Asian Journal of Chemistry Vol. 20, No. 1 (2008), 236-240

Derivative Spectrophotometric Estimation of Metformin Hydrochloride and Rosiglitazone Maleate

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A simple, sensitive and rapid spectrophotometric method has been developed for simultaneous estimation of rosiglitazone maleate and metformin hydrochloride from tablets. Rosiglitazone maleate has absorbance maxima at 316 nm and metformin hydrochloride has absorbance maxima at 232 nm in methanol:water (2:8) mixture. Second derivative ultraviolet spectrophotometric method was used for estimation of metformin hydrochloride and rosiglitazone maleate was estimated directly from its absorbance at 316 nm. This method involves no extraction or separation for estimation of the two drugs. A calibration curve was obtained for metformin hydrochloride by plotting absorbances from the second derivative spectra at 236 nm against the concentration, over a range of 05 to 35 µg/mL in seven mix standards. The slope, intercept and correlation coefficient for this curve were calculated to be 0.0005, -0.0012 and 0.990702, respectively. Similarly, a calibration curve for rosiglitazone maleate was obtained by plotting the absorbance at its sampling wavelength 316 nm against the concentration range of 15 to 105 µg/mL in seven mixed standards. The slope, intercept and correlation coefficient for this curve were calculated to be 0.0087, 0.0332 and 0.997836, respectively. Results of this method were validated statistically and by recovery studies. The results of tablet analysis in terms of percentage of label claim ± standard deviation were 103.54 ± 0.2272 for metformin hydrochloride and 97.6564 ± 2.42413 for rosiglitazone maleate. The percentage recovery ± standard deviation for metformin hydrochloride was 102.53184 ± 2.7839175 and for rosiglitazone maleate was 107.91954 ± 5.3940276.

Key Words: Metformin hydrochloride, Rosiglitazone maleate, Ultraviolet spectrophotometry.

INTRODUCTION

Metformin hydrochloride, chemically 1,1-dimethyl biguanide hydrochloride is a oral hypoglycemic agent and is official in Indian Pharmacopoeia[1] and British Pharmacopoeia[2]. The two pharmacopoeias suggest a non-aqueous method for estimation of metformin hydrochloride from

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tablet formulation. Several gas chromatographic[3] and HPLC methods[4-6] have been reported for the estimation of metformin hydrochloride from body fluids. Rosiglitazone maleate, chemically (±)-5-[[4-[2-(methyl-2-pyridinylamino)-ethoxy]phenyl]methyl]-2,4-thiazolidinedione, (Z)-2-butenedioate (1:1)[7,8] is a peroxime proliferator-activated receptor agonist. Rosiglitazone, a member of the thiazolidinedione class of antidiabetic agents, improves glycemic control by improving insulin sensitivity while reducing circulating insulin levels. It is not official in IP, BP and USP. Several HPLC methods[9,10] have been reported for estimation of rosiglitazone maleate from pharmaceutical formulations. Both these drugs are available in combined dosage form as an antidiabetic. The extensive literature survey revealed that a number of methods are reported for individual drugs[9] and one method for simultaneous estimation of both drugs in combined dosage form[11]. Here the attempt has been made to develop simple, sensitive and rapid spectrophotometric method for estimation of metformin hydrochloride and rosiglitazone maleate simultaneously from its tablet dosage form. The method can be used successfully for quality control testing of the two drugs from combined tablet dosage form.

EXPERIMENTAL

Standard bulk drug samples of metformin hydrochloride and rosiglitazone maleate were provided by USV pharmaceuticals, Chiplun. Marketed tablets of combined dosage form were procured from local pharmacy namely Result R (Sun Pharmaceuticals), Rosicon MF (Glenmark) and Enselin 2M (Torrent).

A PC based Jasco V-530 recording spectrophotometer with spectral bandwidth of 2 nm and wavelength accuracy ± 0.5 nm (with automatic wavelength correction) was employed for all measurements using a matched pair of 10 mm quartz cell. Shimadzu AY 120 analytical balance was used for weighing.

Stock solutions of both drugs, metformin hydrochloride and rosiglitazone maleate were prepared in methanol and water (2:8) by dissolving 100 mg of drug in two different 100 mL volumetric flasks to get concentrations of 1000 µg/mL. Working standard solutions containing 20 µg/mL of metformin hydrochloride and rosiglitazone maleate were prepared separately by appropriate dilutions. Working standard solutions were scanned in the range of 200-400 nm to determine wavelength of maximum absorption. The wavelengths of maximum absorption were found to be 232 and 316 nm for metformin hydrochloride and rosiglitazone maleate, respectively.

Second order derivative spectra of the two drugs revealed that metformin hydrochloride and rosiglitazone maleate showed zero absorbance at 243 and 236 nm, respectively. As at the zero crossing point on the second order

derivative spectrum of rosiglitazone maleate, metformin hydrochloride is having substantial absorbance. This wavelength was used for the estimation of metformin hydrochloride whereas rosiglitazone maleate was estimated directly from its absorbance at 316 nm.

