Digest Journal of Nanomaterials and Biostructures Vol. 4, No. 4, December 2009, p. 739 - 746

APPLICATION OF VIERODT'S AND ABSORPTION CORRECTION SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF ROSIGLITAZONE MALEATE AND GLIMEPIRIDE IN TABLETS

P. B. KHEDEKAR*, S. M. DHOLE[a], K. P. BHUSARI[a]
University Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur-440 033 (M.S.), India
[a]Department of Pharmaceutical Chemistry, Sharad Pawar College of Pharmacy, Wanadongri, Hingna Road, Nagpur-441 110 (M.S.), India

Two new UV-spectrophotometric methods have been developed for simultaneous estimation of rosiglitazone maleate and glimepiride in tablets. The first method was based on application of vierodt's method which involves the formation and solving of simultaneous equations at 247.0 and 228.0 nm, as absorbance maxima of rosiglitazone maleate and glimepiride, respectively. The second method employed was absorption correction method which involves direct estimation of rosiglitazone maleate at 311.5 nm, as at this wavelength glimepiride has zero absorbance and shows no interference. For estimation of glimepiride, corrected absorbance was calculated at 228.0 nm due to the interference of rosiglitazone maleate at this wavelength. Calibration curves were linear with correlation coefficient between 0.99-1.0 over the concentration range of 2-20 μg/mL for both the drugs. The mean percent recovery was found in the range of 99.41-99.80 and 100.36-100.52 for vierodt's method and 99.18-99.80 and 99.64-99.92 for absorption correction method, for rosiglitazone maleate and glimepiride, respectively. The results of analysis were validated statistically and proven to be rugged. The proposed methods are simple, rapid, accurate, precise, economical and can be used successfully in the quality control of pharmaceutical formulations and routine laboratory analysis.

(Received September 18, 2009; accepted October 2, 2009)

Keywords: Rosiglitazone maleate; Glimepiride; Vierodt's method; Absorption correction method; Validation.

1. Introduction

Type-2 diabetes disorder is characterized by disturbed insulin production leading to high blood glucose level. To control this disorder, combination therapy is often used. Rosiglitazone maleate and glimepiride are widely used to treat type-2 diabetes. Rosiglitazone maleate, chemically (±)-5-{p-[2-(methyl-2-pyridyl)amino]ethoxy]- benzyl}-2,4-thiazolidinedione maleate (Fig.1), is a potent oral antihyperglycemic agent that reduces insulin resistance in patients with type-2 diabetes by binding to peroxisomal proliferator-activated receptors gamma (PPAR-γ) [1-2].

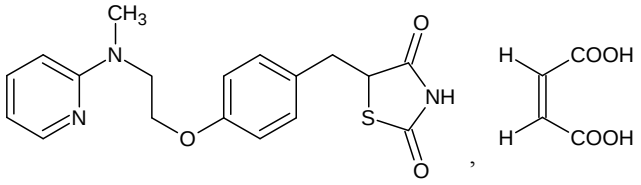

Fig.1. Chemical structure of rosiglitazone maleate.

* Corresponding author: pb_khedekar@rediffmail.com, seemadhole@gmail.com.

Few capillary electrophoresis [3], LC/MS HPLC in human plasma [4], LC in pharmaceutical formulation and human plasma [5-6], MEKC and HPLC [7] and solid phase extraction coupled with LC-MS/MS [8] methods have been reported for analytical monitoring of Rosiglitazone maleate. Glimepiride, chemically trans-3-ethyl-2,5-dihydro-4-methyl-*N*-{2-[4-[[[[(4-methylcyclohexyl)amino]carbonyl]amino]sulfanoyl]phenyl]- ethyl}-2-oxo-1*H*-pyrrole-1-carboxamide, is a sulphonylurea antidiabetic drug and its structure is shown in Fig.2 [9].

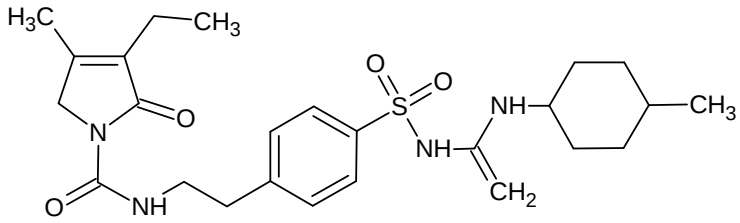

Fig.2. Chemical structure of glimepiride.

