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A VALIDATED SPECTROPHOTOMETRIC METHOD FOR DETERMINATION OF SAROGLITAZAR IN PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

In the present research work two simple, accurate, precise methods of UV-visible spectrophotometric method was developed and validated for the estimation of Saroglitazar in phamaceutical dosage form. Two methods were used for estimation of Saroglitazar using methanol. Method A involves zero order spectroscopy at absorption maximum of 295nm and Method B involves first order derivative at 319 nm. Overlay linearity graph were taken using different concentration of Saroglitazar. The developed methods were validated according to ICH guidelines. The developed methods were found to be linear in concentration range of 5-30 µg/ml with regression equation Y = 0.028x + 0.007. The mean percentage label claim of Saroglitazar was within the acceptable range. The recovery of the drug was ranged between 99.28-101.58 %. The developed methods were found to be accurate and precise. The % RSD values were within the limits. These methods can be used for the routine analysis of Saroglitazar in pharmaceutical dosage form.

***Keyword**: Spectrophotometric Method, Saroglitazar, Validation.*

1. INTRODUCTION

Saroglitazar is a novel glitazar compound developed indigenously in India and gained regulatory approval from the Indian regulatory authority DCGI in June 2013[1]. It was developed by Zydus Cadilla. The chemical name for Saroglitazar is (αS)-α-Ethoxy-4- [2-[2-methyl-5-[4-(methylthio) phenyl]-1H-pyrrol-1-yl] ethoxy] benzenepropanoic Acid (Fig. 1) with Empirical formula - [C25H28NO4S]2Mg and Molecular mass- 900 g/mole. Saroglitazar is a dual PPAR activator with predominant PPAR-α and moderate PPAR-γ agonist action. PPAR-activation increases the fatty acid oxidation process in the liver and also reduces secretion of triglycerides and VLDL (very low-density lipoproteins) which promotes fatty acid uptake by liver, thus decreasing fatty acid synthesis and peripheral triglyceride levels[2]. It also activates lipoprotein lipase and decreases production of apolipoprotein C-III (inhibitor of lipoprotein lipase) thereby promoting lipolysis. There is also increase in synthesis of apolipoprotein A-I, A-II and HDL-C (high density cholesterol) and a reduction in inflammation. Saroglitazar, via PPAR-γ activation, activates the genes involved in glucose metabolism (adiponectin, CD 36 etc.) and increases the insulin sensitivity, glucose uptake and utilization. It also increases fatty acid uptake and decreases post-prandial surge in

their levels. As a result, metabolic burden on liver and muscle is reduced. Saroglitazar was conceptualized and developed keeping in mind the needs of type 2 diabetes patients suffering from dyslipidemia and not controlled by statin therapy. Its dual mode of action provides dual benefit in dyslipidemia and hyperglycemia[3].

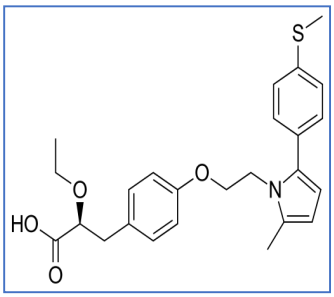

Fig. 1: Saroglitazar: structural formula

Literature survey revealed that few analytical methods such as UV[4,5], HPLC[6,7] and HPTLC[8] methods were reported for the determination of Saroglitazar in pharmaceutical dosage form. Hence the objective of the proposed method is to develop and validate a simple, accurate, precise UV spectroscopic methods in accordance with ICH guidelines[9] for the determination of Saroglitazar in pharmaceutical dosage form.

2. MATERIALS AND METHODS

2.1 Reagents and Chemicals

Pure drug, Saroglitazar was procured from Swapnroop Pharmaceuticals, Aurangabad, Maharashtra, India. Marketed formulation was procured from local Pharmacy. All the chemicals and reagents used were of A.R. grade.

2.2 Instrumentation: A double beam UV spectrophotometer (UV-1800, Shimadzu, Japan) with UV probe software version (2.31) and 10 mm quartz cells was used. All weights were taken on an electronic balance (Schimadzu - 220h).