For each drug appropriate aliquots were pipetted out from standard stock solution in to the series of seven 10 mL volumetric flasks. Calibration curve of metformin hydrochloride was plotted at 236 nm by recording the absorbance of second derivative spectra of seven mixed standard solutions having concentrations of 5, 10, 15, 20, 25, 30 and 35 µg/mL of metformin hydrochloride and 2, 4, 6, 8, 10, 12 and 14 µg/mL of rosiglitazone maleate. Calibration curve for metformin hydrochloride was constructed by taking absorbances from the second derivative spectra at 236 nm. Calibration curve of rosiglitazone maleate was plotted by preparing seven mixed standard solutions having concentrations of 0, 15, 30, 45, 60, 75, 90 and 105 µg/mL of metformin hydrochloride and 35, 30, 25, 20, 15, 10, 5 and 0 µg/mL of rosiglitazone maleate. Calibration curve for rosiglitazone was constructed by taking absorbance directly at 316 nm from spectra of mixed standard against its concentration. By using the quantitative mode of instrument intercept and slope values were obtained. The slope values for metformin hydrochloride and rosiglitazone maleate were 0.0005 and 0.0087 respectively. -0.0012 and 0.0332 were the intercept values of metformin hydrochloride and rosiglitazone maleate, respectively. The co-relation coefficients for metformin hydrochloride and rosiglitazone maleate were 0.990702 and 0.997836, respectively. The concentration of these two drugs were calculated by using the following equations,

$$Abs_{Met} = A + B \times C_{Met} \quad (1)$$

$$Abs_{Ros} = A + B \times C_{Ros} \quad (2)$$

where C_{Met} = concentration of metformin hydrochloride, C_{Ros} = concentration of rosiglitazone maleate, Abs_{Met} = absorbance of metformin hydrochloride at 236 nm and Abs_{Ros} = absorbance of rosiglitazone maleate at 316 nm. By applying the slope and intercept values so obtained, the concentration of metformin hydrochloride and rosiglitazone maleate was found out using formula $Abs_{Met} = -0.0012 + 0.0005\ C_{Met}$ and $Abs_{Ros} = 0.0332 + 0.0087\ C_{Ros}$.

Analysis of marketed tablet formulations of two manufacturers containing 500 mg of metformin hydrochloride and 2 mg of rosiglitazone maleate were procured from a local pharmacy and analyzed using this method. From the triturate of 20 tablets, an amount equivalent to 500 mg of metformin hydrochloride and 2 mg of rosiglitazone maleate was weighed. To this 4 mg of pure rosiglitazone maleate was added. Standard addition of rosiglitazone maleate was done to improve the accuracy and precision of the method. It was then dissolved in methanol:water (2:8) and filtered

through Whatmann filter paper no. 41 to get a stock solution containing 50000 µg/mL of metformin hydrochloride and 600 µg/mL of rosiglitazone maleate. After appropriate dilutions the absorbances were measured and the concentration of each analyte was determined with the equations generated in the method. The statistical data of the results obtained after replicated determinations (n = 6).

To study the recovery of metformin hydrochloride and rosiglitazone maleate different quantities of pure drugs were added to preanalyzed formulation samples within the analytical concentration range of the proposed method. The statistical data of the results obtained from recovery studies after replicated determinations (n = 5).

RESULTS AND DISCUSSION

The proposed method was validated by preliminary analysis of authentic laboratory, samples, marketed formulations and recovery studies. The statistical data obtained form analysis of the authentic laboratory and the marketed formulations is given in Table-1. The standard deviation values in the range of 2.783 to 5.394 indicate that the method is reproducible. The recoveries obtained for each drug (Table-2) do not differ significantly from 100 % and there was no interference from common excipients used in the formulation indicating accuracy and reliability of the method.

TABLE-1
RESULT OF ANALYSIS OF TABLET FORMULATION

Drug	% Label claim estimated* ± SD	Coefficient of variance
Metformin hydrochloride	103.5400 ± 0.2272	0. 2194
Rosiglitazone maleate	97.6564 ± 2.4241	2.4823

*Average of seven determinations; SD stands for standard deviation.

TABLE-2
RESULTS OF RECOVERY STUDIES

Drug	% Label claim estimated* ± SD	Coefficient of variance
Metformin hydrochloride	102.53 ± 2.783	2.71
Rosiglitazone maleate	107.91 ± 5.394	4.99

*Average of seven determinations; SD stands for standard deviation.

The proposed method for derivative spectrophotometric estimation of metformin hydrochloride and rosiglitazone maleate was found to be simple, economical, accurate, rapid and reproducible for routine estimation of drugs in tablet formulations.

ACKNOWLEDGEMENTS

The authors are thankful to USV pharmaceuticals, Chiplun and Pune for supplying gift samples of metformin hydrochloride. The authors acknowledges Dr. H. N. More, Principal, Bharti Vidyapeeth College of Pharmacy, Kolhapur, for providing the necessary facilities to carry out this work.

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(*Received*: 22 September 2006; *Accepted*: 5 September 2007) AJC-5812