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DETERMINATION OF RIZATRIPTAN IN BULK AND ITS TABLET DOSAGE FORMS BY UV SPECTROSCOPIC METHOD.

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ABSTRACT

Rizatriptan is a selective 5-HT1B/1D agonist which is used in the treatment of migraine headaches. Zero order spectroscopic method has been developed for the determination of rizatriptan. Rizatriptan in its 0.1 N HCl solutions was determined at the wavelength ranges of 220–400 nm by the spectroscopic method. Rizatriptan showed an absorption peak at 226 nm. Linearity ranges were found as 1-5 µg/ml. for the zero order UV spectroscopic method. Limit of quantitation was determined as 0.0944 µg/ml whereas limit of detection was calculated as 0.0311 µg/ml for the same measurements, respectively. No interference was found from tablet excipients at the selected wavelengths and assay conditions. Developed method was found to be validated and showed good precision and reproducibility. Proposed method was successfully applied to the assay of rizatriptan in pure and tablet dosage forms and assessed as to be rapid, sensitive, accurate and relatively inexpensive.

INTRODUCTION: Rizatriptan benzoate (**fig. 1**) belongs to a group of medicines known as serotonin (or 5HT) agonists. It is used in the treatment of migraines. Rizatriptan binds to serotonin receptors in the brain, which causes the blood vessels to narrow. By decreasing the width of blood vessels in the brain Rizatriptan relieves the pain [1].

Methods for the determination of rizatriptan in biological materials which have been reported previously 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 [2-8]. Although UV estimation of Rizatriptan benzoate in phosphate buffer and base was reported [9, 10] but estimation of the drug in other solvents has not been reported.

In the present study simple, accurate and precise spectroscopic methods have been developed for the estimation of Rizatriptan benzoate in bulk as well as in pharmaceutical formulations.

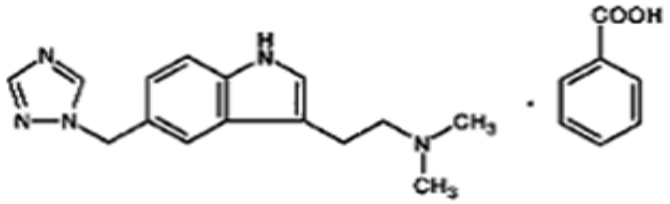

FIG. 1: CHEMICAL STRUCTURE OF RIZATRIPTAN BENZOATE

MATERIALS AND METHOD: A LABINDIA UV 3000$^+$ UV/Vis double beam spectrophotometer with 1 cm matched quartz cells was used for spectral measurement. Schimadzu AX200 analytical balance was used for weighing purposes. The reference standard of Rizatriptan benzoate was procured as a gift sample from Apotex Research Pvt. Ltd. (Bangalore) as a gift sample with 99.9% w/w assay value and

Rizatriptan benzoate tablets (10 mg) were utilized for the study. All chemicals and reagents used were of analytical grade. Rizatriptan benzoate tablets were purchased from market.

Selection of Analytical Wavelength: Appropriate dilutions were prepared for drug from the standard stock solution and the solutions were scanned in the wavelength range of 220-400 nm. The absorption Spectra thus obtained was derivatized for Zero order. This Zero order Spectrum was selected for the analysis of the drugs.

Preparation of Stock Solutions: Standard Rizatriptan 10 mg was weighed and transferred to a 10 ml volumetric flask and dissolved in 0.1 N HCl. The flask was shaken and volume was made up to the mark with 0.1 N HCl to give a solution containing 1000 µg / ml. From this stock solution, pipette out 1 ml and placed into 10 ml volumetric flask. The volume was made up to mark with 0.1 N HCl to give a solution containing 100 µg / ml.

Selection of Analytical Concentration Ranges: From the standard stock solution of Rizatriptan benzoate, appropriate aliquots were pipetted out in to 10 ml volumetric flasks and dilutions were made with 0.1 N HCl to obtain working standard solutions of concentrations from 1 - 5 µg / ml. Absorbance for these solutions were measured at 226 nm. For the standard solution analytical concentration range was found to be 1 - 5 µg / ml and those values were reported in **Table 1.**

Calibration curve for the Rizatriptan benzoate (1-5 µg/ml): Appropriate volume of aliquots from standard Rizatriptan benzoate stock solutions were transferred to different volumetric flasks of 10 ml capacity. The volume was adjusted to the mark with 0.1 N HCl to obtain concentrations of 1, 2, 3, 4 and 5µg / ml. Absorbance spectra of each solution against 0.1 N HCl as blank were measured at 226 nm and the graphs of Zero order overlain Spectra in **Fig. 2.** The Regression equation and Correlation coefficient (r^2) were determined and presented in **Table 2.**

