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Study of Simultaneous Equation and Partial Simultaneous Equation Methods for the Spectrophotometric Estimation of Rosiglitazone Maleate and Glimepiride in Tablets

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Two new, simple, sensitive, accurate and reproducible spectrophotometric methods were developed for the simultaneous estimation of rosiglitazone maleate and glimepiride in combine dosage form. The methods employed are simultaneous equation method and partial simultaneous equation method. **Method I** employed generation and solving simultaneous equations using 248.5 and 228.5 nm as two analytical wavelengths and **method II** employed 312 and 228.5 nm as λ_3 and λ_2. Both drugs obeyed Beer's law in the concentration ranges of 2 to 16 μg/mL. Statistical analysis and recovery studies validated the method. The method is found to be rapid, precise and accurate and can easily be employed in the laboratory for routine estimation of drugs.

Key Words: Rosiglitazone, Glimepiride, Spectrophotometric estimation, UV-Visible spectrophotometer.

INTRODUCTION

Rosiglitazone maleate (ROSI) is chemically (±)-5-{*p*-[2-(methyl-2-pyridylamino)ethoxy]benzyl}-2,4-thiazolidinedione. It is selective agonist for paroxisome proliferator-activated receptor gamma (ppar-γ)[1,2]. Literature survey revealed that several methods including spectrophotometric[3], HPLC[4,5], liquid chromatography[6] have been reported for the estimation of rosiglitazone. Glimepiride (GLIM) is a sulfonylurea antidiabetic drug. Chemically, it is 1-({[-2-(3-ethyl-4-methyl-2-oxo-3-pyrroline-1-carboxamido)-ethyl]phenyl}sulfonyl-3-(*trans*-4-methylcyclohexyl)urea[7,8]. A number of spectrophotometric[9] and HPLC[10,11] liquid chromatography[12] methods have been reported in the literature for the estimation of GLIM. The combination of rosiglitazone maleate (ROSI) and glimepiride (GLIM) is available only in tablet form in the market. Exhaustive literature survey revealed that no UV spectrophotometric method is reported for simultaneous estimation of these two drugs in combination. Hence, in the present paper a comparative

study is made between simultaneous equation and partial simultaneous equation methods for the spectrophotometric estimation of rosiglitazone maleate and glimepiride in tablets.

EXPERIMENTAL

A GBC Cintra-10 double beam UV-Visible spectrophotometer (Australia) equipped with 10 mm matched quartz cells was used in the present investigation. Methanol used was AR grade (Qualigens, Mumbai). Gift sample of ROSI and GLIM were obtained from M/s Aristo Pharmaceuticals Ltd., Mumbai and M/s Synmedic Lab, Faridabad, respectively. A combination of both drugs, rosiglitazone maleate 2 mg and glimepiride 1mg in each tablet dosage form is marketed by M/s Torrent Pharmaceuticals Ltd., under the trade name Enselin 2G.

Preparation of standard stock solution: Standard stock solutions of individual compounds were prepared by dissolving accurately weighed amount of each drug in methanol to make final concentration of 1000 µg/mL. The absorbance against methanol was measured at 248.5 and 312 nm for ROSI and 228.5 nm for GLIM. Both the drugs obeyed Beer's law individually and in mixture within the concentration range of 2-16 µg/mL.

Preparation of sample stock solution: The average weight of each tablet was calculated by weighing 20 tablets. Tablets were powdered finely in a glass mortar. The tablet powder equivalent to 100 mg of ROSI and 50 mg of GLIM was accurately weighed and extracted with 4 successive 20 mL portions of methanol and transferred quantitatively into 100 mL volumetric flask after filtering through Whatmann filter paper. The required volume was made up with methanol. Further dilutions were made to get the required concentration.

Simultaneous equation method (method I): In **method I**, two wavelengths selected for the generation of simultaneous equations were 248.5 and 228.5 nm. Absorption was determined at these two wavelengths for both the drugs separately. The molar absorptivity for the two drugs is presented in Table-1. Molar absorptivity values of ROSI is 2.6279×10^4 L mol^{-1} cm^{-1} at 248.5 nm and 2.7274×10^4 L mol^{-1} cm^{-1} at 228.5 nm, while molar absorptivity values for GLIM is 9.4199×10^3 L mol^{-1} cm^{-1} at 248.5 nm 2.7426×10^4 L mol^{-1} cm^{-1} at 228.5 nm.

The simultaneous equations formed were

$$\text{At } 248.5 \text{ nm } A_1 = 0.0555\ C_X + 0.0192\ C_Y \quad (1)$$

$$\text{At } 228.5 \text{ nm } A_2 = 0.0576\ C_X + 0.0559\ C_Y \quad (2)$$

where, A_1 and A_2 are absorbances of sample solution at 248.5 and 228.5 nm, respectively. C_X and C_Y are the concentrations of ROSI and GLIM respectively, (µg/mL) in sample solution. By substituting the value of C_Y from eqn. 2 into eqn. 1, the value of C_X can be obtained.

