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Development and validation of a Reverse Phase-HPLC method for the determination of Rosiglitazone Maleate in tablet dosage form

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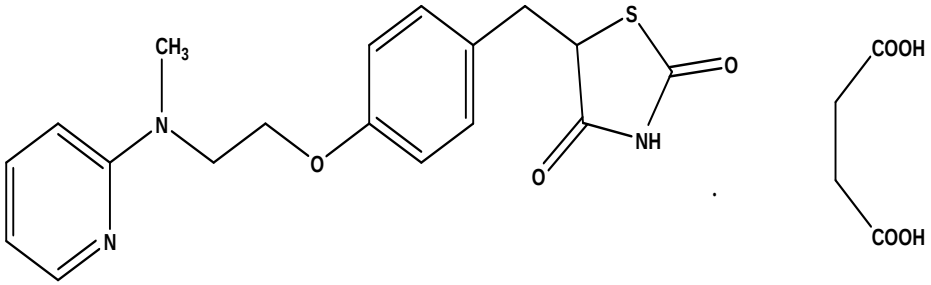
ABSTRACT

A rapid reverse phase high performance liquid chromatography method has been developed and validated for the determination of Rosiglitazone maleate in tablets. Isocratic chromatography was performed on a Kromasil C18 (250X4.6mm) with buffer:acetonitrile:methanol in the ratio of 65:25:10 as a mobile phase at a flow rate of 1.0 ml min^{-1} and the detection was monitored out by photodiode array detector at 235 nm. The retention time for Rosiglitazone maleate was found to be 5.720 min. Good linearity was demonstrated in the range of 160-260 µg/ml (r~0.9975). Various chromatographic parameters including precision, accuracy, system suitability, specificity, LOD, LOQ and robustness have been evaluated. The proposed method was statistically evaluated and can be applied for routine quality control analysis of Rosiglitazone maleate

Keywords: RP-HPLC, Rosiglitazone maleate, Validation, Anti-diabetic, Isocratic.

INTRODUCTION

Rosiglitazone maleate (1) is an anti-diabetic drug in the thiazolidinedione class of drugs(1-3). It works as an insulin sensitizer, by binding to the PPAR receptors in fat cells and making the cells more responsive to insulin(4-7)**.** It is marketed by the pharmaceutical company GlaxoSmithKline as a stand-alone drug (Avandia) and in combination with Metformin (Avandamet) or with Glimepiride(8-10) (Avandaryl).



(1)

Objective

A new, sensitive, accurate and precise Reverse Phase-High Pressure Liquid Chromatography method has been developed for the routine determination of Rosiglitazone maleate in tablet formulation in the quality control department.

MATERIALS AND METHODS

Chemicals

Dichromolactose, Macro crystalline cellulose, Sodium starch glycollate, Magnesium sterate were supplied by E.Merck Ltd, Germany. Acetonitrile, Methanol, Potassium dihydrogen orthophosphate were purchased from Sun Pharmaceuticals Ltd. Mumbai. Rosiglitazone maleate , Rosiglitazone Tablet, Placebo granular powder were purchased from Aldrich Chemicals (USA).

Buffer preparation

Potassium dihydrogen ortho phosphate was dissolved in 1000 ml of distilled water and 5 ml of triethylamine was added and the pH was adjusted to 6.0 with orthophosphoric acid.

Preparation of mobile phase

About 65 volumes of 0.01 M potassium dihydrogen ortho phosphate was added and its pH was adjusted to 3.0 with 25 volumes of acetonitrile and 10 volumes of methanol.