Sample preparation for determination of Rizatriptan benzoate from dosage form: Twenty formulation (Tablet I) were weighed and finely powdered. The powder equivalent to 10 mg of Rizatriptan benzoate was accurately weighed and transferred to volumetric flask of 10 ml capacity containing 7 ml of the 0.1 N HCl and sonicated for 30 min. The flask was shaken and volume was made up to the mark with 0.1 N HCl to give a solution of 1000 µg / ml. The above solution was filtered through Whatmann filter paper (No. 41). From this solution, 1 ml was taken and diluted to 10 ml with 0.1 N HCl to give a solution of 100 µg / ml and used for the estimation of Rizatriptan benzoate.

Validation of Zero order Spectroscopic method [10, 11]:

Linearity and Range: The linearity of analytical method is its ability to elicit test results that are directly proportional to the concentration of analyte in sample within a given range and was given in **Fig. 3.** The range of analytical method is the interval between the upper and lower levels of analyte that have been demonstrated to be determined within a suitable level of Precision, Accuracy and Linearity. The optical characteristics were summarized in **Table 2.**

Accuracy: Accuracy is the closeness of the test results obtained by the method to the true value. To study the Accuracy, twenty tablets of each formulation were weighed and powdered and analysis of the same was carried out. Recovery studies were carried out by adding known amount of standard addition method (50, 100 and 150%) to the sample solution. % Recovery was calculated and reported in **Table 3.**

Precision: The Precision of an analytical method is the degree of agreement among individual test results, when the method is applied repeatedly to multiple samplings of homogenous samples. It provides an indication of random error results and was expressed as % relative standard deviation (% RSD).

Intra and inter-day precision: Variations of results within the same day (intra-day), variation of results between days (inter-day) were analyzed. Intra-day precision was determined by analyzing Rizatriptan benzoate for six times in the same day at 226 nm. Inter-day precision was determined by analyzing daily once for six days at 226 nm and % RSD was calculated and shown in **Table 4.**

Ruggedness: The solutions were prepared and analyzed with change in the analytical conditions like

different laboratory conditions and different analyst and reported in **Table 5.**

RESULTS AND DISCUSSION:

Linearity and range: Rizatriptan benzoate exhibits its maximum absorption at 226 nm and obeyed Beer's law in the range of 1-5 µg/ml. Linear regression of absorbance Vs concentration yielded equation y=0.122x+0.0117 with a correlation coefficient of 0.996. The results are summarized in **Table 1.**

