

## **Simultaneous spectrophotometric analysis of rosiglitazone maleate and gliclazide in bulk drug and pharmaceutical formulation**

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### **ABSTRACT**

*A novel, simple, sensitive, rapid spectrophotometric method has been developed for simultaneous estimation of Rosiglitazone (RSG) and Gliclazide (GLZ). The method involved solving simultaneous equations based on measurement of absorbance at two wavelengths 245nm and 226 nm,  $\lambda_{max}$  of RSG and GLZ respectively. Beer's law was obeyed in the concentration range of 4-40 $\mu$ g/ml and 5-50  $\mu$ g/ml for RSG and GLZ respectively. The method was validated for accuracy, precision and recovery studies. Statistical analysis proved the method was precise, reproducible, selective, specific, and accurate for analysis of RSG and GLZ. The wide linearity range, sensitivity, accuracy, and simple procedure imply that the proposed technique demonstrated to be appropriate for routine analysis and quality control assays of tablets.*

**Keywords:** Rosiglitazone, Gliclazide, Simultaneous Equation Method.

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### **INTRODUCTION**

Rosiglitazone in the thiazolidinedione class of drugs, works as an insulin sensitizer, by binding to the PPAR receptors in fat cells and making the cells more responsive to insulin[1]. PPARs are receptors on the membrane of the cell nucleus. Thiazolidinediones enter the cell, bind to the nuclear receptors, and affect the expression of DNA. There are several PPARs, including PPAR $\alpha$ , PPAR $\beta/\delta$ , and PPAR $\gamma$ . Thiazolidinediones bind to PPAR $\gamma$ [2]. Rosiglitazone also appears to have an anti-inflammatory effect in addition to its effect on insulin resistance. Nuclear factor kappa-B (NF- $\kappa$ B) is a signaling molecule which stimulates the inflammatory pathways. NF- $\kappa$ B inhibitor (I $\kappa$ B) is an inhibitor which downregulates the inflammatory pathways. When patients take rosiglitazone, NF- $\kappa$ B levels fall and I $\kappa$ B levels increase[3]. Gliclazide is an oral hypoglycemic (anti-diabetic drug) and is classified as a sulfonylurea. It is marketed as Glizid, Glyloc and Reclide in India and Diamicon in Canada[4]. Gliclazide undergoes extensive metabolism to several inactive metabolites in humans, mainly methylhydroxygliclazide and carboxygliclazide. CYP2C9 is involved in the formation of hydroxygliclazide in human liver microsomes and in a panel of recombinant human P450s in vitro [5-6]. Some individual methods have been developed on gliclazide that are found reported[7-9]. Even some methods have been developed individually on rosiglitazone[10]. Some simultaneous methods are also available in the literature but based on HPLC, UPLC, HPTLC etc. But no methods are published for the given drugs with UV-Visible Spectrophotometry[11-12]. The objective of this investigation was to devise a simple, precise, rapid and economical method for the simultaneous estimation of Rosiglitazone maleate and Gliclazide in bulk drug and in the tablet formulation.

**MATERIALS AND METHODS****Materials and Reagents:**

The pure sample of Rosiglitazone Maleate was obtained from Actavis pharmaceuticals LTD, Indrad, Dist.Mehsana (Gujarat) and Gliclazide from Panacea biotech LTD, Baddi, Dist.Solan (H.P.) Laboratory mixture of Rosiglitazone maleate and Gliclazide prepared in the laboratory.