2.3 Method development

2.3.1 Preparation of standard stock solution

The standard stock solution of Saroglitazar was prepared by dissolving accurately weighed 10 mg of Saroglitazar in 10 ml volumetric flask containing 5 ml of methanol, shaken for 5 min then volume was made up with methanol to get concentration of 1000 µg/ml. From the above solution working standard solution of concentration 100µg/ml was prepared diluting with distilled water. From these aliquots were prepared to get a concentration range of 5-30 µg/ml.

2.3.2 Preparation of calibration curve[10]

Method A: zero order spectroscopic method

The wavelength was selected by preparing a solution of concentration 20µg/ml by diluting the standard solution with distilled water. The solution was scanned under spectrum mode over a wavelength range of 210- 400 nm using distilled water as blank. The UV spectrum showed λ_{max} at 295 nm. The calibration graph was plotted taking absorbance on Y-axis against concentration of standard solution on x-axis over a concentration range of 5-30 µg/ml. The regression equation was calculated. Linearity was observed through overlain spectra of various concentration of saroglitazar.

Method B: first order derivative spectroscopy

The spectra obtained through method A were derivatized to get first-order derivative spectra and the response (dA/dλ) of the spectra were measured at 319 nm (Fig. 5). The calibration graph was constructed by plotting the concentration versus response (dA/dλ) over a concentration range of 5-30 µg/ml (Fig. 6). The regression equation was calculated. Stacked view of zero and first order spectra is given.

2.4 Estimation of Saroglitazar in tablet dosage form

2.4.1 Preparation of sample solution

For the estimation of saroglitazar in the commercial formulations, 20 tablets each containing 4 mg of saroglitazar were weighed and the average weight was calculated. The tablets were crushed and powdered in glass mortar. Powder equivalent to 10 mg of saroglitazar was transferred into a 10 ml volumetric flask and dissolved in sufficient quantity of methanol and sonicated. The final volume made upto the mark with methanol and the solution was filtered through whatman filter paper no.41.Further dilutions of the stock solution were made in distilled water to get required concentration of 20µg/ml. The concentration of saroglitazar in formulation was determined by above developed methods. The assay procedure was repeated six times (n= 6) for each method.

2.5 Method Validation

The methods were validated according to ICH guidelines[9] to study linearity, precision and accuracy.

2.5.1 Linearity: The linearity of the proposed UV spectroscopic method was evaluated by analyzing different concentrations of standard solutions of saroglitazar and linearity graph was plotted by taking absorbance of analyte on Y axis against concentrations on X-axis. Beer's law was obeyed for both methods in the concentration range of 5-30 µg/ml. A good linear relationship (R^2=0.999) was observed between the concentrations of saroglitazar and the corresponding absorbance. The regression analysis was done to obtain slope, intercept and correlation coefficient values. The slope, intercept and the correlation coefficient of the drug were shown.

2.5.2 Accuracy: Accuracy is expressed as the degree of closeness of experimental value to the true value. To study the accuracy of the proposed method and to check the interferences from excipients used in the dosage form, recovery experiments were carried out by the standard addition method. This parameter is evaluated by percent recovery studies at concentration levels of 80,100 and 120% which includes the addition of known amounts of saroglitazar working standard to a pre-quantified sample solution. Each of the dilution was observed six times. The samples were reanalyzed by proposed methods. The amount of saroglitazar was estimated by applying obtained values to the regression equation. The percentage recovery of the drug was calculated.

2.5.3 Precision: Precision is the level of repeatability of results as reported between samples analyzed on the same day (Intra-day) and samples run on three different days (Inter-day). To check the intra-day and inter-day variation of the methods, solutions containing 15, 20 and 25µg/ml concentrations of saroglitazar were subjected to the proposed spectrophotometric methods of analysis and the recoveries obtained were noted. The precision of the proposed method i.e. the intra and inter – day variations in the absorbance of the drug solutions was calculated in terms of % RSD. Statistical evaluation revealed that the relative standard deviation of standard drug at different concentration was less than 2.0.

