Research Article

Estimation of Rizatriptan Benzoate Tablet by Using UV Spectophotometric Methods

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ABSTRACT

Rizatriptan benzoate is a selective 5-Hydroxy Triptamine1B/1D (5-HT 1B/1D) receptor agonist, used as an antimigraine[1] agent. Two simple, precise, accurate and economical UV spectrophotometric methods[3] have been developed and validated for the routine estimation of Rizatriptan benzoate (RB) in bulk drug and pharmaceutical preparations. The drug showed maximum absorption at 280nm and obeyed Beer-Lambert's law in the concentration range of 0.5-80 µg/ml at 280nm. From the same spectrum AUC was measured. In AUC method the drug showed linearity in the concentration range of 0.5-80µg/ml. The linear regression equations were calculated to be y=0.0141x+0.016 (R^2=0.999) for D_0 at 280nm, y=0.140x+0.020 (R^2=0.999) for AUC. The results of estimation of marketed tablet formulations were found to be 101.06±0.230-100.77±0.520 with their %RSD less than 2. Recovery studies were carried out by addition of known amount of standard drug (80, 100 and 120% of labeled claim of a tablet) to the preanalyzed tablet solution. The % recovery was found to be 103.423±0.921-101.02±0.952, which indicates accuracy and reliability of the validated method as well as non-interference from excipients to the developed method. The intraday and inter day assay was within 2%. The methods were then validated statistically as per the ICH guidelines.

Keywords: Rizatriptan benzoate, λ_{max}, UV visible spectrophotometer, area under curve (AUC).

INTRODUCTION

Migraine is a mysterious disorder characterize by pulsating headache, usually restricted to one side, which comes in attacks lasting 4-48 hours and is often associated with nausea, vomiting, sensitivity to light and sound, flashes of light, vertigo, loose motion and other symptoms[1]. It was formerly believed that migraine headache was simply caused by vasodilatation that caused the release of chemicals from nerve fibers that coil around the large arteries of the brain. While these blood vessels do indeed enlarge, advanced imaging studies of blood flow in the brain have shown that changes in blood flow cannot be solely responsible for all features of migraine. Instead, complex processes within the nervous system are believed to initiate the development of migraine headache[2]. RB chemically 3-[2-(dimethylamino) ethyl] - 5-(1H-1, 2, 4-triazol-1-ylmethyl) indole monobenzoate][3-5] which is used in acute treatment of migraine headache. The mechanism action of Rizatriptan benzoate is through activation of post synaptic 5-HT 1B receptors within cerebral and dural vessel walls causing vasoconstriction of perivascular nerveterminals[6]. Rizatriptan is not official in any pharmacopoeia. Analysis part is an important aspect of formulation development of any drug molecule. A suitable and validated method should be available for the analysis of drug in the bulk, in drug delivery systems, for release dissolution studies and estimation of drug in biological samples.

The literature survey reveals that various methods for the determination of Rizatriptan benzoate are reported. Among these methods liquid chromatography for the determination of rizatriptan in human plasma[7] Mass spectrometry and NMR methods used for the identification of metabolites excreted in urine, and use for the pharmacokinetic study[8]. However no suitable AUC method is reported till date for the estimation of Rizatriptan benzoate. In the present study simple, accurate and precise spectrophotometric methods have been developed for the estimation of Rizatriptan benzoate in bulk as well as in pharmaceutical formulations.

MATERIALS AND METHODS

Reagents and solutions

Pharmaceutical grade of Rizatriptan benzoate was gifted by Alembic Limited, Vadodara, India and certified to contain 99.8% of Rizatriptan benzoate. The NaOH used was of analytical grade produced by NICE laboratory Reagents, India. Spectral and absorbance measurements were made on a Shimadzu-1800 double beam UV-visible spectrophotometer by using 1 cm quartz cells. Denver electronic balance was used for weighing the samples.