**Instrumentation**

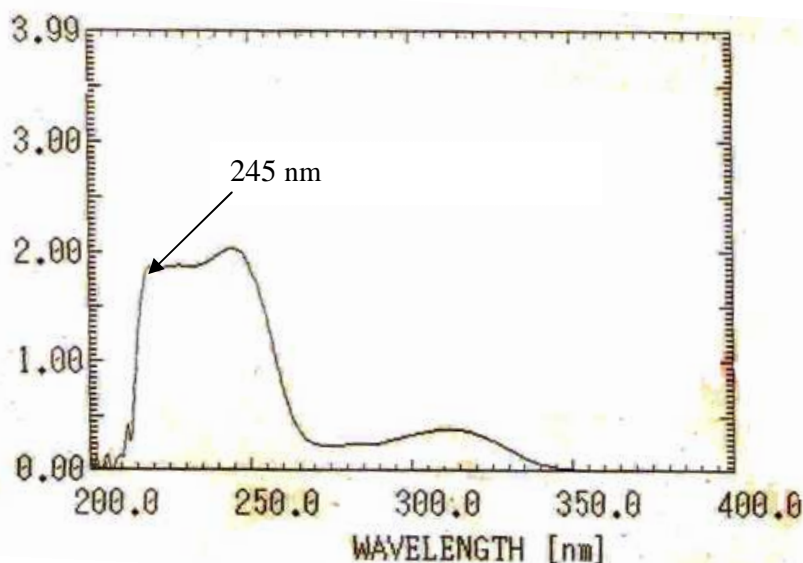
Shimadzu 1700 U.V visible spectrophotometer with 1cm matched quartz cells, and 0.1 N NaOH was used as solvent for the experiment.

**Preparation of standard Stock Solution**

Rosiglitazone maleate 10mg and Gliclazide 10mg were accurately weighed and dissolved separately in 100ml volumetric flask in sufficient quantity of 0.1 N NaOH, sonicated and diluted to 100ml with the same so as to get the concentration of 100 $\mu$ g/ml.

**Estimation of drug from laboratory mixture****Preparation of mix standard Stock Solution**

Rosiglitazone Maleate 10mg + Gliclazide 20mg were accurately weighed and dissolved in 100ml volumetric flask in sufficient quantity of 0.1 N NaOH,sonicated and diluted to 100ml with the same so as to get the concentration of 100  $\mu$ g/ml and 200 $\mu$ g/ml. Further dilutions were made from this stock solution. Estimation of Rosiglitazone Maleate and Gliclazide were done by Simultaneous equation and Absorption ratio method.



**Fig. 1:**  $\lambda_{\max}$  for Rosiglitazone Maleate

**Estimation of drug from dosage form (Tablet)****Sample solution**

20 tablets containing 80 mg of Gliclazide and 4 mg of Rosiglitazone Maleate were weighed and powdered in glass mortar. For the analysis of drugs, a standard addition method was used. An accurately weighed 36 mg of pure Rosiglitazone Maleate was added to finely powdered sample to bring the concentration of Rosiglitazone Maleate in linearity range. With this addition, the ratio of Rosiglitazone Maleate to Gliclazide was brought to 1:2. Quantity of powder equivalent to 20 mg of Gliclazide and 10 mg of Rosiglitazone was transferred to 100 ml volumetric flask, dissolved in sufficient quantity of 0.1N NaOH, sonicated and volume was adjust up to mark with 0.1N NaOH to obtain a stock solution of 200 $\mu$ g/ml of Gliclazide and 100 $\mu$ g/ml of Rosiglitazone Maleate. This solution was then filtered through Whatmann filter paper # 41. Further dilutions were made from this stock solution to get required

concentration. Absorbances of these solutions were measured at appropriate wavelengths, and values were substituted in the respective formula to obtain concentrations.

#### Determination of $\lambda_{\max}$

##### Rosiglitazone Maleate

The standard solution of Rosiglitazone Maleate (40  $\mu\text{g/ml}$ ) was scanned at different concentrations in the range of 200-400 nm and  $\lambda_{\max}$  was found to be 245 nm against reagent blank.

##### Gliclazide

The standard solution of Gliclazide (50  $\mu\text{g/ml}$ ) was scanned at different concentrations in the range of 200-400 nm and  $\lambda_{\max}$  was found to be 226 nm against reagent blank.