Literature survey revealed that derivative spectrophotometric [10], HPLC [11] and HPLC-ESI-MS-MS [12] methods are available for GLIME. In the present work, an attempt has been made to develop two UV-spectrophotometric methods for simultaneous estimation of rosiglitazone maleate and glimepiride in tablet dosage form.

2. Experimental

2.1. Instrument

Double beam UV/VIS spectrophotometer, Shimadzu model 1601 with a pair of 10 mm matched quartz cells was used to measure absorbance of the resulting solution.

2.2. Chemicals and reagents

Pharmaceutically pure sample of rosiglitazone maleate and glimepiride were obtained as generous gifts from Panacea Biotec Ltd., Malpur, Solan (H.P.), India and Medley Pharmaceuticals Ltd., Bari Brahmana, Jammu, India, respectively. All chemicals were of analytical grade. A combination of rosiglitazone maleate (2.0 mg) and glimepiride (1.0 mg) in tablet formulation was procured from local market (Rosicon-G, Glenmark Pharmaceuticals Ltd., Baddi, H.P., India).

2.3. Preparation of standard stock solution

Standard stock solution of rosiglitazone maleate and glimepiride were prepared separately by dissolving 10.0 mg each (accurately weighed) of standard rosiglitazone maleate and glimepiride in methanol and made the volume up to 100 mL with same solvent in 100 mL volumetric flask. Working standard solutions (10.0 µg/mL) were prepared by diluting aliquot portion of standard stock solution of each drug in 100 mL volumetric flasks separately and made the volume up to 100 mL with methanol.

2.4. Study of spectral and linearity characteristics

Each working standard solution was scanned between the range 200-400 nm in 1cm cell against blank and the overlain spectra was recorded (Fig.3). Rosiglitazone maleate shows two absorbance maxima (λ_{max}) at 247.0 and 311.5 nm wavelengths, where as glimepiride shows single absorbance maxima (λ_{max}) at 228.0 nm.

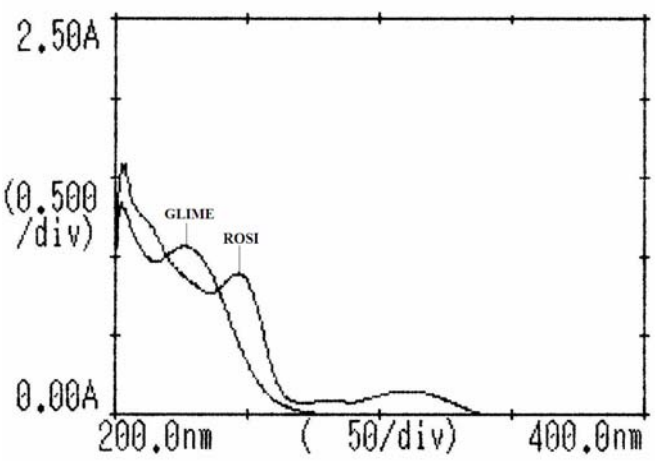

Fig.3. Overlain spectra of rosiglitazone maleate (ROSI) and glimepiride(GLIME).

The calibration curves for rosiglitazone maleate and glimepiride were prepared in the concentration range of 2-20 µg/mL at selected wavelengths by diluting aliquot portions of standard stock solution of each drug. The plots of Beer's law limit are shown in Fig.4 and Fig.5 and the regression parameters are depicted in Table 1.

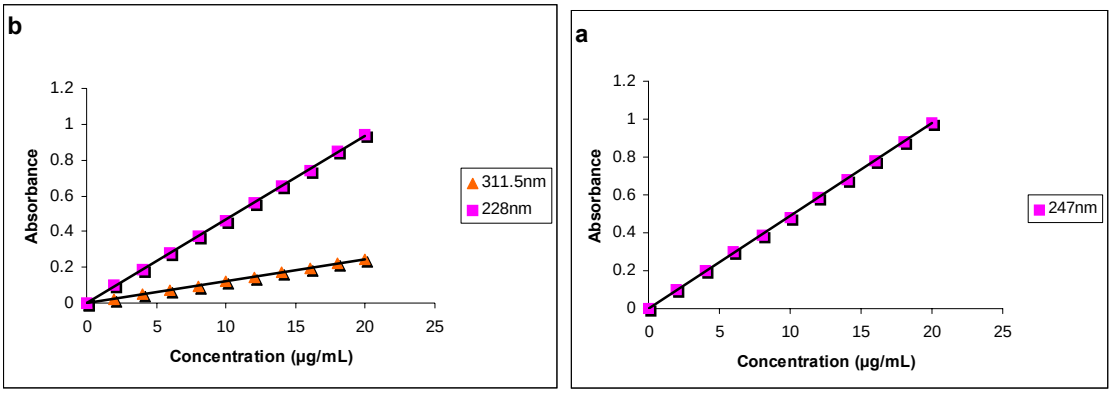

Fig.4. Calibration curve of rosiglitazone maleate in methanol. (a) at 247.0 nm; (b) at 228.0 and 311.5 nm.