Instruments and Chromatographic conditions

The HPLC system (Shimadzu Co, Tokyo, Japan) consisted of a Shimadzu model LC-10 ATVp, A Shimadzu model SPD-6AV variable wavelength detector (Possessing deuterium lamp with a sensitivity of 0.005 AUFs and adjusted to an absorbency of 240nm)

Stationary phase	:	Kromasil C18 250 x 4.6mm
Buffer	:	0.01 M Potassium dihydrogen orthophosphate adjusted to pH 3.0 with Orthophosphoric acid.
Mobile phase ratio	:	65:25:10 (Buffer:Acetonitrile:Methanol)
Flow rate	:	1.0 ml/min
Injection Volume	:	10 µl
Detection	:	235 nm

Calculation of Rosiglitazone Maleate

$$\frac{\text{Spl.area}}{\text{Std.area}} \times \frac{\text{Std.Wt}}{100} \times \frac{100}{\text{Spl.wt}} \times \frac{\text{Std.purity}}{100} \times \text{Avg.Wt} \times \text{Conversion factor}$$

$$\text{Conversion factor: } \frac{\text{Rosiglitazone}}{\text{Rosiglitazone maleate}} = \frac{357.43}{473.51} = 0.7548$$

Validation of parameters

System suitability

System suitability parameters are evaluated by following ICH guidelines injecting five replicates of 200 µg/ml concentration of standard Rosiglitazone maleate solution. Resolution factor, theoretical plate and tailing factor were evaluated by following ICH guidelines. The results are presented in Table.1 and Fig.1

Linearity

Linearity of the peak area response was determined by making six measurements at six different concentrations point in the range of 160-260 µg/ml of sample Rosiglitazone maleate respectively. The linear regression coefficient was calculated. The results are presented in Table.2 and Fig.2.

Accuracy

Accuracy was assessed by using a minimum of three different concentration (standard Rosiglitazone maleate 80%, 100%, and 120%) and 310 mg of placebo spiked into the standard solution of Rosiglitazone maleate. The mean, standard deviation and RSD were calculated. The results are presented in Table.3

Specificity

Specificity is the degree to which the procedure applies to a single analyte and is checked in each analysis by comparing the blank chromatogram with the chromatogram obtained for the drug spiked with internal standard(placebo) to trace out the interfering peaks.

The specificity of the method was investigated by the analysis of blank preparations spiked with standard Rosiglitazone maleate and the sample Rosiglitazone maleate and internal standard (placebo) is also added. The result is presented in Table.4

Limit of quantitation (LOQ)

LOQ, the peak area response was determined by analysing five times of 20 µg/ml concentration of standard Rosiglitazone maleate and the sample solution Rosiglitazone maleate of 20 µg/ml. The mean, standard deviation and RSD were calculated. The result is presented in Table.4.

Limit of detection (LOD)

LOD is the peak area response was determined by making twenty one measurements at seven different concentrations of the sample Rosiglitazone maleate in the range of 2 µg/ml – 10 µg/ml. The mean, standard deviation and RSD were calculated. The result presented in Table.4.

Precision

i) Reproducibility

Reproducibility of the method assessed by analysing five times 200 µg/ml of standard solution of Rosiglitazone maleate. The mean, standard deviation and RSD of Reproducibility were calculated. The results are presented in Table.4.

ii) Repeatability

Repeatability of the peak area response was determined by making six measurements at six different concentration points in the range of 336.1 - 338.5 mg/ml of sample Rosiglitazone maleate respectively and it is compared with that of the standard Rosiglitazone maleate 26.5 mg/ml. The results are presented in Table.4.

Robustness

Robustness was determined by injecting triplicate injection of standard and three sample solutions in single and at different concentration with respect to control condition.

Robustness of the method was checked by varying the instrumental condition Wavelength ±2 nm, temperature 2° C. and the %RSD was calculated.The results are presented in Table-4

RESULTS AND DISCUSSION

Method development

The present RP-HPLC method for the quantification of Rosiglitazone maleate in bulk and Pharmaceutical dosage forms, revealed as simple, accurate, presise, robust, specific and stability indicating. The method has the significant retention time of 5.720 min.

