Research Article

NEW DERIVATIVE SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF RIZATRIPTAN BENZOATE IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

Two simple, rapid and sensitive first derivative spectrophotometric methods were developed for the determination of Rizatriptan Benzoate in pharmaceutical formulations in water and hydrochloric acid. Beer's law was obeyed in a concentration range of 1-35 µg/ml in water and 0.5-30 µg/ml in hydrochloric acid with correlation coefficient of r^2 = 0.998 in both the methods. The linear regression equations are found to be y = 0.01x + 0.003 and y = 0.009x + 0.003 in water and hydrochloric acid respectively. The % RSD for intra-day and inter-day precision studies were found to be 0.0477 and 0.0543 in water and 0.4786 and 0.7288 in hydrochloric acid respectively which is less than 2.0 indicating that the methods are precise. The % RSD in accuracy studies was also found to be less than 2.0. The proposed methods are suitable for the determination of Rizatriptan Benzoate in pharmaceutical formulations. No interferences were observed from the excipients in the formulations. The methods were validated according to ICH guidelines.

Keywords: Rizatriptan benzoate, Derivative spectrophotometry, Validation.

INTRODUCTION

Rizatriptan benzoate[1] (RZB), dimethyl ({2-[5-(1H-1, 2, 4-triazol-1-ylmethyl)-1H-indol-3-yl] ethyl}) amine is a selective agonist of serotonin (5-hydroxytryptamine; 5-HT) type 1B and 1D receptors. It has a molecular weight of 269.4 with chemical formula $C_{15}H_{19}N_5$. Rizatriptan is indicated to relieve acute migraine headaches (with or without aura). Rizatriptan is not recommended for treatment of basilar artery migraine or hemiplegic migraine. The mechanism of Rizatriptan Benzoate (Fig. 1) is not been established clearly. It is thought that agonist activity at the 5-hydroxytryptamine (5-HT) $_{1B}$ and 5-HT $_{1D}$ receptor subtypes provides relief of headaches[2]. Rizatriptan is a highly selective agonist at these receptor subtypes; it has no significant activity at 5-HT $_2$ or 5-HT $_3$ receptor subtypes or at adrenergic, dopaminergic, histamine, muscarinic, or benzodiazepine receptors. It has been proposed that constriction of cerebral vessels resulting from 5-HT $_{1B/1D}$ receptor stimulation reduces the pulsation that may be responsible for the pain of migraine headaches. It has also been proposed that Rizatriptan may relieve migraine3 headaches by decreasing the release of pro-inflammatory neuropeptides. Literature survey reveals that various methods for the determination of Rizatriptan Benzoate have been developed which include HPLC methods[4-12] for evaluation of pharmaceutical formulations, LC[13], LC-MS[14], LC-MS/MS[15] methods for biological fluids and spectrophotometric[16-17] methods. Joseph Sunder Raj et al isolated, identified and characterized the process related impurities in Rizatriptan[18].

In the present study, two novel simple, rapid and cost-effective derivative spectrophotometric methods were developed for the routine analysis of RZB in pharmaceutical formulations in water (Method A) and hydrochloric acid (Method B) and they are validated as per the ICH guide lines[19].

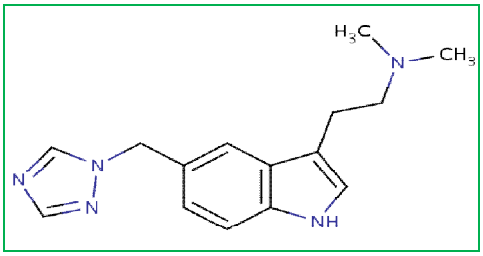

Figure 1: Chemical structure of Rizatriptan Benzoate (RZB)

MATERIALS AND METHODS

Instrumentation

A double beam UV-VIS spectrophotometer (UV-1800, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe was employed with spectral bandwidth of 1nm and wavelength accuracy of ±0.3 nm with a pair of 10 mm matched quartz cells. All weights were taken on electronic balance (Denver, Germany). For scanning, the wavelength range selected was from 400 nm to 200 nm with medium scanning speed. All experiments were performed at room temperature (25 ± 1)°C.