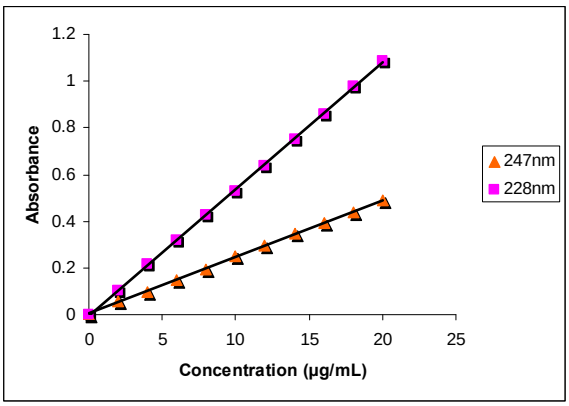

Fig.5. Calibration curve of glimepiride in methanol at 247.0 and 228.0 nm.

Table 1. Spectral and linearity characteristics data.

Parameters	Method I*			Method II**	
	Rosiglitazone maleate	**Glimepiride**		**Rosiglitazone maleate**	**Glimepiride**
λ_{max} (nm)	247.0	228.0		311.5	228.0
Linearity range (µg/mL)	2-20	2-20		2-20	2-20
Regression equation (y=mx+c)					
Slope (m)	0.0488	0.0543		0.0121	0.0543
Intercept (c)	0.0001	-0.0058		0.0004	-0.0058
Correlation coefficient (r^2)	0.9999	0.9997		0.9997	0.9997

*Vierodt's method; **Absorption correction method; y=mx+c, y: concentration (µg/mL); m: slope; x: absorbance; c: intercept.

The absorptivity coefficients of each drug at selected wavelengths were determined. The absorptivity coefficients reported are the mean of five independent determinations and shown in Table 2.

Table 2. Absorptivity coefficient values of rosiglitazone maleate and glimepiride.

Drugs		Absorptivity coefficient*		
		228.0 nm	**247.0 nm**	**311.5 nm**
Rosiglitazone maleate	Mean	458.36	473.94	120.56
	± S.D.	0.858	0.846	0.128
Glimepiride	Mean	520.40	224.73	–
	± S.D.	0.893	0.642	–

* Average of five determinations.

2.5. Method I: Application of Vierodt's method

In quantitative estimation of two components by vierodt's (simultaneous equation) method, two wavelengths i.e. 247.0 nm as λ_{max} of rosiglitazone maleate and 228.0 nm as λ_{max} of glimepiride were selected from the overlain spectra, at which both drugs has absorbance. A set of two simultaneous equations were formed using absorptivity coefficients at selected wavelengths. The concentrations of two drugs in the mixture were calculated using set of two simultaneous equations.

$$C_x = A_2\, ay_1 - A_1\, ay_2 / ax_2\, ay_1 - ax_1 ay_2 \quad (1)$$

$$C_y = A_1\, ax_2 - A_2\, ax_2 / ax_2\, ay_1 - ax_1 ay_2 \quad (2)$$

Where, A_1 and A_2 are absorbance of sample solution at 247.0 nm and 228.0 nm; ax_1 and ax_2, absorptivity coefficients of rosiglitazone maleate at 247.0 nm and 228.0 nm, respectively; ay_1

and ay_2, absorptivity coefficients of glimepiride at 247.0 nm and 228.0 nm, respectively; C_x and C_y are concentrations of rosiglitazone maleate and glimepiride in mixture.

2.6. Method II: Application of Absorption correction method

From the overlain spectrum of rosiglitazone maleate and glimepiride in methanol (Fig.3), it was observed that glimepiride has zero absorbance at 311.5 nm, where as rosiglitazone maleate has substantial absorbance. Thus rosiglitazone maleate was estimated directly at 311.5 nm with no interference of glimepiride. Firstly, for estimation of glimepiride, the absorbance of rosiglitazone maleate was measured at 228.0 nm using standard solution of rosiglitazone maleate (10.0 µg/mL). The contribution of rosiglitazone maleate was deducted from the total absorbance of sample mixture at 228.0 nm. The calculated absorbance was called as corrected absorbance for glimepiride. The concentration of glimepiride was determined from calibration curve at 228.0 nm using the corrected absorbance (Fig.5).