System suitability

System suitability test was employed to establish the parameters such as tailing factor, theoretical plates and retention time. The tailoring factor is 1.768 and the theoretical plate is 7229.377. The results are presented in Table-1. The typical chromatogram of Rosiglitazone maleate is shown in Fig.1

Linearity

Linearity was evaluated by plotting peak area as a function of analyte concentration for Rosiglitazone maleate. From the linear studies the specified range determined was 160-260 µg/ml. The linear regression coefficient and the correlation coefficient were found to be 0.99975 and 0.099988. It obeys the linear equation Y= 29836.83 X - 96983.4 (n =6). The results are shown in Table-2 and Fig-2.

Precision

Reproducibility of the method was studied by injecting standard Rosiglitazone maleate for five times (n=5). The % RSD was found to be 0.0177, for all the solution tested. The percentage RSD less than 2 indicates good Reproducibility of the method

Repeatability of the method was studied by obtaining data from the precision experiments for six multiple injections at six different of samples of Rosiglitazone maleate 336.4, 337.2, 337.4, 336.1, 336.6, 338.5 during precision. The method showed %RSD of 0.5769 which is less than 2 % for all the solution tested. This indicates good Repeatability of the method.

Accuracy

The accuracy of a method can be measured in several ways. One way is based on recovery as determined by spiking analytes into a blank matrix, and we should get 100% recovery. The method showed % RSD of 0.7513 for all the solution tested which is less than 2. This indicates good accuracy of the method.

LOD and LOQ

The LOD of Rosiglitazone maleate was found to be 2 µg/ml and the LOQ was 20 µg/ml. Overall summary of validation parameters are presented in Table-4

Table-1. System suitability parameters of Rosiglitazone maleate

Retention Time	16.001
Theoretical Plates	7229.377
Tailing Factor	1.768

Table-2. Linearity for Rosiglitazone maleate

S.No	Concentration (µg/ml)	Volume of stock solution(ml)	Volume made up to (ml)	Area
1	160	4	50	4673534
2	180	9	100	5279654
3	200	5	50	5874826
4	220	11	100	6472821
5	240	6	50	7031955
6	260	13	100	7679710

Linear regression coefficient 0.99757

Correlation coefficient 0.099988

Standard deviation 19254.14

Table-3. Accuracy for Rosiglitazone maleate

S.No	%Recovery/ Concentration	Placebo wt in mg	Standard wt in mg	Standard area	Syn.mix. area	%Recovered
1	Standard	---	26.5	6091250 6092015	--	----
2	80	308.2	22.3	---	5132056	100.11
3	80	307.6	22.1	---	5132934	101.04
4	80	308.4	22.4	---	5134018	99.71
5	100	307.5	27.8	---	6471253	101.26

6	100	307.6	27.7	---	6441786	101.71
7	100	306.8	27.5	---	6429289	101.71
8	102	310.4	31.8	---	7363602	100.73
9	102	309.8	31.3	---	7322708	101.77
10	102	310.6	31	---	7265276	101.95
					MEAN	101.05
					SD	0.7592
					RSD in %	0.7513

