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Visible Spectrophotometric Methods For The Determination Of Rizatriptan In Pure Form And In Pharmaceutical Formulations

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ABSTRACT

Three simple spectrophotometric methods (A, B and C) are described for the determination of rizatriptan (RZT) in pure form and in pharmaceutical formulations. Method A is based on the oxidative coupling reaction between RZT with 2, 6- dichloroquinone - 4 -chlorimide (DCQC) and the color developed was measured at 610 nm. Method B is based on the replacement of sulfonate group of 1, 2 - napthoquinone - 4- sulphonic acid (NQS) by an imino group of indole moiety of RZT producing a colored product which absorbs maximally at 480 nm. Method C is based on the oxidative coupling reaction between RZT and brucine in presence of sodium metaperiodate and the color developed was measured at 530 nm. The optimum experimental parameters for the color production are selected. Beer's law is valid with in a concentration range of 5.0 - 25.0 μg/ml for method A, 15-75 μg/ml for method B and 8 -40 μg/ml for method C. The results obtained are reproducible and are statistically validated and found to be suitable for the assay of RZT in pharmaceutical formulations.

KEYWORDS

Rizatriptan;
Spectrophotometry;
DCQC;
NQS;
Brucine;
Determination.

INTRODUCTION

Rizatriptan[1-3] (RZT) is a antimigraine/ antiheadache drug and is chemically known as N, N-dimethyl-5(1H-1,2,4-triazol-1-ylmethyl)-1H-indole-3-ethanamine monobenzoate (Figure 1). It is not official in any of the pharmacopoeia. It acts by binding with the 5-$HT_{1B/1D}$ receptors on the extra cerebral, intracranial blood vessels that become dilated during a migraine attack and on nerve terminals in

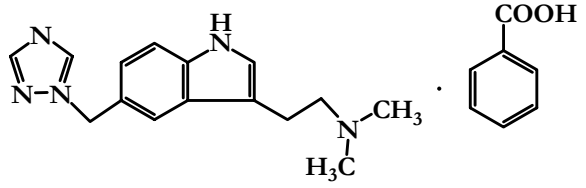

Figure 1: Structure of riaztriptan benzoate

the trigeminal system.

Literature survey reveals that, few chromatographic methods[4-9] have been reported for the estimation of RZT in biological fluids included high performance liquid chromatography (HPLC) with tandem-mass spectrometry, electrospray liquid chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry (LC-MS/MS), NMR and liquid chromatography-atmospheric pressure chemical ionization mass spectrometry. To the best of our knowledge, there is no work in the literature reported about the visible spectrophotometric methods for the analysis of RZT in either biological fluids or pharmaceutical formulations. Hence the author has made an attempt to develop simple and sensitive spectrophotometric methods for the estimation of RZT in pure drug and in pharmaceutical formulations. Method A is based on the oxidative coupling reaction between RZT with 2,6-dichloroquinone-4-chlorimide (DCQC) and the color developed was measured at 530 nm. Method B is based on the replacement of sulfonate group of 1,2-napthoquinone-4-sulphonic acid (NQS) by an imino group of indole moiety of RZT producing a colored product which absorbs maximally at 480 nm. Method C is based on the oxidative coupling reaction between RZT and brucine in presence of sodium metaperiodate and the color developed was measured at 530 nm.

EXPERIMENTAL

Apparatus

All spectral and absorbance measurements were made on a systronic model 106 digital spectrophotometer with 10mm matched quartz cells.

Reagents and standards

All chemicals used were of analytical reagent grade. Double distilled water was used throughout. RZT was obtained from Cipla Ltd, Mumbai. Rizact is the commercial tablet formulation labeled to contain 5/10 mg of RZT per tablet respectively.

DCQC (0.04%) solution was prepared by dissolving 40 mg of DCQC in 100 ml of isopropanol. pH 9.4 buffer solution was prepared by mixing 250 ml of 0.2 M boric acid with 160 ml 0f 0.2 N NaOH solution and diluted to 1000 ml with distilled water and pH was adjusted to 9.4. NQS (0.5%) solution was prepared by dissolving 500 mg of NQS in 100 ml of distilled water. pH 8.0 buffer solution was prepared by mixing 30 ml of potassium hydrogen phosphate (0.067 M) and 770 ml of disodium hydrogen phosphate (0.067 M) and the pH of the solution was adjusted to 8.0. Brucine (0.2%) solution was prepared by first dissolving 200 mg of brucine in few drops of sulphuric acid (H_2SO_4) and diluted to 100 ml with distilled water. 2.3 M H_2SO_4 was prepared by diluting 126 ml of H_2SO_4 to 1000 ml with distilled water. 0.2% sodium metaperiodate ($NaIO_4$) was prepared by dissolving 200 mg of $NaIO_4$ in 100ml of distilled water.

Stock standard solution (1000μg/ml) was freshly prepared by dissolving 100mg of RZT in 100ml of distilled water and then this solution was further diluted with distilled water so as to obtain a working standard solution of 100, 300, 400 μg/ml for method A,B and C respectively.