2.7. Analysis of tablet formulation

Twenty tablets were weighed and average weight was calculated. The tablets were triturated to a fine powder. An accurately weighed quantity of powder equivalent to 20.0 mg of rosiglitazone maleate was transferred to 100 mL volumetric flask and dissolved in 50 mL of methanol by intermittent shaking and volume was adjusted up to 100 mL with same solvent. The solution was filtered through Whatman filter paper No. 41 and aliquot portion of filtrate was diluted to obtain a solution of 10 µg/mL and 5 µg/mL of rosiglitazone maleate and glimepiride, respectively. The absorbance of sample solution was measured at selected wavelengths. The content of rosiglitazone maleate and glimepiride in sample solution of tablet was calculated by using vierodt's method (equations 1 and 2) and absorption correction method. The analysis procedure was repeated six times and the result of analysis are shown in Table 3.

Table 3. Results of analysis of tablet formulation.

Drugs	**Labeled Claim (mg)**	**Method I % ± S.D.* (n=6)**	**Method II % ± S.D. (n=6)**
Rosiglitazone maleate	2.0	100.40±0.7340	100.09±0.6377
Glimepiride	1.0	100.01±0.9199	99.95±0.5622

* Standard deviation.

2.8. Validation of methods

The methods were validated with respects to linearity, LOD (Limit of detection), LOQ (Limit of quantitation), precision, accuracy and ruggedness [13].

2.8.1. Linearity

Linearity was checked by preparing standard solutions at ten different concentrations, ranges from 2-20 µg/mL for both the drugs. Calibration curves (n=5) were plotted in the range 2-20 µg/mL between absorbance and concentration of drugs. The results of linearity study of rosiglitazone maleate and glimepiride with two methods, measured in methanol were given in Table 1.

2.8.2. Sensitivity

The limit of detection (LOD) and limit of quantitation (LOQ) parameters were calculated using the following equations; LOD=3.3σ/s and LOQ=10σ/s, where σ is standard deviation of y intercept of calibration curve (n=5) and s is slope of regression equation. The results of the same are shown in Table 5.

2.8.3. Precision

The precision of the method was established by carrying out the analysis of the analytes (n=6) using the proposed developed methods. The low value of standard deviation showed that the methods were precise. The results are shown in Table 3.

2.8.4 Accuracy

To check the accuracy of the developed methods and to study the interference of formulation excipients, analytical recovery experiments were carried out by using standard addition method, at 80, 100, 120% levels. From the total amount of drug found, the percentage recovery was calculated. The results revealed no interference of excipients. The results of recovery studies were summarized in Table 4.

2.8.5. Ruggedness

The ruggedness test of analytical assay method is defined as degree of reproducibility of assay results obtained by the successful applications of assay over different time, day and among multiple analysts. In this study, the proposed methods for determination of rosiglitazone maleate and glimepiride were carried out at different time interval, day and two analysts. The results are shown in Table 5.

Table 4. Result of recovery studies.

Methods	Drugs	% Amount added	% Recovery	±SD(n=3)
Method I	Rosiglitazone maleate	80	99.41	0.3889
		100	99.74	0.7529
		120	99.87	0.0265
	Glimepiride	80	100.50	1.0171
		100	100.52	0.4725
		120	100.36	0.4186
Method II	Rosiglitazone maleate	80	99.80	0.6484
		100	99.18	0.4165
		120	99.77	0.5810
	Glimepiride	80	99.88	0.4392
		100	99.92	0.5209
		120	99.64	0.8279

Table 5. Validation parameters.

Parameters	Method I			Method II	
	Rosiglitazone maleate	**Glimepiride**		**Rosiglitazone maleate**	**Glimepiride**
LOD* (μg/mL)	0.2028	0.1215		0.4161	0.1215
LOQ** (μg/mL)	0.6147	0.3680		0.9230	0.3680
Precision (±S.D.)	0.7340	0.9199		0.6377	0.5622
Intra day (n=3) %± S.D.	100.04±0.3189	100.12±0.4537		99.82±0.4358	99.44±0.3055
Inter day (n=3) %± S.D.	100.42±0.8055	99.89±0.7553		99.80±0.6806	99.89±0.8326
Different analyst (n=3) %± S.D.	100.12±0.4537	99.56±0.5529		100.08±0.7937	100.24±0.4124

* Limit of detection; ** Limit of quantification.

