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UV-SPECTROSCOPIC METHODS FOR ESTIMATION OF RIZATRIPTAN BENZOATE IN PHARMACEUTICAL PREPARATIONS

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ABSTRACT: Rizatriptan benzoate is a triptan drug and it is a selective 5-Hydroxy Triptamine1B/1D (5-HT 1B/1D) receptor agonist, used as an antimigraine agent. Three simple, precise, accurate and economical UV spectrophotometric methods have been developed and validated for the routine estimation of rizatriptan benzoate in bulk drug and pharmaceutical preparations. The drug shows maximum absorption at 227nm and 281nm and obeyed Beer-Lambert's law in the concentration range of 0.5-20µg/ml at 227nm and 0.5-80 µg/ml at 281nm respectively. The same spectrum was derivatised into first order and second order derivative, the amplitude of the trough at 233nm for D_1 and amplitude of crest at 238nm for D_2 were measured. In D_1 and D_2 method the drug showed linearity in the concentration range of 0.5-20µg/ml. The linear regression equations were calculated to be y=0.1182x+0.003(R^2=0.9997) for D_0 at 227nm, y=0.0135x+0.0094(R^2=0.9991) for D_0 at 281nm, y= -0.0467x-0.0005(R^2=0.9998) for D_1 and Y=0.0238x +0.0031 (R^2=0.9993) for D_2. The results of estimation of marketed tablet formulations were found to be 97.51±0.0381-101.58±0.223 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 preanalysed tablet solution. The % recovery was found to be 97.104±0.094-100.035±0.193, 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 which yielded good results concerning range, precision, accuracy, specificity, robustness and ruggedness.
Keywords: Rizatriptanbenzoate, Spectrophotometry, Validation.

INTRODUCTION

Rizatriptan benzoate is chemically described as 3-[2-(dimethylamino) ethyl] - 5-(1H-1, 2, 4-triazol-1-ylmethyl) indole monobenzoate [1]. It is a selective serotonin 5-HT1B/1D receptor agonist which is used in the acute treatment of migraine headaches [2]. The literature survey reveals that various methods for the determination of Rizatriptan benzoate are reported among these methods Liquid chromatography[3], Identification of impurities [4], LC-MS/MS[5-6], HPLC method for Rizatriptan benzoate[7-8], Application and Development of Improved RP-LC-DAD for Rizatriptan and its degradation products[9], Disposition and pharmacokinetics of rizatriptan[10] etc. However no suitable derivative spectrophotometric 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

Apparatus

Absorbance measurements were made on THERMO UV_1 UV/Visible double beam spectrophotometer with

spectral bandwidth 2 nm and 10mm matched quartz cuvettes.

Reagents and solutions

Pharmaceutical grade of Rizatriptan benzoate was gifted by Alembic Limited, Vadodara, India and certified to contain 99.8% of Rizatriptan Benzoate .It was used without further purification. The NaOH used was of analytical grade produced by NICE laboratory Reagents, India.

Preparation of calibration curve

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 shows maximum absorption at 227nm and 281nm (fig-1). The same spectrum was derivatised into first order and second order derivative, the amplitude of the trough at 233nm for D_1 (fig-2) and amplitude of crest at 238nm for D_2 (fig-3) were measured. In Do, drug shows linearity in the range of 0.5-20µg/ml at 227nm and 0.5-80 µg/ml at 281nm respectively. In D_1 and D_2 method the drug showed linearity in the concentration range from 0.5-20µg/ml. The linear regression equation were calculated to be $y=0.1182x+0.003$($R^2=0.999$) for D_0 at 227nm (fig-4), $y=0.0135x+0.0094$($R^2=0.9991$) for D_0 at 281nm (fig-5), $y=-0.0467x0.0005$ ($R^2=0.9998$) for D_1 (fig-6) and $Y=0.0238x+0.0031$($R^2=0.9993$) for D_2 (fig-7)**.**

Analysis of tablet

Twenty 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 Whattmann 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). The same spectrum was derivatised into first order and second order derivative, the amplitude of the trough at 233nm for D_1 and amplitude of crest at 238nm for D_2 were measured. The amount of drug present in the tablet was calculated from the standard graphs. (Table-3)