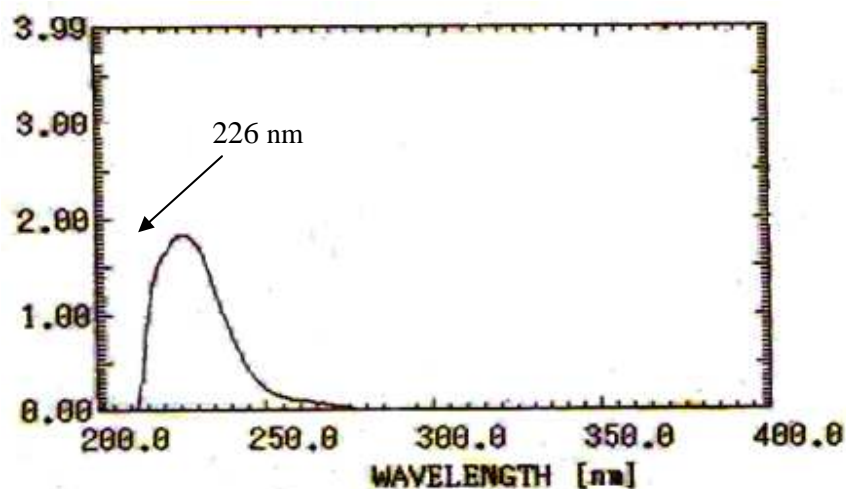


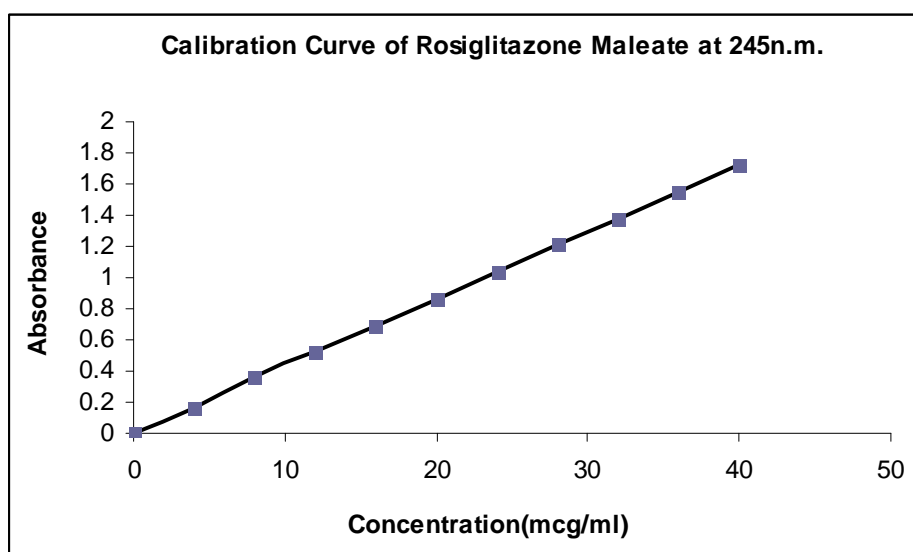
Fig.2  $\lambda_{\max}$  for Gliclazide

Simultaneous equation method

#### Calibration Curve

##### Rosiglitazone Maleate at 245nm and 226nm

The absorbances were recorded for 4-40  $\mu\text{g/ml}$  at 245nm. ( $\lambda_{\max}$  of Rosiglitazone Maleate) and 226nm ( $\lambda_{\max}$  of Gliclazide). From this calibration curve was plotted.



