INTERNATIONAL JOURNAL OF ADVANCES IN PHARMACY, BIOLOGY AND CHEMISTRY

Research Article

# Development of Spectrophotometric method of Saroglitazar in Bulk and Pharmaceutical formulations using 1, 10 – phenanthroline

**Manjusha D.Karad and V.D.Barhate***

Department of Chemistry, VES College of Arts Science and commerce,

Chembur Mumbai, India – 400071.

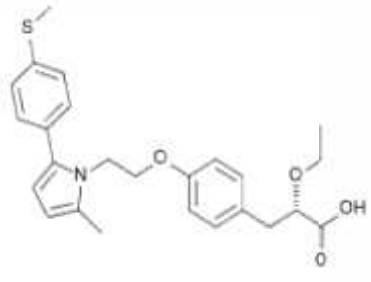
**ABSTRACT**

A new, simple, precise, sensitive, accurate, and reproducible spectrophotometric method have been developed for the determination of saroglitazar in pure and dosage forms. Method is based on oxidation of the drug with 1, 10 phenanthroline producing orange colored chromogen which is measured at 510 nm. Beer's law is obeyed in the concentration range of 3-15 µg/mL for the developed method. The molar absorptivity and sandell sensitivity are found to be 6347.7 L $mol^{-1}cm^{-1}$and 0.069 µg/$cm^2$ respectively. The regression equation for saroglitazar was found to be y = 0.045X + 0.003 and the correlation coefficient for the regression line was 0.9985. Different experimental parameters affecting the color development and stability of colored product are carefully studied and optimized. The developed method could be successfully applied to pharmaceutical formulations. The results obtained are in good agreement with those obtained using standard method.

**Keywords:** Saroglitazar, Spectrophotometric method, 1, 10-phenanthroline ,LIPAGLYN Marketed formulation

## INTRODUCTION

Saroglitazar, chemically, it is (2S) - 2- Ethoxy - 3- [4- (2- {2-methyl-5- [4- (methylsulfanyl)phenyl] -1H-pyrrol-1-yl} ethoxy)phenyl] propanoic acid. The chemical formula is C25H29NO4S and the molecular weight is 439.56 g/mol. Saroglitazar is a drug for the treatment of type 2 diabetes mellitus and dyslipidemia. It is approved for use in India by the Drug Controller General of India.




Saroglitazar

Saroglitazar is indicated for the treatment of diabetic dyslipidemia andhypertriglyceridemia with type 2 diabetes mellitus not controlled by statin therapy. In clinical studies, saroglitazar has demonstrated reduction of triglycerides (TG), LDL cholesterol, VLDL cholesterol, non-HDL cholesterol and an increase in HDL cholesterol. It has also shown favorable glycemic control by reducing the fasting plasma glucose and HbA1c in diabetes patients. The recommended dose of saroglitazar is one tablet of 4 mg once a day. Saroglitazar is novel first in class drug which acts as a dual PPAR agonist at the subtypes α (alpha) and γ (gamma) of the peroxisome proliferator-activated receptor (PPAR). Agonist action at PPARα lowers high blood triglycerides, and agonist action on PPARγimproves insulin resistance and consequently lowers blood sugar[1]. Literature surveys reveal pharmacokinetics and bioavailability studies[2-9] and spectrophotometric determination of Saroglitazar in pharmaceutical preparations by $KMnO_4$ method[10] and the estimation of Saroglitazar

in bulk and pharmaceutical dosage form by Rp-HPLC[11]. In present investigation we developed simple accurate, precise and validated method for determination of Saroglitazar in pharmaceutical preparations

## EXPERIMENTAL

### Instrumentation

An ELICO SL-159 model, 2nm high resolution, double beam, 1cm length quartz coated optics and a Wavelength range of 190-1100nm. High stability, linearity, precision of instrument is used for all the spectral measurements. All chemicals and reagents used in the analysis are of analytical grade and doubly distilled water is used for the preparation of all the solutions.