Reagents and chemicals

Analytical grade reagents were used. Rizatriptan Benzoate was supplied as gift sample from Optimus Pharma Pvt. Ltd., India (purity 99.8%). Rizatriptan Benzoate (RZB) stock was prepared daily by dissolving 25 mg of the drug in 25 ml of methanol in a volumetric flask (1000 µg/ml) and working standard solutions were obtained by proper dilution of this stock solution with water and hydrochloric acid solution for method A and B respectively.

Rizatriptan Benzoate is available commercially as tablets and orally disintegrating tablets with brand names MAXALT® and MAXALT-MLT® (containing 5 mg and 10 mg of the drug content) respectively and twenty tablets from each brand were procured from the local market.

Preparation of stock solution and calibration curve

2.5 ml of Rizatriptan Benzoate (RZB) stock solution was transferred into two 25 ml volumetric flask and diluted with water and 0.1N HCl separately to get the working standard solution (100 µg/ml) and from this a series of standard solutions (0.1-100 µg/ml) were prepared in water and 0.1N HCl at room temperature (25ºC).

The above solutions were scanned 200-400 nm against their reagent blank and the absorption spectra were recorded for both methods A and B. The absorption spectra were transformed in to first derivative spectrums and the corresponding values were recorded.

Assay of commercial formulations

For the determination of RZB in pharmaceutical formulations, twenty tablets were weighed, finely powdered and powder equivalent to about 25 mg of Rizatriptan Benzoate was accurately weighed and transferred into a 25 ml volumetric flask. Methanol was added and sonicated for 30 min and made up to volume with methanol. The resulting mixture was filtered and suitable dilutions were made with water and 0.1N HCl for method A and B separately and analyzed according to the recommended procedure.

Precision and Accuracy

The precision study was done by recording the response of six replicates in Method A (10µg/ml) and Method B (10µg/ml) and the % RSD was calculated. Accuracy was evaluated by the percent recovery studies by the addition of 80%, 100%, and 120% of pure sample solution to the pre-analysed formulation solution. For the present study 10 µg/ml of RZB solution extracted from the formulation was taken and 80%, 100%, and 120% of pure sample solution (i.e. 8, 10 and 12 µg/ml) and the % RSD was calculated.

RESULTS AND DISCUSSION

In Method A the derivative spectrum (Fig. 2) shows maxima (216.64 nm) and minima (233.78 nm) in water and therefore the amplitude was chosen for the analytical determinations.

In Method B the derivative spectrum (Fig. 3) shows maxima (216.8 nm) and minima (234.06 nm) in hydrochloric acid and therefore the amplitude was chosen for the analytical study. A graph was drawn by taking the concentration on the x-axis and the corresponding derivative absorbance on the y-axis for both method A and B.

Beer-Lambert's law was obeyed over the concentration range of 1-35 µg/ml (Fig. 4) and 0.5-30 µg/ml (Fig. 5) for methods A and B respectively. The linear regression equations for method A and B were found to be y = 0.01x + 0.003 (r^2 = 0.998) and y = 0.009x + 0.003 (r^2 = 0.998) respectively.

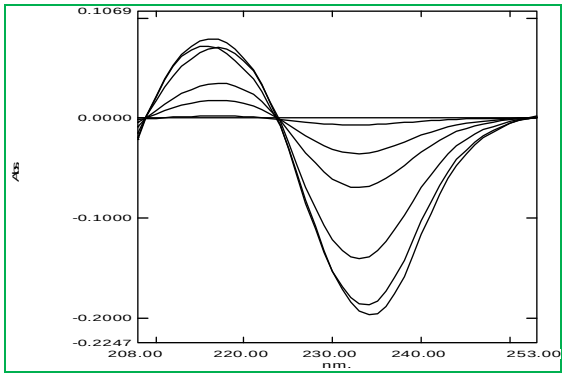

Figure 2: First order derivative overlay spectrum of Rizatriptan Benzoate in water (1-35 µg/ml)