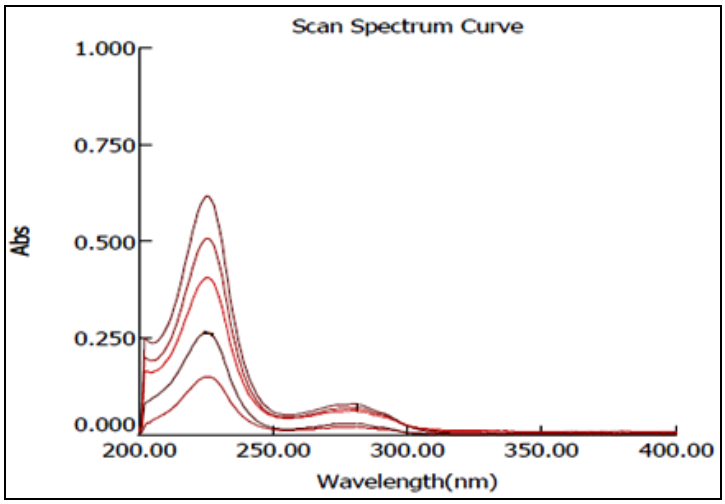

FIG. 2: ZERO ORDER SPECTRA OF RIZATRIPTAN BENZOATE AT 226nm

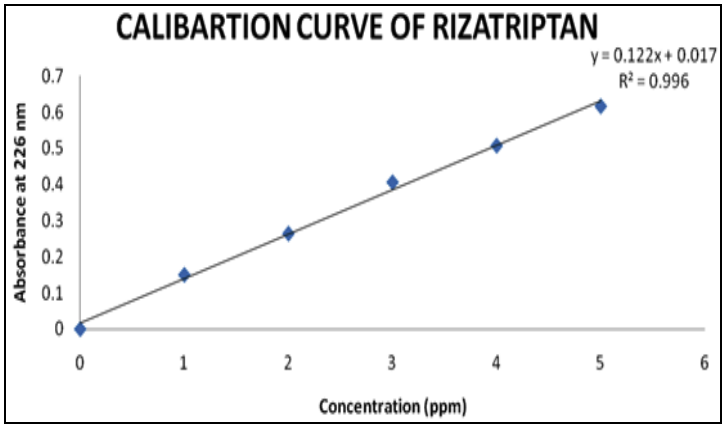

FIG. 3: LINEARITY CURVE FOR RIZATRIPTAN BENZOATE AT 226nm BY ZERO ORDER SPECTROSCOPIC METHOD

TABLE 1: RESULTS OF CALIBRATION CURVE AT 226nm FOR RIZATRIPTAN BENZOATE BY ZERO ORDER SPECTROSCOPIC METHOD

Sl. No.	Concentration (µg/ml)	Absorbance at 226 nm
1	1	0.150
2	2	0.264
3	3	0.406
4	4	0.507
5	5	0.616

TABLE 2: OPTIMUM CONDITIONS, OPTICAL CHARACTERISTICS AND STATISTICAL DATA OF THE REGRESSION EQUATION IN ZERO ORDER SPECTROSCOPIC METHOD

Parameters	UV Method
λ_{max} (nm)	226
Beer's law limits (µg / ml)	1 – 5
Molar extinction coefficient ($Lmol^{-1} cm^{-1}$)	5.0750×10^4
Sandell's sensitivity (µg/cm^2-0.001 absorbance units)	0.07389
Regression equation (Y*)	Y = 0.122 X + 0.077
Slope (b)	0.122
Intercept (a)	0.077
Correlation coefficient (r^2)	0.996
LOD (µg/ml)	0.0311
LOQ (µg/ml)	0.0944

*Y= m X + c where X is the concentration of Rizatriptan benzoate in µg/ml and Y is the Absorbance at the respective $\lambda_{max.}$

Accuracy: In order to ascertain the suitability and reproducibility of the proposed method, recovery studies were carried out by adding known quantities of standard Rizatriptan benzoate (50,100,150%) to the tablet and the mixtures were analyzed by the proposed method. The percentage recovery of Rizatriptan benzoate was found to be 99.004-100.5 % (**Table 3**) indicating that there is no interference by the excipients in the method.

TABLE 3: DETERMINATION OF ACCURACY RESULTS FOR RIZATRIPTAN BENZOATE BY ZERO ORDER SPECTROSCOPIC METHOD

Level of Recovery Amount of sample (µg/ml)	Amount of drug added (µg/ml)	Amount Recovered (µg/ml)	% Recovery ± SD**
50%	5	4.8	98.9±0.17
100%	10	10	100.5±0.15
150%	15	14.85	99.004±0.18

**Average of six determinations

Precision: Intra-day precision was evaluated by analyzing six test samples of Rizatriptan benzoate. The intermediate precision (inter-day precision) of the method was determined by evaluating the samples of Rizatriptan benzoate on different days. The relative standard deviation (RSD) values are 0.4470 and 0.132 respectively (**Table 4**).

TABLE 4: DETERMINATION OF PRECISION RESULTS FOR RIZATRIPTAN BENZOATE AT 226nm BY ZERO ORDER SPECTROSCOPIC METHOD

Sr. No.	Concentration (µg/ml)	Intra-day	Inter-day
1	3	0.419	0.413
2	3	0.420	0.413
3	3	0.420	0.412
4	3	0.418	0.412
5	3	0.415	0.412
6	3	o.419	0.413
Avg.		0.4185	0.412
SD*		0.001871	0.0005
%RSD*		0.4470	0.132

***** is average of 6 determinations

Ruggedness: In the ruggedness study, % recovery of Rizatriptan benzoate in bulk drugs samples was found to be 100.05 by analyst-1 and 99.8 by analyst-2 respectively (**Table 5**).

TABLE 5: RUGGEDNESS RESULTS FOR RIZATRIPTAN BENZOATE AT 226nm BY ZERO ORDER SPECTROSCOPIC METHOD

Sample	Label claim (mg)	Analyst I		Analyst II	
		Amount found (mg)	% Recovery ± SD**	Amount found (mg)	% Recovery ± SD**
Tablet I	10	10.05	100.05 ± 0.001	9.98	99.80 ± 0.011

** Average of six determinations

CONCLUSION: A zero-order UV spectroscopic method was developed for the determination of Rizatriptan benzoate. The developed method was found to be simple, sensitive, accurate, precise, reproducible and can be used for routine quality control analysis of Rizatriptan benzoate in bulk and tablet formulation.

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