### Materials and Methods

### Preparation of Standard solution of drug

An accurately weighed 4 mg of Saroglitazar is dissolved in 25 ml of ethanol .The final volume is adjusted with 50% ethanol to 50ml in standard flask.

### Preparation of Reagents

0.241%(w/v) Fe (III) solution is prepared by dissolving 241mg of anhydrous ferric ammonium sulphate in 100mL of double distilled water, 0.991% (w/v) o-phenanthroline is prepared by dissolving 991mg of the reagent in 100mL of alcohol and 0.15% (v/v) O-phosphoric acid solution is prepared by diluting 0.15 mL of laboratory reagent (AR Grade) of o-phosphoric acid to 100mL with distilled water.

### Experimental Procedure

Different portions (1.0- 5.0mL, 75µg/mL) of standard Saroglitazar solution is delivered into a series of 25mL calibrated standard flask and then 1.0 mL of $5.0x10^{-3}$M of Fe (III) solution, 1.0mL of $5.0x10^{-2}$M o-phenanthroline are added successively. The total volume in each flask is brought to 16mL with distilled water. The flasks are kept on a boiling water bath for 30minutes. The flasks are removed and cooled to room temperature.2.0mL of $2.0x10^{-2}$M of o-phosphoric acid is added and volume in each flask is made up to the mark with distilled water. The absorbance of the colored complex solution is measured after 5 minutes against a reagent blank prepared at 510nm (Fig.1). The amount of the Saroglitazar is computed from the appropriate calibration graph (Fig.2).

### Analysis of pharmaceutical sample

Tablets powdered equivalent to 4 mg of the drug is weighed accurately and transferred into 100ml beaker and shaken with 25 ml ethanol by following standard method. The standard solution is filtered into 50ml standard flask and volume is adjusted with 50% ethanol. Suitable aliquots of this solution used for the determination of Saroglitazar contents by procedure describe earlier.

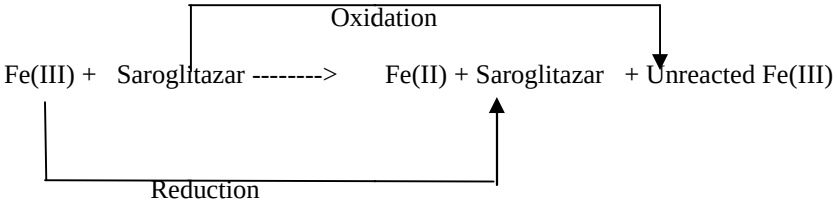
## RESULTS AND DISCUSSION

In order to test whether the colored product formed in this method adhere to Beer's law, the absorbance at maximum wavelength of a series of eight concentrations are plotted against concentration of the drug in µg/mL (Fig2). Beer's law is obeyed within the limits 3-15 µg/mL of Saroglitazar, molar absorptivity and sandell sensitivity is found to be 6347.7L $mol^{-1}$ $cm^{-1}$ and 0.069 µg /$cm^2$ .Regression analysis of the Beer's law plots at $\lambda_{max}$ reveals a good correlation. The graphs show negligible intercept and are described by the regression equation $y = 0.045X + 0.003$ (where Y is the absorbance of 1 cm layer, b is the slope, a is the intercept and C is the concentration of the measured solution in µg/mL). The high molar absorptivity of the resulting colored complex indicates the high sensitivity of the method.

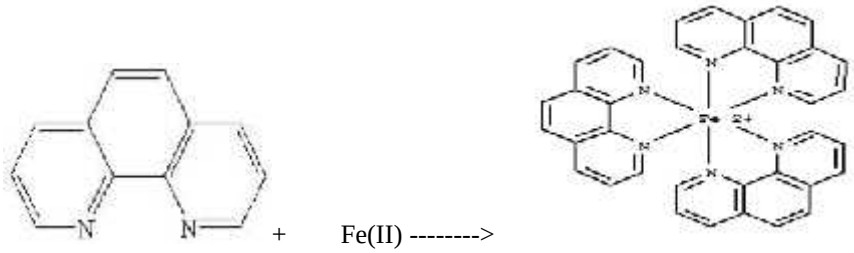
To determine the accuracy of the method, three different amounts of drug sample within the linearity limits are prepared and analyzed by the developed method. The percent recoveries of the drug by this method is found to be within the range which indicates that the developed method is accurate. Variation from mean at 95% level confidence limit percent are calculated for the developed method. Optical characteristics, linear regression parameters, precision and accuracy of the proposed method is shown in Table-1. The method has been successfully applied for the determination of Saroglitazar in pharmaceutical preparations.