3. RESULTS AND DISCUSSION

The proposed methods for estimation of saroglitazar were found to be simple, precise, accurate and economical. The Absorption maxima for method A were found to be 295 nm (Fig. 2). The calibration graph was plotted taking absorbance on Y-axis against concentration of standard solution on x-axis, which was linear over a concentration range of 5-30 µg/ml (Fig. 3). Linearity was observed through overlain spectra of various concentration of saroglitazar (Fig. 4). The Absorption maxima for method B were found to be 319 nm (Fig. 5). The first order calibration curve was plotted (Fig. 6) which was found to be linear in the concentration range of 5-30 µg/ml (Table 1). Stacked view of zero and first order spectra is given in fig. 7. The % assay by both methods was found to be in the range 99.16-100.74% for

saroglitazar (Table 2). No interference was observed from the pharmaceutical excipients in accuracy. The recovery studies in range of 99.28-101.58 for method A and 98.33-100.97 for method B showed that the methods were accurate and reproducible. The results revealed that any change in the drug concentration could be accurately determined by the proposed method. Accuracy of the proposed methods was further confirmed by percent recovery values, as shown in Table 3. Percentage RSD values for repeatability and inter-day precision were less than 2.0 as shown in Table 4. The proposed methods were validated in terms of linearity, precision and accuracy. Characteristic parameters and summary of validation parameters for both the methods were given in Table 5.

By observing the validation parameters, the methods were found to be simple, accurate, precise and economical. Hence these methods can be employed for the routine analysis of saroglitazar in tablet formulations.

Table 1: Assay results of Saroglitazar by two methods

Parameter	Method A	Method B
Absorption maxima	295	319
Linearity Range µg/ml	5-30	5-30
Regression equation (Y = a+ bc)	y = 0.028x + 0.007	y = 0.001x + 0.000
Correlation coefficient (r2)	0.998	0.999
Slope (a)	0.028	0.001
Intercept (b)	0.007	0

Table 2: Linearity studies of the Proposed Method

Analysis method	Label claim (mg/tablet)	Amount found (mg) (n= 6)	% amount found	% RSD
A	4	4.03	100.74	0.44
B	4	3.97	99.16	2.05

Table 3: Accuracy studies of Saroglitazar by 2 methods

Concentration taken (µg/mL)	Spiked level (%)	Amount added (mg)	Amount found (mg) (n = 6)		% Recovery	
			A	B	A	B
20	80	16	16.16	15.93	101.04	99.58
20	100	20	19.85	19.66	99.28	98.33
20	120	24	24.38	24.23	101.58	100.97

Table 4: Precision studies of Saroglitazar

Concentration taken (µg/mL)	Intra-day precision		Inter-day precision	
	*mean ±SD	% RSD	*mean ± SD	% RSD
2	0.444±0.002	0.67	0.447±0.001	0.37
3	0.572±0.002	0.33	0.576±0.003	0.65
4	0.698±0.003	0.44	0.703±0.003	0.50

**RSD of six independent determinations*

Table 5: Summary of Optical Characteristics and Validation Parameters

Parameter	Method A	Method B
λ_{max}	295	319
Beer's limit (µg/mL)	5-30	5-30
Linearity indicated by correlation coefficient	0.998	0.999
Accuracy indicated by % recovery	99.28-101.58	98.33-100.97