General procedure and calibration

Method A (using DCQC)

In to 10 ml measuring flasks, different aliquots of working standard solution (0.5-2.5 ml) were transferred to provide final concentration range 5.0 -25.0 μg/ml. To each flask, 5 ml of buffer solution (pH 9.4) and 1.5 ml of DCQC were successively added and kept a side for 15 min. The solutions were made up to volume with distilled water. The absorbance of each solution was measured at 610 nm against the reagent blank. The calibration graph was then prepared by plotting the absorbance versus concentration of the drug. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

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Method B (using NQS)

In to 10 ml measuring flasks, different aliquots of working standard solution (0.5-2.5 ml) were transferred to provide final concentration range 15.0-75.0 μg/ml. To each flask, 1.5ml of NQS and 5 ml of buffer solution (pH 8.0) were successively added and kept a side for 30 min. The solutions were made up to volume with distilled water. The absorbance of each solution was measured at 480 nm against the reagent blank. The calibration graph was then prepared by plotting the absorbance versus concentration of the drug. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

Method C (using Brucine)

In to 25 ml measuring flasks, different aliquots of working standard solution (0.5-2.5 ml) were transferred to provide final concentration range 8.0-40.0 μg/ml. To each flask, 3 ml of brucine, 1.5 ml of $NaIO_4$ and 2.0 ml of 2.3 M sulphuric acid were successively added and heated on a boiling water bath for 15 min. The solutions were cooled and made up to volume with distilled water. The absorbance of each solution was measured at 530 nm against the reagent blank. The calibration graph was then prepared by plotting the absorbance versus concentration of the drug. The concentration of the unknown was read from the calibration graph or computed from the regression equation.

Determination procedure for RZT in pharmaceutical formulations

Thirty tablets were weighed accurately and ground in to a fine powder. An amount of powder equivalent to 100 mg of RZT was weighed into a 100ml volumetric flask, 50 ml of the distilled water was added and shaken thoroughly for about 10 min, then the volume was made up to the mark with the distilled water, mixed well and filtered using a quantitative filter paper. The assay of the tablets was completed according to the general procedures.

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law lim-

TABLE 1: Optical and regression characteristics, precision and accuracy of the proposed methods for RZT

Parameter	Method A	Method B	Method C
λ_{max} (nm)	610	480	530
Beer's law limits (μg ml^{-1})	5.0 – 25.0	15.0 - 75.0	8.0 - 40.0
Detection limits (μg ml^{-1})	0.134	0.412	0.220
Molar absorptivity (L $mole^{-1}$ cm^{-1})	1.34 x 10^4	4.3 x 10^3	8.1 x 10^3
Sandell's sensitivity (μg cm^{-2} / 0.001 absorbance unit)	0.029	0.09063	0.048
Optimum photometric range(μg ml^{-1})	6.0 - 23.0	16.0 - 73.0	9.0 - 38.0
Regression equation (Y = a + bC)			
Slope (b)	3.4 x 10^{-2}	1.1 x 10^{-2}	2.0 x 10^{-2}
Standard deviation of slope (S_b)	0.09 x 10^{-3}	0.03 x 10^{-3}	0.06 x 10^{-3}
Intercept (a)	1.8 x 10^{-3}	0.50 x 10^{-3}	0.70 x 10^{-3}
Standard deviation of intercept (S_a)	1.53 x 10^{-3}	1.52 x 10^{-3}	1.52 x 10^{-3}
Standard error of estimation (S_e)	1.46 x 10^{-3}	1.45 x 10^{-3}	1.45 x 10^{-3}
Correlation coefficient (r)	0.9999	0.9999	0.9999
Relative standard deviation (%) [a]	0.163	0.193	0.159
% Range of error(Confidence limits)[a]			
0.05 level	0.137	0.162	0.133
0.01 level	0.203	0.240	0.197
% Error in bulk samples[b]	-0.018	0.038	-0.094

[a] Average of eight determinations, [b] Average of three determinations. In Y =a + bC, Y is absorbance and C is concentration

its, Sandell's sensitivity, molar absorptivity, percent relative standard deviation (calculated from eight replicate samples containing 3/4th of the amount of the upper beer's law limits) were calculated for all the methods and the results are summarized in TABLE 1. Regression characteristics like standard deviation of slope (S_b), standard deviation of intercept (S_a), standard error of estimation (S_e), % range of error (0.05 and 0.01 confidence limits) and detection limit were calculated for all the methods and are shown in TABLE 1.

Commercial formulations of RZT were successfully analyzed by the proposed methods and the values obtained are presented in TABLE 2. As an additional demonstration of accuracy, recovery experiments were performed at two levels by adding 5 mg and 10 mg of pure drug to the pre-analyzed formulations. The percentage recovery values (average ± S.D. of five determinations) are 99.99±0.3, 100.01±0.05 and 99.98±0.2 for the first level; 100.01±0.08, 100.03±0.5 and 99.99±0.4 for the second level for tablets-1; and 100.01±0.06, 100.0±0.7 and 100.01±0.9 for the first level; and 100.03±0.4, 99.99±0.8 and 100.02±0.8 for the second level for tablets-2 for methods A, B and C respectively. Interference studies revealed that the common excipients and other additives usually present in dosage form did not interfere in the proposed methods.

TABLE 2: Results of analysis of tablet formulations containing RZT

Formulation	Labeled amount	%Recovery*		
		Method A	Method B	Method C
Tablets-1	5	100.01	100.03	99.99
Tablets-2	10	100.00	100.01	100.01

*** Recovery amount was the average of six determinations**

CONCLUSIONS

The proposed methods are simple, accurate and offer advantages of reagent availability and stability, less time consumption and high sensitivity. Hence these methods can be useful for routine quality control analysis of RZT in pure as well as in pharmaceutical formulations.

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