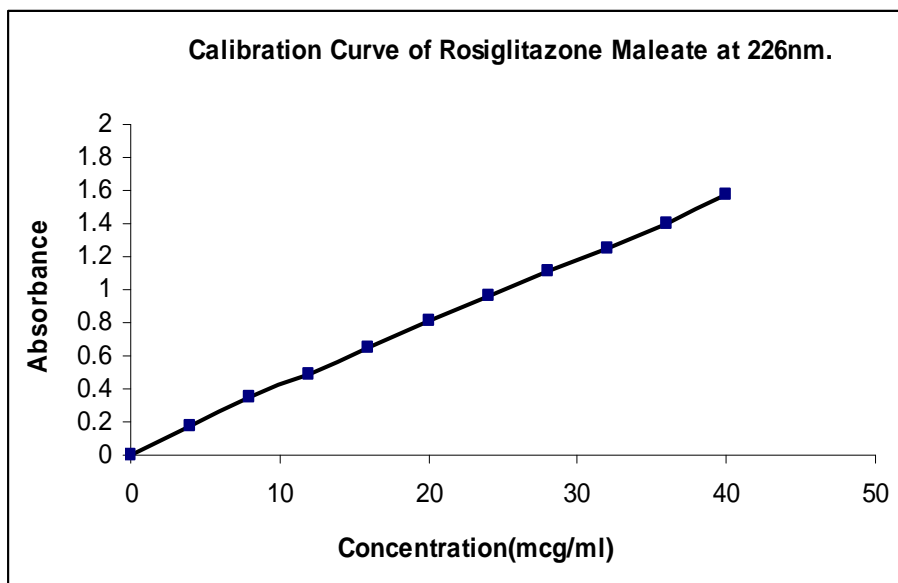
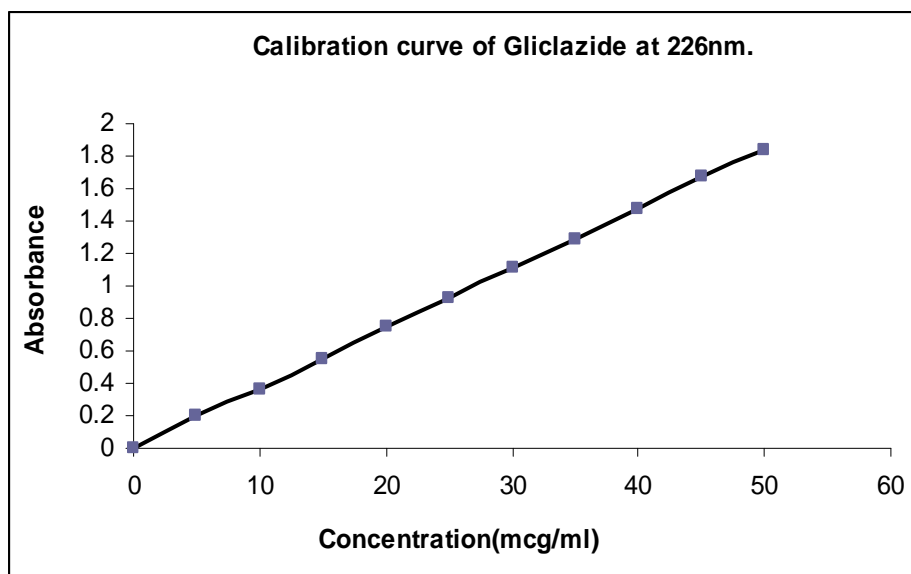


Fig.3 : Calibration Curve for Rosiglitazone Maleate

#### Gliclazide at 245nm and 226nm

The absorbances were recorded for 05-50 $\mu$ g/ml at 245nm ( $\lambda_{\text{max}}$  of Rosiglitazone Maleate) and 226nm ( $\lambda_{\text{max}}$  of Gliclazide). From this calibration curve was plotted.



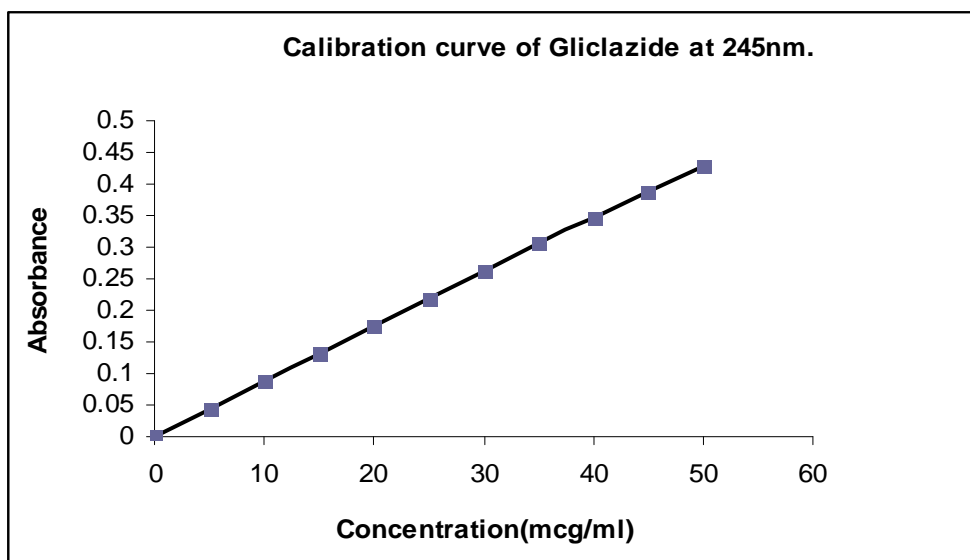


Fig.4 : Calibration curve for Gliclazide

Table-1: Results of analysis of Rosiglitazone Maleate and Gliclazide in the laboratory prepared mixture