Method Validation

The developed methods were validated for its accuracy, precision, reproducibility and selectivity. The accuracy of the methods was determined by performing recovery studies on tablet formulation and for prepared solutions containing known amount of drug by standard addition method in which preanalyzed samples were taken and standard drug was added at three different levels (80%.100% and 120%). The results are shown in table 4. Also, the experiments were repeated three times in a day to determine intra-day precision and on three different days to determine inter-day precision. The percent relative standard deviations (%RSD) were calculated at each concentration level and the results are given in table 2 .The reproducibility was confirmed by repeating the methods by three different analysts and the % RSD were calculated. The selectivity of the methods was checked by monitoring a standard solution of Rizatriptan Benzoate 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.

RESULTS AND DISCUSSION

The proposed methods are simple, rapid and precise and do not suffer from any interference due to excipients of tablet. Various optical characteristics are shown in the table 1.The proposed spectrophotometric methods were found to be linear in the range of 0.5-20µg/ml at 227nm and 0.5-80 µg/ml at 281nm respectively in Do. In D_1 and D_2 methods the drug showed linearity in the concentration range from 0.5-20µg/ml with correlation coefficients (R^2) for Do, D_1, D_2 were found to be 0.999, 0.9998, 0.9993 respectively. The regression equations are shown in the table 2. The methods were validated in terms of accuracy, precision, reproducibility and the results are recorded in table 2and 4. The accuracy of the method was determined by performing recovery studies by standard addition of method in which preanalyzed 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 in table 4 indicating %RSD of less than 2% at each level clearly indicate that the proposed method is precise enough for the analysis of the drug. The reproducibility of the methods was confirmed by performing the proposed method by three different analysts. 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. The excipients 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

Three 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 D_1 and D_2 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, reproducible and can be successfully applied to the pharmaceutical formulations without interference of excipients.

Table 1 Optical characteristics for Rizatriptan benzoate

Parameters	Obtained Values			
	Do	**Do**	**D_1**	**D_2**
λ_{max}	227	281	233	238
Beer's Law limit(µg/ml)	0.5-20	0.5-80	0.5-20	0.5-20
Sandell's sensitivity (µg/cm²/0.001 AU)	0.0838	0.0714	-0.0217	0.04
Molar extinction Coefficient(L.mole^{-1}.cm^{-1})	4.6×10^4	5.4×10^3	-1.8×10^4	9.7×10^3
%RSD	1.37	1.81	-1.67	1.20
Regression equation(Y)*	0.1182x+0.003	0.0135x+0.0094	-0.0467x-0.0005	0.0238x+0.0031
%Range of error 0.05 confidence limits 0.01 confidence limits	 ±1.137 ±1.497	 ±0.2076 ±0.2733	 ±0.4899 ±0.6449	 ±0.2126 ±0.2798
Correlation co-efficient	0.999	0.9991	0.9998	0.9993

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

Table 2 Validation Parameters

Sl No.	Parameters		D_0		D_1 (at 233nm)	D_2 (at 238nm)
			At 227nm	**At 281nm**		
1	Linearity	µg/ml	0.5-20	0.5-80	0.5-20	0.5-20
		Regression eq^n	0.1182x+0.003	0.0135x+0.0094	-0.0467x-0.0005	0.0238x+0.0031
		R^2	0.999	0.9991	0.9998	0.9993
2	Precision	Mean	1.193125	0.165125	-0.4225	0.253625
		S.D	0.016418	0.002997	0.007071	0.003068
		%RSD	1.37%	1.81%	-1.67%	1.20%
3	Intraday	Mean	1.197	0.1685	-0.4655	0.25175
		S.D	0.016842	0.003109	0.005508	0.004031
		%RSD	1.40%	1.84%	-1.18%	1.60%
4	Interday	Mean	0.19475	0.16825	-0.467	0.25025
		S.D	0.018081	0.003304	0.005944	0.004573
		%RSD	1.51%	1.96%	-1.27%	1.82%

Table 3 Analysis of tablet formulation

Formulation	Label claim	Observed amount* ± S.D	%Recovery of pure drug	%R.S.D
RITZA Tablet (By NATCO Pharma Ltd)	10mg	9.75183 ± 0.038148253	97.5183	0.391191