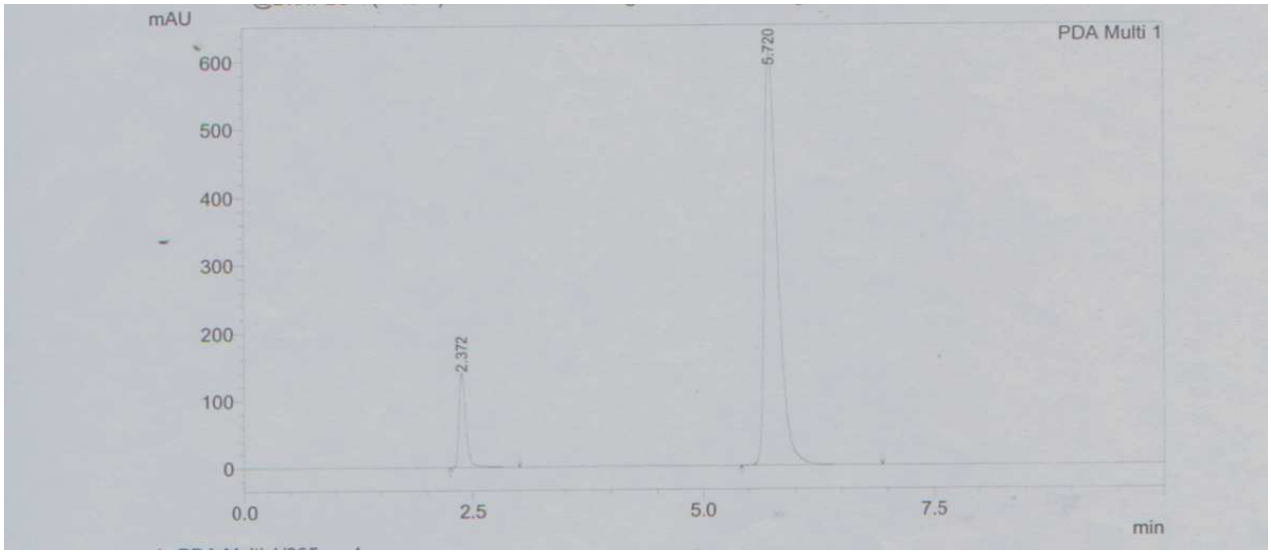


Fig.-1 Typical chromatogram of Rosiglitazone Maleate

Table-4. Summary of Validation parameters

S.no	Parameters	Results
1	Limit of detection(LOD) (µg/ml)	2 µg/ml
2	Limit of quantitation (LOQ) (µg/ml)	20 µg/ml
3	Reproducibility (% RSD)	0.0177
4	Repeatability (% RSD)	0.5729
5	Robustness	
	(1) Change in wavelength (Mean % Assay)	99.68
	(2) Change in Temperature (Mean % Assay)	100.46
6	specificity	No interference of other peak, so the system is specific.

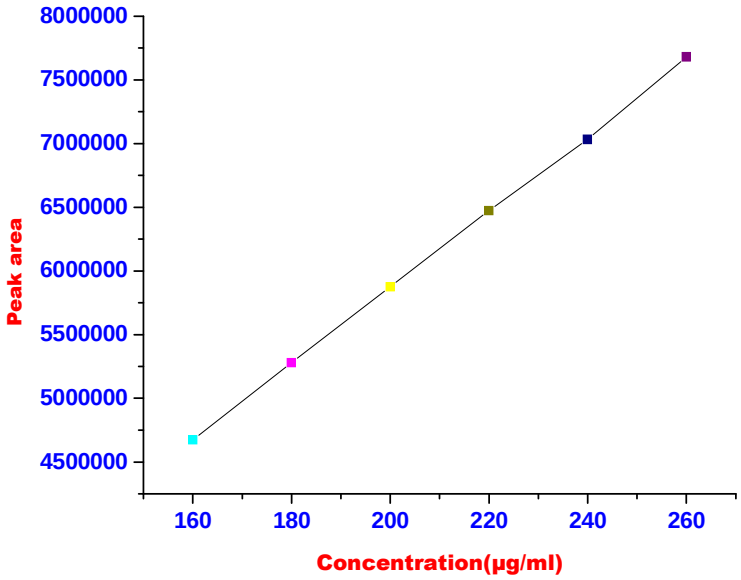


Fig-2. Linear graph of Rosiglitazone Maleate

CONCLUSION

This developed RP-HPLC method for the estimation of Rosiglitazone maleate is accurate, precise, robust, specific, and stability-indicating. The method has been found to be better because of its less retention time, use of an economical and readily available mobile phase, and good resolution of peaks. The run time is relatively short, which will enable rapid quantification of many samples in routine and quality-control analysis of various formulations containing Rosiglitazone maleate. All these factors make this method suitable for quantification of Rosiglitazone maleate in bulk drugs and in pharmaceutical dosage forms without any interference. The results of stress testing undertaken according to the International Conference on Harmonization (ICH) guidelines reveal that the method is selective and stability-indicating.

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