Sr. No	Concentration present ( $\mu\text{g/ml}$ )		Concentration found ( $\mu\text{g/ml}$ )		% Estimated	
	RSGN	GLZ	RSGN	GLZ	RSGN	GLZ
1	10	20	9.85	20.12	98.5	100.6
2	10	20	9.88	19.87	98.8	99.35
3	10	20	9.93	19.95	99.3	99.75
4	10	20	10.14	20.04	101.4	100.20
5	10	20	9.98	20.08	99.8	100.40
6	10	20	10.06	19.93	101.6	99.65
Mean	-	-	-	-	99.74	99.99
$\pm$ S. D.	-	-	-	-	1.106	0.483
%RSD	-	-	-	-	1.11	0.49

Table-2: Results of analysis of Rosiglitazone Maleate and Gliclazide in tablet formulation

Formulation	Label claim (mg/ tablet)		Amount found* (mg/ tablet)		Percentage found	
	RSGN	GLZ	RSGN	GLZ	RSGN	GLZ
Glyroz-4	4	80	3.97	79.75	99.25	99.69

\* Mean of six readings

Table-3: Results of analysis and Recovery studies

Formulation	Label claim (mg/ tablet)		% Estimated*		% Recovery*	
	RSGN	GLZ	RSGN	GLZ	RSGN	GLZ
Glyroz-4	4	80	99.25	99.69	100.525	100.45

Table-4: Statistical analysis of recovery study results

\* Mean of six readings

SD-Standard deviation, COV-Coefficient of Variation, SE- Standard Error

RSGN- Rosiglitazone Maleate

GLZ-Gliclazide

**Method Validation:**

**Specificity-** Pure Rosiglitazone Maleate and Gliclazide is spiked with common excipients and was assayed by proposed method and it was found that the assay results were unaffected by the presence of such excipients.

**Linearity-** Linearity of Rosiglitazone Maleate and Gliclazide was observed in the range of 4-40 µg/ml and 5-40 µg/ml respectively at all two wavelengths 245nm, 226, 235nm in both simultaneous equation and Q analysis methods. The calibration curve yielded coefficient of correlation (r) near to 0.999.

**Assay results-** A tablet dosage form containing both drugs i.e. Rosiglitazone Maleate and Gliclazide was analyzed by Simultaneous equation and Absorption ratio and method, the percentage of both drugs in tablet were determined and presented in table. Assay results obtained are within the limit.

**Accuracy and precision** –The low values of S.D and %COV interval indicate that method is precise. % recovery of both methods was found to be within limit indicate the non interference from the formulation excipients and confirm the accuracy and precision of the method.

### RESULTS AND DISCUSSION

The proposed methods described for the simultaneous analysis of RSGN and GLZ in combined tablet dosage form has been found to be simple, accurate, rapid, economical and sensitive to be applied in routine analysis of tablets. In described method, there is no additional extraction or separation procedures to extract the drug from the formulation excipients matrix, therefore decreasing the error in quantitation.

The developed method involving formation and solving of simultaneous equation is based on the absorptivity coefficient of two drugs that are on the wavelength maxima of both drugs i.e. RSGN (245 nm) and GLZ (226nm). Once the equations were framed, it is just required to measure the absorbance of sample solution at selected wavelengths and few calculations that can be manually done. Framed equations were validated using laboratory prepared mixtures of two drugs which gave satisfactory results.

In the developed method, six replicate analysis were carried out to test the precision of the method. To confirm the accuracy of the method, recovery studies were performed by adding known amount of pure drug to the preanalyzed formulation and reanalyzing the mixture by proposed method. The results of recovery studies were found close to 100% for both RSGN and GLZ, standard deviation was low indicating accuracy and reproducibility of the methods. Recovery studies were satisfactory which shows that there is no interference of excipients. The developed methods were found to be simple, rapid and accurate that can be used for routine estimation of RSGN and GLZ from tablet formulations.

### CONCLUSION

The %recovery of Rosiglitazone Maleate in Simultaneous equation method was found to be in the range of 99.47-100.49% whereas % recovery of Gliclazide in the range of 100.50-100.72% which is close to 100% indicating reproducibility and accuracy of the method. Hence, the proposed method were found to be accurate, simple and rapid for the routine analysis of Rosiglitazone Maleate and Gliclazide in combine dosage form tablet or capsule.

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