*Average of three determinations

Table-4 Accuracy

Sample ID	Pure drug concentration (µg/ml) A	Formulation (µg/ml) B	Total concentration (µg/ml) A+B				%Recovery of pure drug			Statistical analysis (Mean,S.D,%RSD)		
			D_0		D_1	D_2	D_0	D_1	D_2	D_0	D_1	D_2
			At 227nm	At 281nm								
80%	4	5	8.747	8.785	8.768	8.907	97.198	97.43	98.972	97.104	99.333	98.972
80%	4	5	8.73	8.859	9.089	8.781	97.01	100.999	97.572	0.094	1.796	1.4
80%	4	5	8.739	8.785	8.961	9.033	97.104	99.571	100.373	0.096	1.808	1.415
100%	5	5	9.966	9.822	9.946	9.915	99.661	99.464	99.159	99.661	99.536	99.299
100%	5	5	9.949	9.748	10.01	9.831	99.492	100.107	98.319	0.1692	0.538	1.0574
100%	5	5	9.983	9.97	9.903	10.042	99.83	99.036	100.42	0.1697	0.541	1.064
120%	6	5	10.981	11.081	10.91	10.84	99.83	99.182	98.548	100.035	99.766	99.694
120%	6	5	11.006	10.933	10.974	11.008	100.061	99.766	100.076	0.1935	0.5839	1.0106
120%	6	5	11.023	11.155	11.038	11.05	100.215	100.35	100.458	0.1934	0.5853	1.0136

Figure-1: Over lain spectra of Rizatriptan (D_0)

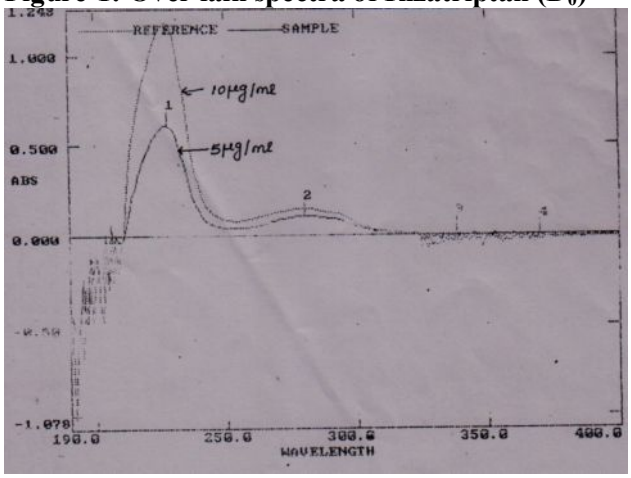


Figure-2: Over lain spectra of Rizatriptan (D_1)

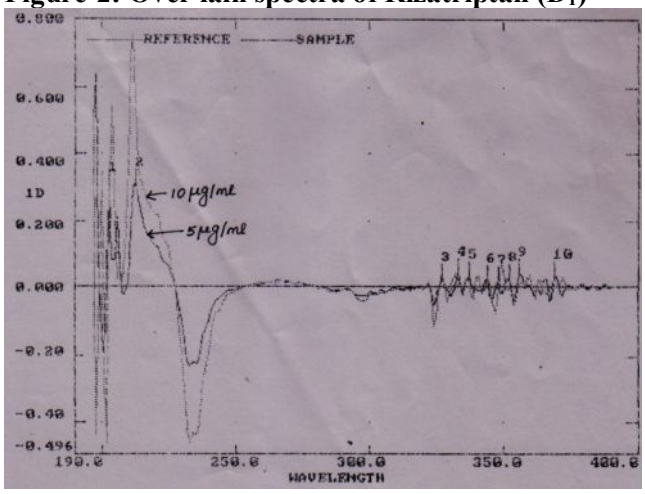


Figure-3: Spectrum of Rizatriptan (D_2)

