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A Validated Method Development For Estimation Of Pioglitazone By First Order Derivative Spectroscopy

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Abstract: Pioglitazone is an oral hypoglycemic agent. It selectively stimulates the nuclear receptor peroxisome proliferator-activated receptor gamma (PPAR-γ). Literature review revealed that 1st order derivative spectroscopic method is not available. The aim of this study is to develop a simple, accurate, precise and economical procedure for estimation of Pioglitazone by first order derivative spectroscopy. The method is based upon determination of D1 value of Pioglitazone at 231.5 nm, in 0.1N NaOH. Different analytical performance parameters such as linearity, range, system precision, robustness, sensitivity and accuracy were determined according to the ICH guidelines. Pioglitazone at its λ max shows linearity in the concentration range 15-65µg/mL.

Keywords: Pioglitazone, Uv spectroscopy, 1st order derivative spectroscopy, method development and validation.

Introduction:

Pioglitazone is an oral ant diabetic agent belonging to the class of thiazolidinediones that acts primarily by decreasing insulin resistance. It is used in the management of type 2 diabetes mellitus. It improves sensitivity to insulin in muscle and adipose tissue and inhibits hepatic gluconeogenesis also improves glycemic control while reducing circulating insulin levels. Pioglitazone [(±) - 5- [[4- [2- (5- ethyl- 2- pyridinyl) ethoxy] phenyl] methyl] -2,4-] thiazolidinedione monohydrochloride belongs to a different chemical class and has a different pharmacological action than the sulfonylureas, metformin, or α glucosidase inhibitors[1]. Determination of pioglitazone by various analytical methods like spectrophotometric method[2,3] and HPLC and MECK method[4] in tablet dosage form, HPLC and solid phase extraction method in human serum[5] and in dog serum[6], HPLC and LC MS in human plasma[7] have been reported. But these methods are sophisticated, expensive and time consuming when compared to simple UV spectrophotometric method.

Pioglitazone is not official in any pharmacopoeia. There is a need for a simple, rapid, cost effective and reproducible method for assay of Pioglitazone in its dosage forms. Therefore, it was thought of interest to develop simple, speedy, accurate and cost effective method for the analysis of Pioglitazone in its tablet formulation. This paper describes development and validation of simple, specific, sensitive, accurate and precise

1st order derivative UV spectrophotometric method[8,9,10] for the estimation of Pioglitazone in bulk and its formulation.

Materials And Methods:

Pioglitazone was kindly supplied by Aurobindo Pharmaceuticals, Aurangabad. It was tested for purity by measuring its melting point and thin layer chromatography and no impurities were found. Pharmaceutical preparations of Pioglitazone (Pionorm and Pioz) were obtained from local pharmacies. NaOH from Qualigens Fine chemicals, Mumbai. The pH of solutions was measured by a pH meter (Model LT-11). The spectrophotometric measurements were carried out by using a SHIMADZU 1800 model UV-VIS spectrophotometer. All other chemicals used were of analytical grade. Double-distilled water was used throughout the study.

Preparation of Standard Solution of Pioglitazone: Pioglitazone hydrochloride (25 mg) was weighed accurately and transferred in 25 mL volumetric flask. It was dissolved in 0.1N NaOH and was filtered. Then the filtered solution was diluted up to the mark with 0.1N NaOH. The resulting solution contained 1000 µg of Pioglitazone per ml of the solution was taken as stock solution(1000 µg/mL). The solution (1 mL) was diluted further to 10 mL with the same solvent. The final solution contained 100 µg of Pioglitazone per mL of the solution was used as a working stock solution.

Determination of Absorption Maxima and Calibration Curve: Before the analysis of solutions containing Pioglitazone, the spectrophotometry was adjusted with 0.1N NaOH. The spectrum was recorded from 200 nm to 400 nm. Standard solutions (15 µg/mL) were scanned against a solvent (0.1N NaOH) as blank between 200-400 nm. Spectrum was recorded and the suitable absorption maxima were selected as 231.5 nm. Various aliquots of standard stock solution were taken and diluted to 10 mL with 0.1N NaOH to give a final analyte concentration (15,25,35,45,55 upto 65 µg/mL). Then the absorbance of these solutions was measured at 231.5 nm and the corresponding values were plotted as a calibration curve.

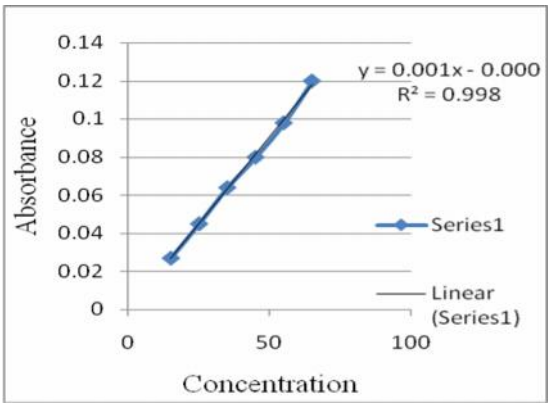

Fig. 1: Calibration Curve Of Standard Pioglitazone

Development and Validation of Analytical Method: 1st order Derivative Spectrophotometric method for the determination of Pioglitazone was developed and validated by determining the linearity, precision, accuracy, LOD and LOQ, sensitivity. Detection wavelength of 231.5 nm was selected for analysis because the drug has sufficient absorption and lesser interference and low quantities of drug may be detected correctly.