3. Results and discussion

The proposed two methods are based on spectrophotometric simultaneous estimation of rosiglitazone maleate and glimepiride in UV region using methanol as solvent. The absorbance spectral analysis shows the maximum absorbance at 247.0, 311.5 nm for rosiglitazone maleate and 228.0 nm for glimepiride. Method I is based on vierodt's (simultaneous equation) method which involves generation and solving of simultaneous equations using absorptivity coefficient values and absorbance at 247.0 and 228.0 nm for estimation of rosiglitazone maleate and glimepiride in sample solution. Method II is based on absorbance correction method which involves correction of absorbance at 228.0 nm for estimation of glimepiride and the estimation of rosiglitazone maleate was done at 311.5 nm directly with no interference of glimepiride.

Beer's law obeyed in the concentration range of 2-20 μg/mL for both the drugs. The correlation coefficients were found to be in between 0.99-1.0 which shows the good linear relationship for both components. The results of optical characteristics such as Beer's law limits, correlation coefficient, slope, intercept and absorptivity coefficient values were summarized in Table 1 and Table 2 for method I and method II.

The tablet assay results obtained by proposed methods were very closed to labeled claim and low valve of standard deviation, suggesting that the developed methods has high precision.

In order to check the accuracy of the developed methods, known quantities of standard drugs of rosiglitazone maleate and glimepiride in three different levels were added to its preanalyzed tablet sample and analyzed by the developed methods. The results of recovery studies are shown in Table 4. The mean percentage recoveries were found in the range of 99.0-101.0 and it indicated the non interference of the excipients in the tablet formulation.

Ruggedness test was determined between different time intervals, days and analysts. The result shows (Table 5) no statistical difference between different analysts, time and days, suggesting that the developed methods were rugged.

4. Conclusions

The proposed two analytical UV spectrophotometric methods were developed and validated thoroughly for quantitative determination of rosiglitazone maleate and glimepiride in tablets. The developed methods were found to be simple, rapid, accurate, precise, economical and give an acceptable recovery of the analytes, which can be directly and easily applied to the analysis of rosiglitazone maleate and glimepiride in pharmaceutical tablet formulations.

Acknowledgements

Authors are thankful to Panacea Biotec Ltd., Malpur, Solan (H.P.), India and Medley Pharmaceuticals Ltd., Bari Brahmana, Jammu, India for providing the gift samples of drug rosiglitazone maleate and glimepiride, respectively.

References

[1] Indian Pharmacopoeia, Government of India Ministry of Health and Family Welfare, Indian Pharmacopoeia Commission, Ghaziabad **3**, 1674 (2007).
[2] E. A. M. Gale, Lancent, **357**, 1870 (2001).
[3] B. Jamali, G. C. Theill, L. L. Sorensen, J. Chrom. A. **1049**, 183 (2004).
[4] J. He, Y. F. Duan, Z. R. Tan, H. H. Zhou, J. Pharm. Biomed. Anal. **43**, 909 (2004).
[5] T. Radhakrishna, J. Satyanarayana, A. Satyanarayana, J. Pharm. Biomed. Anal. **29**, 873 (2002).
[6] B. L. Kolte, B. B. Raut, A. A. Deo, M. A. Bagool, D. B. Shinde, J. Chrom. B. **788**, 37 (2003).
[7] P. Gomes, J. Sippel, A. Jablonski, M. Steppe, J. Pharm. Biomed. Anal.**36**, 909 (2004).
[8] C. C. Chou, M. R. Lee, F. C. Cheng, D. Y. Yang, J. Chrom. A. **1097**, 74 (2005).
[9] S. Budavari, The Merck Index: An Encyclopedia of Chemicals, Drugs and Biologicals, 13th edn, Merck Research Laboratories, Whitehouse Station, NJ, 790 (2001).
[10] S. Altinoz, D. Tekeli, J. Pharm. Biomed. Anal. **24**, 507 (2001).
[11] P. Kovarikova, J. Klimes, J. Dohnal, L. Tisovska, J. Pharm. Biomed. Anal. **36**, 905 (2004).
[12] I. I. Salem, J. Idrees, J. I. Tamimi, J. Chrom. B. **788**, 37 (2003).
[13] ICH Guidelines Q2B Validation of Analytical Procedures: Methodology International Conference on Harmonization, Geneva, (1996).