Methods

Method-I: UV Spectrophotometry method[3]

Standard stock solution of Rizatriptan benzoate was prepared in 0.1N NaOH. Working standard solutions of Rizatriptan benzoate was prepared by taking suitable aliquots of standard drug solution (1000 µg/ml) and volume was made up to 10 ml with 0.1N NaOH. The resulting solutions were then scanned in the UV range (200-400nm) in a 10 mm matched quartz cells in a UV-Visible double beam spectrophotometer. The drug showed maximum absorption at 280nm (Fig 2). In D_0, drug shows linearity in the range of 0.5-80 µg/ml at

280nm respectively. The linear regression equation were calculated to be y=0.0141x+0.016(R^2=0.999) at 280nm (Fig 4).

Method-II[3]

The AUC (area under curve) method is applicable where there is no sharp peak or when broad spectra are obtained. It involves the calculation of integrated value of absorbance with respect to the wavelength between the two selected wavelengths λ_1 and λ_2. Area calculation processing item calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which area has to be calculated. This wavelength range is selected on the basis of repeated observation so as to get the linearity between area under curve and concentration. The spectra obtained in method I was used to calculated AUC (Fig 2). The calibration curve was constructed by plotting concentration (0.1-80μgml^{-1}) versus AUC (Fig4).
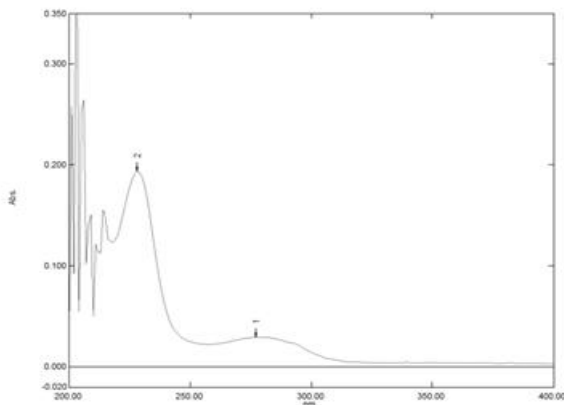

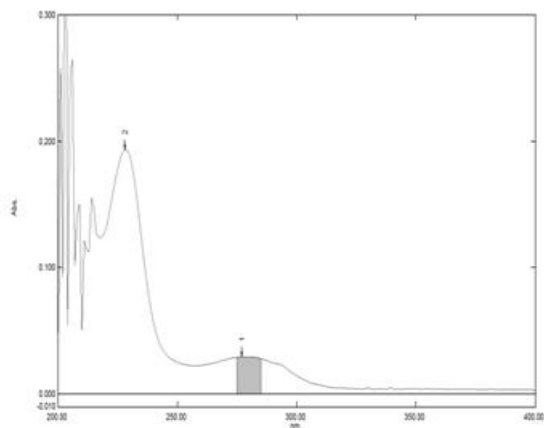**Figure 1:** Spectra of Rizatriptan in 0.1N NaOH (Method-I)

Figure 2: Spectra of Rizatriptan in 0.1N NaOH (Method-II)

Estimation of Rizatriptan Benzoate in commercial formulations

Three tablets were weighed accurately and reduced to fine powder. Drug equivalent to 10mg of Rizatriptan benzoate and 5-7ml of 0.1N NaOH were taken in a 10ml volumetric flask, sonicated for about 30min and the volume was made up to 10ml with 0.1N NaOH and filtered by using Whatman filter paper. From the filtrate an appropriate aliquot was taken in such a way that the