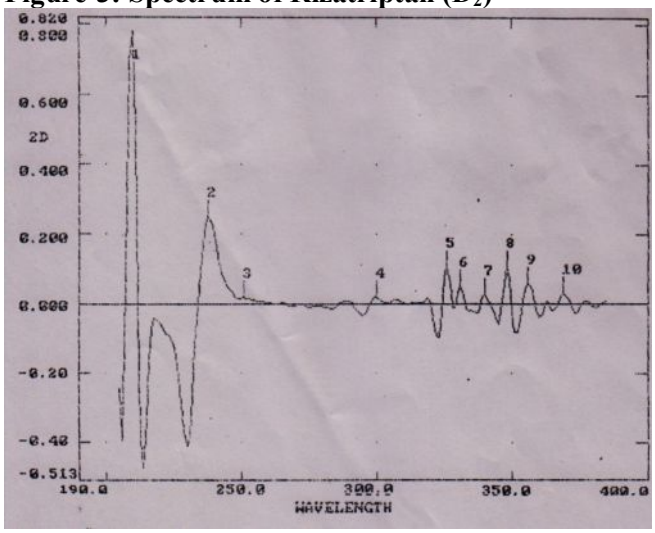


Figure-4: Linearity graph at 227nm (D_O)

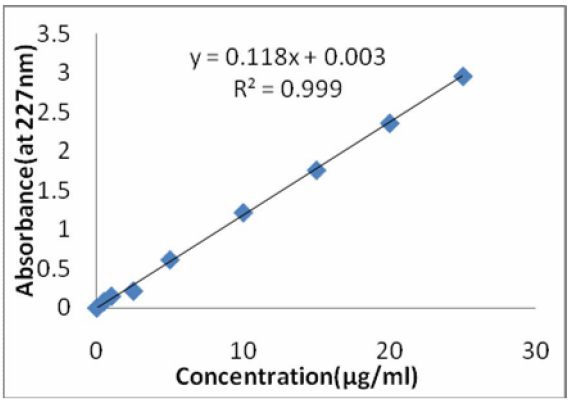


Figure-5: Linearity graph at 281nm (Do)

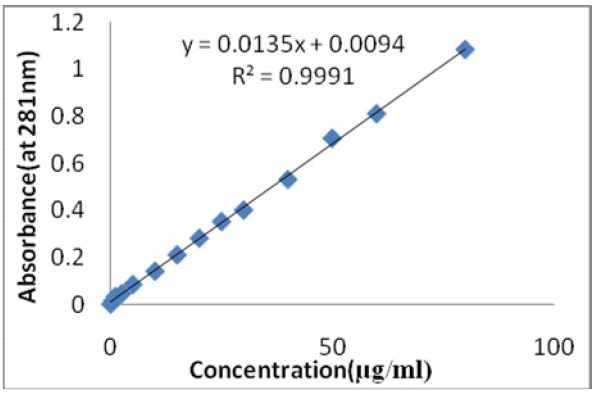


Figure-6: Linearity graph (D_1)

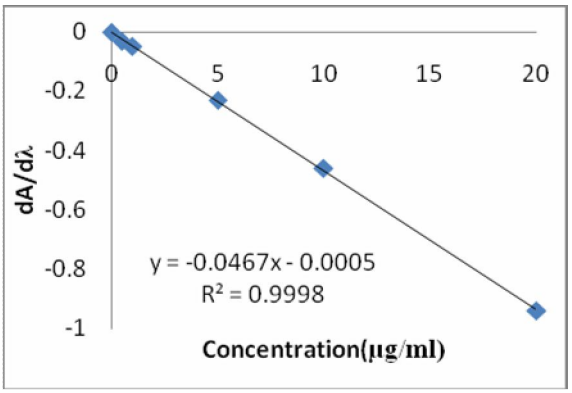
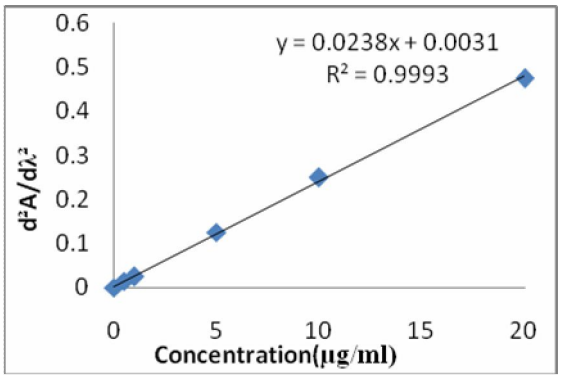


Figure-7: Linearity graph (D_2)



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