Fig. 2: Zero Order Derivative of Saroglitazar

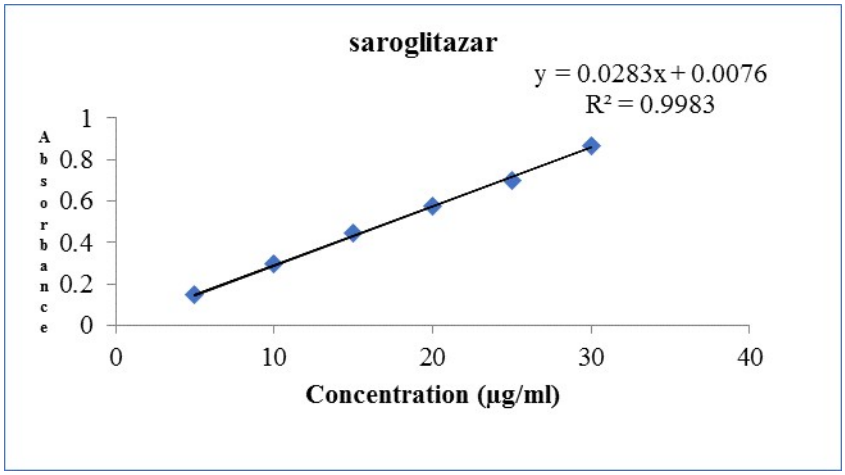

Fig. 3: Calibration graph of Saroglitazar

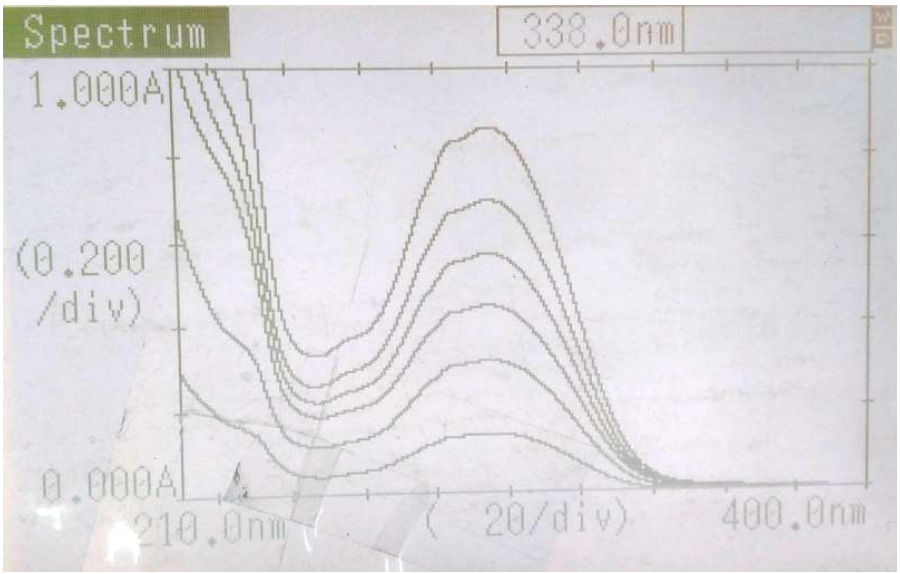

Fig. 4: Overlain spectra for different concentration of Saroglitazar

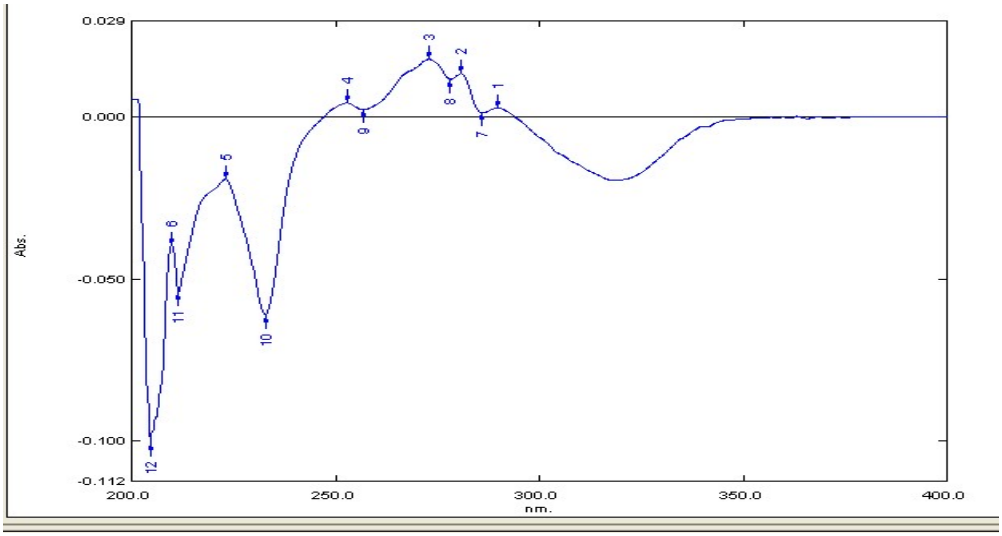

Fig. 5: First Order Derivative of Saroglitazar

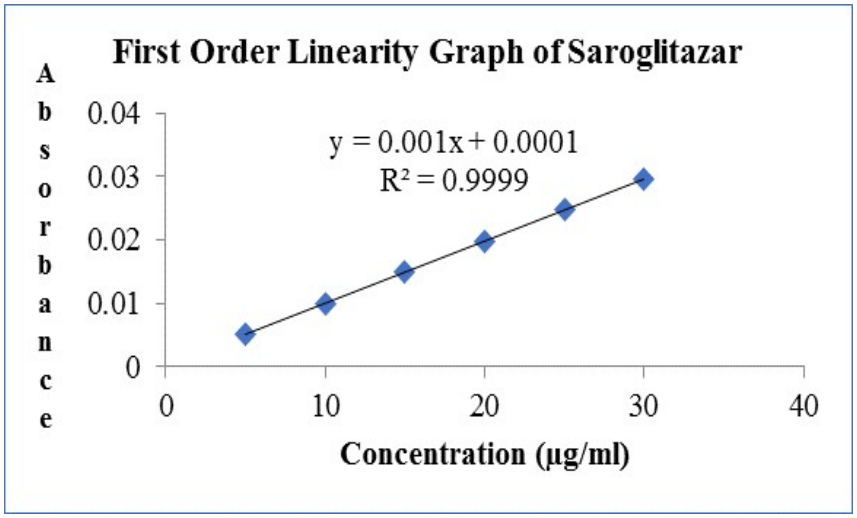

Fig. 6: Calibration graph of Saroglitazar

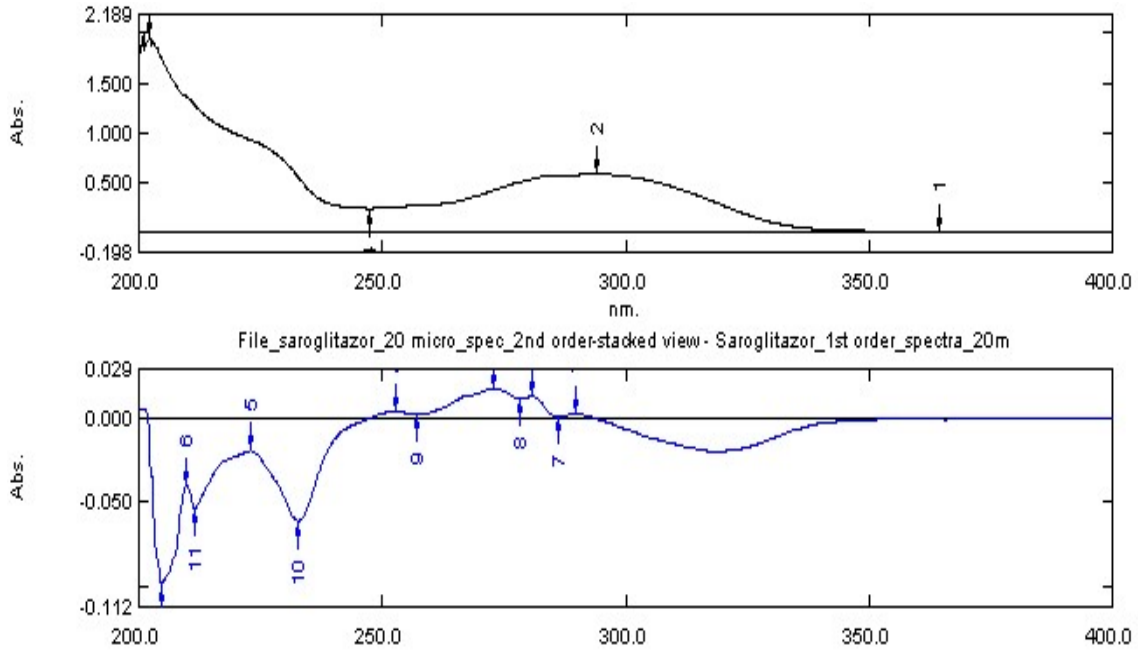

Fig. 7: Stacked view of zero and first order spectra of Saroglitazar

4. CONCLUSION

The two spectrophotometric methods were developed and validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed methods were within the acceptance limits, indicating a high degree of precision of methods. The results of the recovery studies indicate the methods to be accurate and reproducible. Hence, it can be concluded that developed spectropthometric methods were simple, accurate, precise and economical and can be employed successfully in the estimation of saroglitazar in formulation. There is a good scope for estimation of saroglitazar by these two methods to carry out their routine analysis.

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