final concentration in 10ml lies within the range tested and scanned in the UV range (200-400nm).
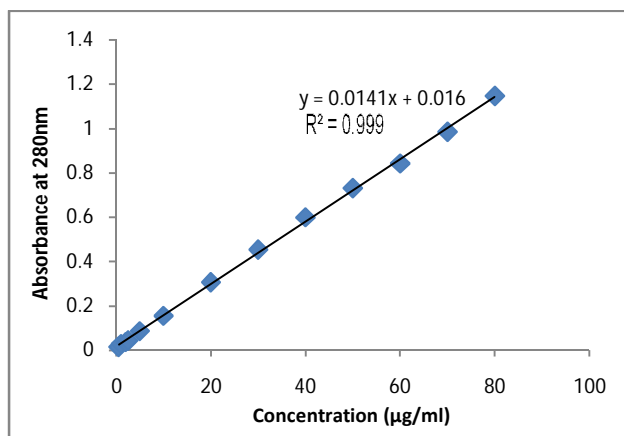
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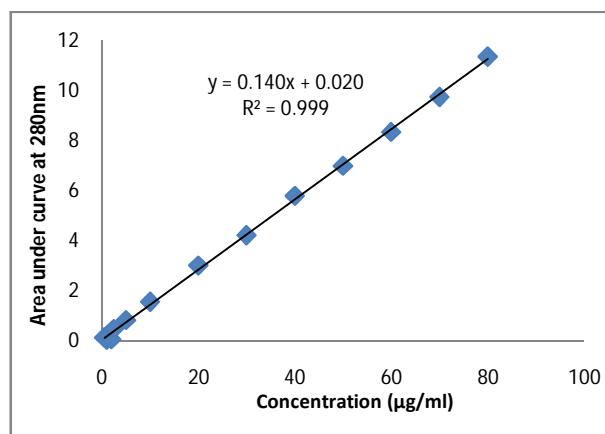

Figure 3: Linearity graph at 280nm (Method-I)

Figure 4: Linearity graph (Method-II)

Method Validation

Precision

The precision of the proposed method was ascertained by actual determination of eight replicates of fixed concentration of the drug within the Beer's range and finding out the absorbance by the proposed method. From these absorbances, mean, standard deviations, %RSD was calculated.

Intraday

The assay procedure is carried out in the same day in the duration of 2 hours to 3 hours at fixed concentration and the results are compared.

Interday

The assay procedure is carried out for 3days with freshly prepared solution from stock solution at fixed concentration at 24hour interval. The readings were shown in the table 4.

Table 1: Concentration Vs Absorbance

Concentration (µg/ml)	Absorbance (Method-I)				AUC (Method-II)			
	A	B	C	Mean	A	B	C	mean
0.5	0.011	0.012	0.012	0.0116	0.11	0.11	0.11	0.11
1	0.029	0.029	0.029	0.029	0.286	0.288	0.287	0.287
2	0.038	0.037	0.038	0.0376	0.375	0.377	0.376	0.376
2.5	0.046	0.046	0.045	0.0456	0.455	0.455	0.455	0.455
5	0.088	0.087	0.087	0.0873	0.809	0.808	0.810	0.809
10	0.155	0.156	0.156	0.156	1.542	1.542	1.542	1.542
20	0.308	0.308	0.308	0.308	3.0	3.001	3.0	3.0
30	0.455	0.455	0.456	0.455	4.216	4.215	4.217	4.216
40	0.601	0.601	0.601	0.601	5.80	5.80	5.80	5.8
50	0.732	0.733	0.734	0.733	7.00	7.00	7.00	7.0
60	0.844	0.845	0.844	0.844	8.368	8.367	8.367	8.367
70	0.985	0.987	0.989	0.987	9.772	9.771	9.773	9.772
80	1.148	1.149	1.150	1.149	11.389	11.387	11.390	11.389

Table 2: Recovery from the formulation

Formulation	Method	Label claim	Observed amount* ± S.D	% Recovery of pure drug	% R.S.D
RITZA Tablet (By NATCO Pharma Ltd)	I	5mg	10.106 ± 0.230	101.06	0.227
	II	5mg	10.077 ± 0.520	103.04	0.64

Table 3: Optical characteristics for Rizatriptan benzoate

Parameters	Obtained Values	
	Do	AUC
λ_{max}	280	280
Beer's Law limit (µg/ml)	0.5-80	0.5-80
Sandell's sensitivity (µg/cm²/0.001 AU)	0.0590	0.0061
Molar extinction Coefficient (L.mole^{-1}.cm^{-1})	7.03×10^3	6.2421×10^4
Regression equation(Y)*	0.0141X+0.016	0.0140X+0.020
Correlation co-efficient	0.999	0.999
Slope	0.0141	0.140

Y*= aX+b, where 'a' is slope, 'b' is intercept, 'X' is concentration in µg/ml and 'y' is absorbance unit.