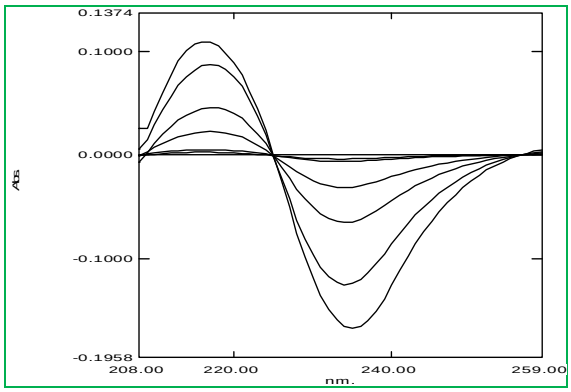

Figure 3: First order derivative overlay spectrum of Rizatriptan Benzoate in Hydrochloric acid (0.5-30 µg/ml)

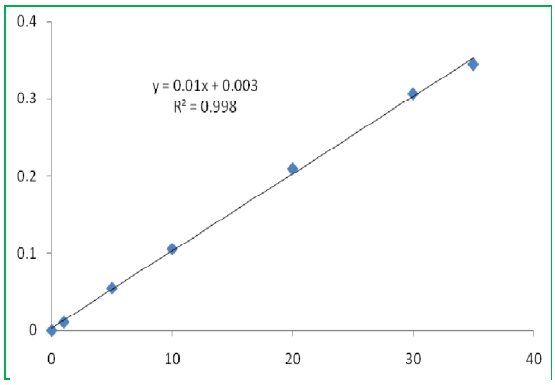

Figure 4: Linearity of Rizatriptan Benzoate in water (1.0-35µg/ml)

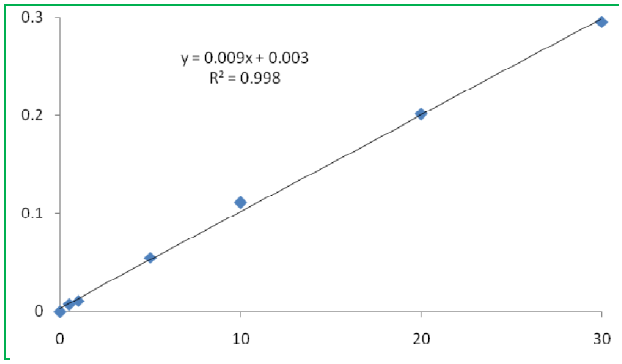

Figure 5: Linearity of Rizatriptan Benzoate in Hydrochloric acid (0.5-30µg/ml)

The % RSD values in precision studies were found to be less than 2% in both methods A and B indicating that the method is more precise. The % RSD values in accuracy studies were also found to less than 2% in both methods A and B indicating that the method is more accurate (table 1).

The % assay was found to be 99.81-99.92 and 99.61-99.83 for methods A and B respectively. Results of recovery studies are represented in table 2.

Table 1: Optical characteristics of Rizatriptan Benzoate

Parameters	Method A	Method B
λ (nm) (Amplitude)	216.64- 233.78	216.80-234.06
Beer-Lambert's range (µg/ml)	1-35	0.5-30
Slope	0.01	0.009
Intercept	0.003	0.003
Correlation coefficient	0.998	0.998
Precision (RSD, %)		
Intra-day (n=3)	0.0477	0.4786
Inter-day (n=3)	0.0543	0.7288
Accuracy (% recovery)	99.81-99.92	99.61-99.83

Table 2: Analysis of Rizatriptan Benzoate commercial formulation (tablets)

Formulation	Labeled claim (mg)	*Amount found (mg)		*Recovery (%)	
		Method A	Method B	Method A	Method B
Brand I	10	9.981	9.961	99.81	99.61
Brand II	10	9.992	9.983	99.92	99.83

*Mean of three replicates

CONCLUSION

The proposed methods result a simple, sensitive, inexpensive, precise and accurate analytical techniques to determine Rizatriptan Benzoate (RZB) in commercial pharmaceutical formulations successfully.

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