[a]Regression equation Y = a+bC , Where Y stands for absorbance and C is concentration in µg/mL
[b]%Relative standard deviation is calculated for ten determination

The proposed method has been used for the analysis of Saroglitazar. The results obtained are comparable with standard method[13] (Table- 2).




Unreacted Fe(III) + O-Phosphoric Acid --------> Fe(III)-O-phosphoric Acid Complex




**Scheme of coloured product**

Ferric salt converts into a ferrous salt upon oxidation and can be easily detected by the usual reagent o-phenanthroline. The reduction product is tris complex of Fe (II), well known as ferroin. The colored product of the reaction is given above.

**CONCLUSIONS**

The developed method is simple, sensitive, accurate and reproducible. The developed method could be successfully applied for determination of Saroglitazar in pharmaceutical formulations. The results obtained are in good agreement with those obtained by using standard method.

**ACKNOWLEDGEMENTS**

The authors are thankful to Principal VES College of Arts Science and commerce, Chembur for providing laboratory facilities**.**

**Table-1**

**Optical characteristics, Regression parameters, Precision and Accuracy of the proposed method**

| Parameters | Method |
|---|---|
| Maximum Wavelength $\lambda_{max}$ | 510 nm |
| Beer's Law Limits µg/mL | 3.0-15 |
| Sandell's Sensitivity (µg/cm$^2$ /0.0001 Absorbance) | 0.069 |
| Molar Absorptivity Lt/mole/cm | 6347.7 |
| Slope(b)[a] | 0.044 |
| Intercept(a)[a] | 0.003 |
| Standard Deviation on intercept($S_a$) | .0023 |
| Standard Deviation on slope ($S_b$) | .0011 |
| Correlation Coefficient ( r ) | 0.9985 |
| Standard Deviation (S) | 5.869 |
| Variation from mean at 95% level confidence limit | ±4.195 |
| Limit of Detection (LOD)µg/mL | 0.1711 |
| Limit of Quantification (LOQ)µg/mL | 0.5185 |

**Table 2**
**Analysis of Pharmaceutical Formulations of Saroglitazar**

| Drug | Manufacturing company | Labelled amount(mg) | *Amount found by Proposed Method(mg) | *Amount found by Referrence Method(mg) |
|---|---|---|---|---|
| Saroglitazar<br>LIPAGLYNMarketed formulation | Zydus cadila | 4.0 | 3.89 | 3.97 |

