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DETERMINATION OF PIOGLITAZONE HYDROCHLORIDE IN BULK AND PHARMACEUTICAL FORMULATIONS BY UV SPECTROPHOTOMETRIC METHOD

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ABSTRACT

UV spectrophotometric method was developed and validated for the analysis of pioglitazone in tablets. The analyses were performed in Phosphate buffer (pH 7.4). Beer's law was valid in concentration range of 10-50 mcg/ml and UV detection was done at 238 nm. The developed method was validated respect to linearity, precision, accuracy, selectivity / sensitivity applied to the determination of Pioglitazone in two pharmaceutical formulations. The obtained data from developed method was compared statistically. It was concluded that the developed method was suitable for the quality control of Pioglitazone in pharmaceuticals.

INTRODUCTION: Pioglitazone is an oral antidiabetic 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] and HPLC and MECK method [3] in tablet dosage form, HPLC and solid phase extraction method in human serum [4] and in dog serum [5], HPLC and LC MS in human plasma [6, 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 UV spectrophotometric method [8, 9, 10] for the estimation of pioglitazone in bulk and its formulation.

MATERIALS AND METHODS: Pioglitazone was kindly supplied by Sun Pharma Limited, Jammu. It was tested for purity by measuring its melting point and thin layer chromatography and no impurities were found. Pharmaceutical preparations of Pioglitazone (Gatilox and Tequin) were obtained from local pharmacies. KH_2PO_4 from S. D. Fine chem. Ltd, Mumbai and 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 using an SHIMADZU 1700 model UV-VIS spectrophotometer. All other chemicals were either reagents or analytical grade were used. Double-distilled water was used throughout the study.

Preparation of Standard Solution of Pioglitazone: Pioglitazone hydrochloride (10 mg) was weighed accurately and transferred in 10 ml volumetric flask. It was dissolved in methanol and filtered it. Then filtered solution diluted up to mark with phosphate buffer (pH 7.4). The final solution contained 1000 µg of Pioglitazone per ml of the solution. The solution (1ml) was diluted further to 10 ml with the same solvent. The final solution contained 100 µg of pioglitazone per ml of the solution as a stock solution.

Determination of Absorption Maxima and Calibration Curve: Before the analysis of solutions containing Pioglitazone, the spectrophotometry was adjusted with phosphate buffer pH 7.4. The spectrum was recorded from 200 nm to 400 nm. Standard solutions (10 mcg/ml) was scanned against a solvent (phosphate buffer pH 7.4) as blank between 200-400 nm. Spectrum was recorded and the suitable absorption maxima were selscted as 238 nm. Various aliquots of standard stock solution were taken and diluted to 10 ml with phosphate buffer (pH 7.4) to give a final analyte concentration of wanted volume (10,20,30,40,50 µg/mL). Then the absorbance of these solutions was measured at 238 nm and the corresponding values were plotted as a calibration curve.

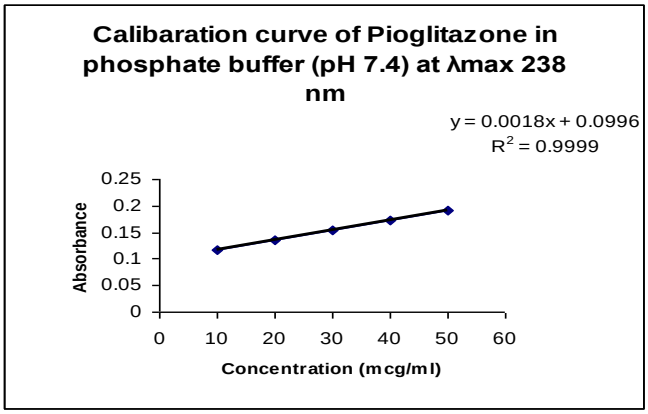

FIG. 1: CALIBRATION CURVE OF STANDARD PIOGLITAZONE

Preparation of Sample Solution: Ten tablets were weighed from each formulation and powdered. The powder equivalent to Pioglitazone (10 mg) was weighed accurately and mixed with methanol and sonicated for 10 minutes. The solution was filtered through Whatman filter paper. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant and diluting them with phosphate buffer (pH 7.4) to give final concentration. Then the absorbance of these solutions was measured.

Development and Validation of Analytical Method: Spectrophotometric method for the determination of pioglitazone was developed and validated by determining the linearity, precision, accuracy, LOD and LOQ. Detection wavelength of 238 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 10 to 50 µg/mL. Pioglitazone calibration curve was constructed with 5 different concentrations. Each concentration was analyzed 6 times. The regression equation was y = 0.0018 x + 0.0996 (n = 6), where y is the absorbance and x is the concentration in µg/mL (r= 0.9999). There was no significant difference between r values (t Calculated = 2.22 > t Tabulated = 2.015 $p < 0.05$).