Linearity and Range: In developed UV method, calibration curve was linear in the range from 15 to 65 µg/mL. Pioglitazone calibration curve was constructed with 6 different concentrations. Each concentration was analyzed 6 times. The regression equation was y = 0.0018 x + 0.0008, where y is the absorbance and x is the concentration in µg/mL (r= 0.9983).

Limit of Detection and Quantification: The LOD (limit of detection) and LOQ (limit of quantification) of Pioglitazone were estimated from the standard deviation of intercept (n=6) and average of slope (n=6). (Indian

drugs 46 (9) 2009) Applying this formula, LOD and LOQ were found to be 6.06 µg and 18.38 µg respectively. And results are clearly indicated in Table 1.

Table 1: Results Of Different Parameter Of Analytical Method

Validation criteria	Result
Absorbance Maxima	231.5nm
Linearity response	15-65µg/mL
Beer' law limit	15-65µg/mL
Slope	0.0018
Intercept	0.0008
Regression equation	y=0.0018x– 0.0008
LOD	6.06µg
LOQ	18.38µg

Precision: Repeatability is the results of the method operating over a short time interval under the same conditions. The low RSD % values of system and method precision showed that the method have high repeatability. Intra-day study was performed by analyzing, any one concentration of drug for different time interval in the same day. Inter-day precision was performed by analyzing any one concentration of the drug for consecutive days in a week at same time. The results are reported in Table 2.

Robustness: Robustness of the proposed method is determined by analysis of six aliquots from homogenous slot by different analysts, different temperature and different pipette using similar operational and environmental conditions. The results are reported in Table 2.

Sensitivity: Sensitivity is the capacity of the test procedure to record small variation in concentration. For spectrophotometry sensitivity is measured in terms of Sandell's Sensitivity (л). Six different sets of dilution were prepared in the range and average D1 was calculated.The results are reported in Table 2.

Table 2: Results Of Different Parameter Of Analytical Method

Validation criteria	Result
System precision	%RSD< 2%
Robustness	%RSD< 2%
Method precision	%RSD< 2%
Intraday precision	Up to 5 hrs
Interday precision	Up to 3 days
Sensitivity	55.672µg/cm^2/0.001 AU

Recovery Studies: The accuracy of a method is expressed as the closeness of agreement between the found value and reference value. The accuracy of the proposed method was assessed by recovery studies at three different levels i.e. 50%, 100%, 150%. The recovery studies were carried out by adding known amount of standard solution of the drug to preanalysed tablet solutions. The resulting solutions were then reanalysed by proposed methods, the results are reported in Table 3.

Table 3: Results Of Recovery Studies By 1st Order Derivative Spectroscopy

Level of recovery	Amt of sample	Amt obtained	% Recovery
50%	12	19.25	110.41
100%	12	25.37	111.41
150%	12	30.36	103.05

Analysis of Pioglitazone from Tablet Dosage form / Assay:

Twenty tablets of formulation were weighed and finely powdered. The powder equivalent to 100 mg of Pioglitazone was accurately weighed and approximately 50-60 mL of 0.1N NaOH was added and stirred until it gets dissolved and sonicated for 5-10 mins. The volume of solution was made upto 100 mL. The solution was filtered. Then 10 mL of filtrate was diluted up to 100 ml with 0.1 N NaOH. 2.1 mL of resulting solution was diluted up to 10 mL. D1 value of the final solution was recorded at 231.5 nm. The result is reported in Table 4.

Table 4.

Drug	Label claim mg/tab	Amt found mg/tab	% Assay
Pionorm	15	15.079	100.52

Results And Discussion

Pioglitazone was freely soluble in Methanol and 0.1 N NaOH. 0.1 N NaOH was choosen as a solvent. The drug has maximum absorbance at 231.5 nm. The optical characteristic of drug was found to be Beer's law limits 15-65 µg/mL, Correlation coefficient is 0.9983. The drug sample was analyzed by UV spectroscopy using 0.1 N NaOH as solvent and the average content of drug present in the formulation was found to be 100.52%. The % RSD of accuracy studies was found to be 108.29±1.352. The %RSD of precision was found to be 0.736 to 1.865%.The Sandell's Sensitivity was found to be 55.672 µg/cm^3/0.001AU. LOD and LOQ were found to be 6.06µg and 18.38µg respectively.

Conclusion

The proposed spectrophotometric method is accurate, precise, economic and reliable for the estimation of Pioglitazone in pharmaceutical dosage form. The % RSD for all parameters were found to be less than two, which revealed the validation of new method and assay results obtained by this method are fairly satisfactory. Hence, it can be concluded that the developed UV spectrophotometric method can be employed successfully as an alternative for HPLC and HPTLC methods for the quantitative estimation of Pioglitazone.

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