Partial simultaneous equation method (method II): In **method II**, two wavelengths selected for the generation of simultaneous equations were 228.5 and 312 nm. Absorption was determined at these two wavelengths for both the drugs separately. The molar absorptivity for the two drugs is presented in Table-1.

TABLE-1
ABSORPTIVITY VALUES FOR ROSIGLITAZONE MALEATE AND GLIMEPIRIDE

Concentration (μg/mL)		Absorptivity at				
		248.5 nm		228.5 nm		312 nm
ROSI	GLIM	ROSI	GLIM	ROSI	GLIM	ROSI
2	2	564	199	608	575	139
4	4	575	200	600	582	122
6	6	545	210	534	594	118
8	8	546	207	507	552	112
10	10	545	185	593	546	125
12	12	551	181	561	535	116
14	14	545	181	610	546	105
16	16	532	176	598	539	106
Mean		555.04	192.38	576.38	558.63	118

Molar absorptivity values of ROSI is 5.5873×10^3 L mol^{-1} cm^{-1}at 312 nm and 2.7274×10^4 L mol^{-1} cm^{-1} at 228.5 nm, while molar absorptivity values for GLIM is 2.7426×10^4 L mol^{-1} cm^{-1} at 228.5 nm.

The simultaneous equations formed were

$$\text{At 312 nm } A_3 = 0.0118C_X \quad (3)$$

$$\text{At 228.5 nm } A_2 = 0.0576C_X + 0.0559C_Y \quad (4)$$

where A_3 and A_2 are absorbances of sample solution at 312 and 228.5 nm, respectively. C_X and C_Y are the concentrations of ROSI and GLIM, respectively (μg/mL) in sample solution. By substituting the value of C_X from eqn. 3 into eqn. 4, the value of C_Y can be obtained.

Estimation of marketed preparation: An aliquot of sample stock solution (0.4 mL) was transferred to 100 mL volumetric flask and volume was made up to the mark with methanol. This solution was scanned in the range 200-400 nm against methanol as blank. Absorbances of these solutions were measured at 248.5, 228.5 and 312 nm as A_1, A_2 and A_3, respectively. The concentration of each drug was then calculated using eqns. 1 and 2 for **method I** and eqns. 3 and 4 for **method II**. Results of analysis of the tablet formulation are reported in Table-2. The experiment was repeated six times to get reproducibility.

TABLE-2
STATISTICAL ANALYSIS FOR ROSIGLITAZONE MALEATE AND GLIMEPIRIDE

Tablet brand	Method	Tablet component	Label claim* (mg/tab)	Amount found* (mg/tab)	SD*	RSD* (%)	SE*
Enselin 2G	I	ROSI	2	2.0147	0.0093	0.4619	0.0038
		GLIM	1	1.0039	0.0080	0.7971	0.0033
	II	ROSI	2	2.0078	0.0073	0.3619	0.0029
		GLIM	1	1.0047	0.0047	0.4708	0.0019

*Average of six determinations.

Recovery studies: To study accuracy, reproducibility and precision of the method, recovery studies were carried out by adding known amount of pure drugs to the analyzed sample of tablet powder and mixture was reanalyzed for the drug content using the proposed method. Results of recovery were found to be satisfactory and presented in Table-3.

TABLE-3
RECOVERY STUDY OF ROSIGLITAZONE MALEATE AND GLIMEPIRIDE

Tablet brand	Method	Tablet component	Label claim* (mg/tab)	Amount found* (mg/tab)	% Recovery ± SD*
Enselin 2G	I	ROSI	2	2	100.61 ± 0.0155
		GLIM	1	1	100.38 ± 0.0192
	II	ROSI	2	2	100.46 ± 0.0086
		GLIM	1	1	100.34 ± 0.0035

*Average of six determinations.

RESULTS AND DISCUSSION

Method I for simultaneous estimation of ROSI and GLIM showed higher values of standard deviation, standard error of mean, coefficient of variation and percentage range of error (within 95 % confidence limit) and thus shows less precision of method. In **method II** the results of analysis of commercial formulations significantly showed low values of these statistical parameters and thus better showed precision of the method. **Method II** was found to be simple, accurate, economical and rapid for routine simultaneous analysis of drugs from the formulation without prior separation. Mean of absorptivity for rosiglitazone at 248.5 and 228.5 nm was 555.04 and 576.38 nm, respectively and for glimepiride was 192.38 and 558.63 at 248.5 and 228.5 nm, respectively. Mean of absorptivity for rosiglitazone at 312 nm was 118. Quantity of rosiglitazone and glimepiride in Enselin 2G

was found to be 2.0147 mg/tab (label claim 2 mg/tab) and 1.0039 mg/tab (label claim 1 mg/tab), respectively by **method I** while 2.0078 mg/tab (label claim 2 mg/tab) and 1.0047 mg/tab (label claim 1 mg/tab) by **method II**.

In this method, once absorptivity coefficients were determined, little time is required for analysis, as it would only require determination of absorbances of the sample solutions at the selected wavelengths. The values of coefficient of variation were satisfactorily low and recovery was close to 100 % for both the drugs by **method II**. Hence, it can be employed for routine analysis in quality control laboratories.

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