Table 4: Method validation

Methods	Mean			SD			%RSD		
	Precision	Intraday	Interday	Precision	Intraday	Interday	Precision	Intraday	Interday
D_0 (at 280nm)	0.307	0.312	0.309	0.004	0.001	0.002	1.302	0.320	0.647
AUC	3.07	3.12	3.09	0.043	0.014	0.025	1.40	0.44	0.80

Table 5: Percentage recovery of pure drug

Sample ID	Pure drug conc (µg/ml) A	Formulation (µg/ml) B	% Recovery of pure drug		Statistical analysis (Mean, S.D, %RSD)	
			D_0	AUC	D_0	AUC
80%	16	20	103.72	103.72	103.423	103.04
80%	16	20	104.16	103.18	0.921	0.662
80%	16	20	102.39	102.40	0.8905	0.64
100%	20	20	102.12	102.13	102.36	102.36
100%	20	20	102.48	102.48	0.207	0.202
100%	20	20	102.48	102.48	0.202	0.19
120%	24	20	100.47	100.47	101.02	101.35
120%	24	20	102.12	102.13	0.952	0.835
120%	24	20	100.47	101.46	0.942	0.82

Accuracy:

To determine the accuracy of the proposed method, recovery studies were carried out by adding different amounts (80%, 100% & 120%) of bulk samples of Rizatriptan Benzoate within the linearity range were taken and added to the preanalyzed formulation of concentration 20µg/ml from that percentage recovery values were calculated. The results were shown in the table 5.

RESULTS AND DISCUSSION

The proposed methods are simple, rapid and precise and do not suffer from any interference due to excipients of tablets. Various optical characteristics are given above. The proposed spectrophotometric methods were found to be linear in the range of 0.5-80µg/ml at 280nm in D_o. In AUC methods the drug showed linearity in the concentration range from 0.5-80µg/ml with correlation coefficients (R^2) for D_0, AUC were found to be 0.999, 0.999 respectively. The regression equations are shown in the graphs. The methods were validated in terms of precision, intraday, interday and accuracy and the results are recorded in tables 3 and 4 respectively. The accuracy of the method was determined by performing recovery studies by standard addition of method in which pre-analyzed samples were taken and standard drug was added at three different levels. Values of recovery ±SD greater than 97.0% indicate that proposed method is accurate for the analysis of the drug. The precision of the proposed method was estimated in terms of inter-day precision and intra-day precision wherein the method was repeated on three different days and repeated for three different time periods in the same day respectively. The results shown %RSD of less than 2% at each level clearly indicate that the proposed method is precise enough for the analysis of the drug. The selectivity of the method was checked by monitoring a standard solution of RB in presence of excipients at the same concentration level as used in tablet using the method described in the procedure for calibration curve in pharmaceutical tablets. Excipients used in the formulation of tablets did not show any effect on the estimation of RB. Hence, the determination of RB in the tablet is considered to be free from interference due to the excipients. Rigorous analysis of the results indicates that the presence of excipients in tablet formulation did not interfere with the final determination of the active component. This reveals that the potential utility of this method for the routine analysis of RB in pharmaceutical preparations.

CONCLUSION

Two new, simple and selective spectrophotometric methods were developed for the analysis of RB in bulk and in pharmaceutical formulation. The D_0 method is useful for tablet formulations where there is no interference of excipients in the absorbance of RB and method AUC can be utilized for formulations containing any interfering excipients. The developed methods were also validated and from the statistical data, it was found that methods were accurate, precise and reproducible and can be successfully applied to the pharmaceutical formulations without interference of excipients.

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Source of Support: Nil, **Conflict of Interest:** None.