* Average of three determinations

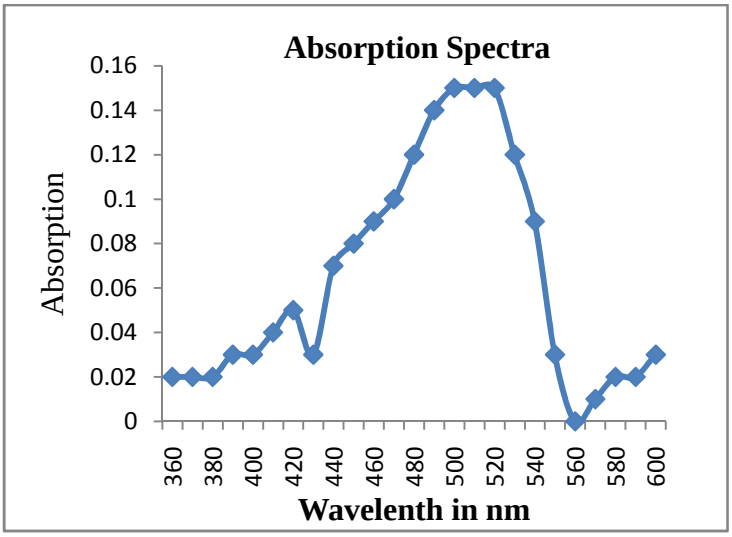



**Fig 1**
**Absorption spectra of Saroglitazar with Fe (III) /O-PHEN**

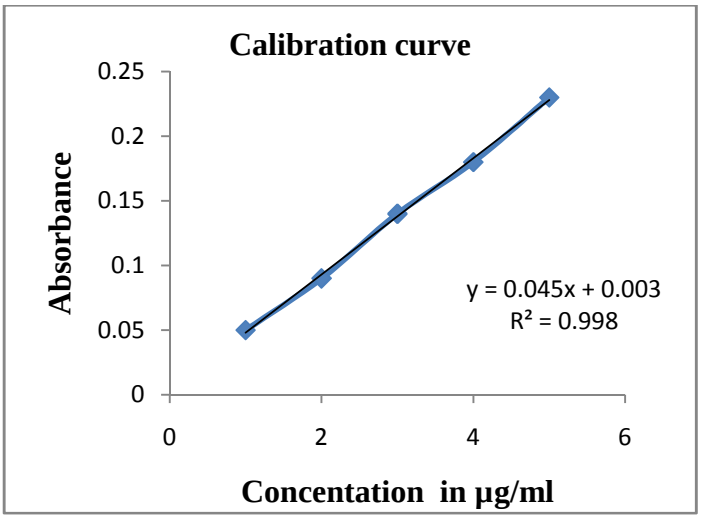



**Fig.2**
**Linear plot of Saroglitazar with Fe (III)/O-PHEN .The calibration curve is found to be linear over the concentration range of 20-320ug/ml of Saroglitazar**

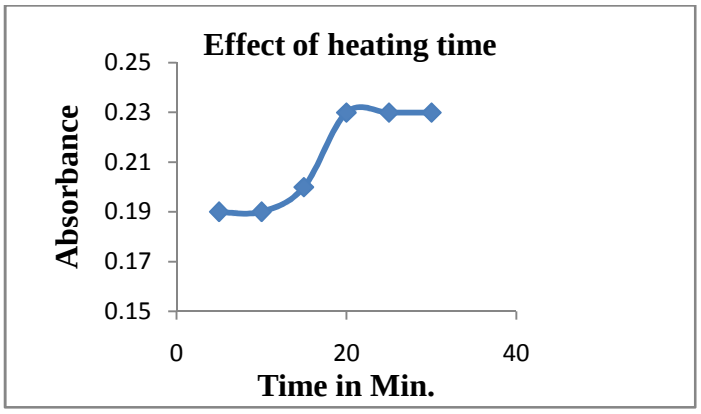



**Fig.3**
**Effect of heating time on absorbance of developed system . 25 minutes are sufficient for full colour development hence 30 minutes time is selected for further studies.**

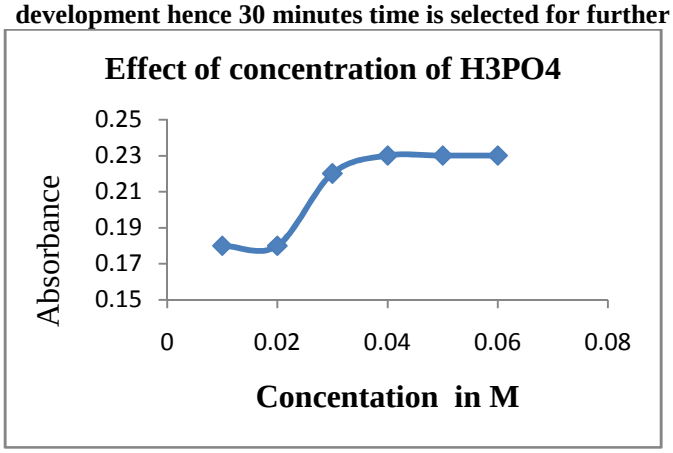



**Fig.4**
**Effect of concentration of $H_3PO_4$ on colour development.Absorbance remains constant after 0.015M concentration of $H_3PO_4$.Hence 0.02M $H_3PO_4$ is usued for colour development and further studies.**