Limit of Detection and Quantification: The LOD (limit of detection) and LOQ (limit of quantization) of Pioglitazone were estimated from the standard deviation of constants (n=6) and average of slope (n=6). (Indian drugs 46 (9) 2009) Applying this formula, LOD and LOQ were found to be 0.0002mcg/ml and 0.0018mcg/ml respectively. And results are clearly indicated in **table 1**.

TABLE 1: RESULTS OF DIFFERENT PARAMETER OF ANALYTICAL METHOD

Validation criteria	Results
Linearity Response	10-50 mcg/ml
Absorption maxima	238 nm
Beers law limit	10-50 mcg/ml
Slope	0.0018
Intercept	0.0996
Regression equation	y = 0.0018 x + 0.0996
LOD	0.0002
LOQ	0.0018

Precision: Repeatability is the results of the method operating over a short time interval under the same conditions. The low RSD % values of intra-day precision (Table I), recoveries assays (Table II) showed that the method have high repeatability.

Intermediate Precision: Three different concentration of Pioglitazone (5, 15 and 45 µg/mL) in the linear range were analyzed in six independent series on the same day (intra-day precision) and six consecutive days (inter-day precision) from three measurements of every sample in each series (Table 1). The RSD % values varied from 0.047 to 0.213 for intra-day and from 0.146 to 0.284 for inter-day precision. RSD % values are represented in Table I are less than 2% that illustrate the good precision of the analytical method.

TABLE 2: PRECISION AND ACCURACY OF THE DEVELOPED UV METHOD FOR THE ANALYSIS OF PIOGLITAZONE (n=6)

Added µg/mL	Intra-Day			Inter-Day		
	Found X mean (µg/mL) ± SE	Accuracy Bias %α	Precision RSD %	Found X mean (µg/mL) ± SE	Accuracy Bias %α	Precision RSD %
5	4.991±0.023	-0.18	0.460	5.01±0.012	0.20	0.239
15	14.99±0.032	-0.06	0.213	15.01±0.022	0.066	0.146
45	45.01±0.021	0.025	0.047	44.99±0.128	-0.022	0.284

% Bias = [(found – added) / added] x 100 , SD : standard Deviation, RSD : Relative standard deviation

Accuracy: The accuracy of a method is expressed as the closeness of agreement between the found value and reference value. It is determined by calculating the percentage relative error between the measured and added concentrations of pioglitazone. The obtained results for intra-day inter-day accuracy were <1.00 (**Table 2**). The mixture of excipients and labeled amount (30 mg) of pioglitazone] were done. The recovery percentages for pioglitazone in synthetic tablets were 99.69 ± 0.13 % (RSD %: 0.33) for Gatilox and 99.93 ± 0.07 % (RSD %: 0.19) for Tequin (Table 3). The low bias values and high recovery percentages indicated that the developed method is highly accurate.

TABLE-3 RECOVERY RESULTS OF PIOGLITAZONE IN MARKETED TABLETS OBTAINED WITH UV METHOD

	Gatilox (30mg)		Tequin (30 mg)	
	Found amount (mg)	Recovery %	Found amount (mg)	Recovery %
Mean ± SD	29.412 ± 0.437	98.04 ± 1.458	29.57± 0.438	99.11± 1.176
SD	0.437	1.458	0.438	1.176
% RSD	1.485	0.014	1.48	1.186

Selectivity: The spectrum obtained from tablet was identical with that obtained spectrum from standard solution containing an equivalent concentration of Pioglitazone. In addition the standard curves were follow the equation y = 0.0018 x + 0.0996 (r = 0.9999). There was not any difference between slopes of standard and tablet solutions. This results show that there was no any interference from matrix components. Therefore it could be said that developed method are highly selective

RESULTS AND DISCUSSION: The proposed simple and rapid UV spectrophotometric method for the determination of Pioglitazone in pharmaceutical formulation has been developed and validated. The linearity ranges, limit of detection and quantification, precision, accuracy, selectivity were performed to determine the suitability of the method. In this study, the developed UV spectrophotometric method for the determination of Pioglitazone in pure and pharmaceutical forms has the advantage of being fast, simple, inexpensive with high precision and accuracy. These full validation assays have been concluded that the developed UV method is linear, sensitive, accurate, precise, and selective for the determination of Pioglitazone.

CONCLUSION: The developed UV spectrophotometric method is cheaper, simpler and faster than other published methods for analysis of Pioglitazone in the pharmaceutical preparations. These advantages encourage the application of this method in routine analysis of Pioglitazone.

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