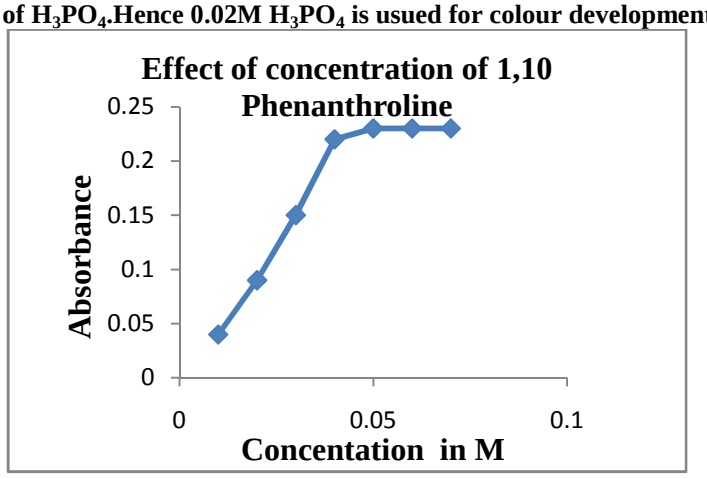



**Fig.5**
**Effect of concentration of 1,10 phenanthroline on absorbance of developed system.**

**REFERENCES**


1. http://en.wikipedia.org/wiki/Saroglitazar
2. Agarwal R, The first approved agent in the Glitazar's Class: Saroglitazar, PubMed.gov, 2014; 5(2): 151-155.
3. Rajendra H. Jani, Kevinkumar Kansagra Mukul R. Jain, and Harilal Patel. Pharmacokinetics, Safety, and Tolerability of Saroglitazar (ZYH1), a predominantly PPARα Agonist with Moderate PPARγ Agonist Activity in Healthy Human Subjects, Clinical Drug Investigation, 2013; 33(11): 809–816.
4. Sonu S. Biliary excretion of ZYH1 in Wistar rats. Ahmedabad: Cadila Healthcare Ltd. Vol 3, Issue 9, 2004.
5. Poonam G. Determination of monodirectional permeability of ZYH1 across Caco2 cell monolayer using LC-MS/MS. Ahmedabad: Cadila Healthcare Ltd; 2011.
6. Robert RH, Michael AL, Sunder M, et al. Effects of the dual peroxisome proliferator-activated receptor-α/γ agonist aleglitazar on risk of cardiovascular disease in patients with type 2 diabetes (SYNCHRONY). Lancet, 2009; 374: 126–35.
7. Fievet, C Fruchart, J.Staels B. PPARα and PPARγ dual agonists for the treatment of type 2 diabetes and the metabolic syndrome. Current Opinion in Pharmacology, 2006; 6 (6):606–614.
8. “Zydus Group launches new diabetic drug”. The Times of India. Jun 6, 2013.
9. Zydus Cadila, "Zydus pioneers a breakthrough with LIPAGLYN, India’s first NCE to reach the market," 5 June 2013.
10. Manjusha D Karad and Dr. VD Barhate Spectrophotometric Determination of an Antidiabetic Drug Saroglitazar Bulk And Pharmaceutical Formulations ,World Journal of Pharmacy and Pharmaceutical Science 2015;4(6): 954-961.
11. Siddartha B, Sudheer Babu I. Method Development and Validation for the Estimation of Saroglitazar in Bulk and Pharmaceutical Dosage Form by rp-HPLC. Word Journal of Pharmacy and Pharmacetical Sciences 2014;3(9):567-575.