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SPECTROPHOTOMETRIC ESTIMATION OF ALMOTRIPTAN MALATE IN BULK AND PHARMACEUTICAL FORMULATIONS BY MULTIVARIATE TECHNIQUE

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ABSTRACT

A sensitive, accurate and economical UV spectrophotometric method with multivariate calibration technique for the determination of almotriptan malate in bulk drug and pharmaceutical formulation has been described. This technique is based on the use of the linear regression equations by using relationship between concentration and absorbance at six different wavelengths. The results were treated statistically and were found highly accurate, precise and reproducible. The method is accurate, precise and linear within the range 2-10µg/ml. There was no interference from the excipients. This statistical approach gives optimum results for the eliminating fluctuations coming from instrumental or experimental conditions.

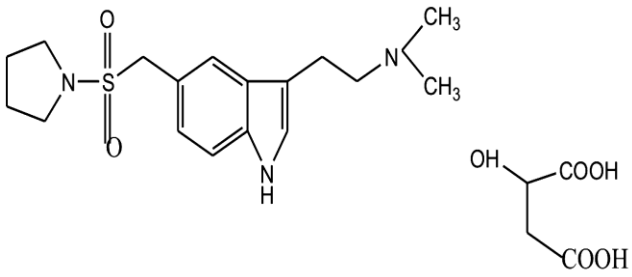
Keywords: UV Spectrophotometry; Multivariate Calibration; Pharmaceutical Formulation.

INTRODUCTION

Almotriptan malate [1] a selective 5-hydroxytryptamine 1B/1D (5HT 1B/1D) receptor agonist. Almotriptan binds with high affinity to 5-HT 1D, 5-HT 1B and 5-Ht 1F receptors. It has weak affinity for 5-Ht 1A and 5-HT 7 receptors, but has no significant affinity or pharmacological activity at 5-Ht 2, 5-HT 3, 5-HT 4, 5-HT 6; alpha or beta adrenergic; adenosine (A1, A2); angiotensin (At 1, AT 2); dopamine (D1, D2); endothelin (ET A, ET B); or tachykinin (NK 1, NK 2, NK 3) binding sites.

Only a few procedures based on liquid chromatography have been reported so far for the quantitative determination of almotriptan in human plasma and urine. Jansat et al.[2] have published a method, using high performance liquid chromatography, for determination of almotriptan levels in plasma. Fleishaker et al [3] have suggested a method, using a validated, sensitive and specific HPLC method for determination of almotriptan concentrations in urine. Earlier a method for the determination of process-related impurities in almotriptan malate API and HPTLC method have been published by Suneetha et al [4,5]. Literature survey reveals that no Spectrophotometric method for determination of almotriptan malate in pharmaceutical dosage forms is reported.

Almotriptan malate



Present study involved development of a simple UV spectrophotometric method for the estimation of almotriptan malate in bulk and tablet dosage forms by using multivariate technique. The proposed method is based on the direct determination of almotriptan malate with a high degree of accuracy and sensitivity. The

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method is easy, least expensive and is applicable to the bulk drug and dosage formulations. This paper describes the application of UV spectral multivariate calibration technique having simple mathematical content for the quantitative determination of almotriptan malate in pharmaceutical formulation. The solubility of almotriptan malate was determined in a variety of solvents, from the solubility studies drug was found to be freely soluble in water. An absorption maximum was found to be 228.8 nm, when the spectrum was scanned for the drug dissolved in water.

EXPERIMENTAL

Materials and Methods

Reference standard of almotriptan malate was procured from SMS Pharmaceuticals Ltd., Hyderabad. The tablet formulation was procured from US market. Spectroscopic analysis was carried out on Elico Double beam UV-Visible spectrophotometer with 1cm matched quartz cells.

Mutivariate Technique

The basis of this method i.e. multivariate spectral calibration contains the use of linear regression functions obtained at six different wavelength set. This approach is based on the reduction of multi-linear regression functions to univariate data set, which provides more sensitive determination than the classical UV method. In case of single wavelength UV spectrophotometry, some errors may occur because of instrumental variations and other sources. Under optimized conditions the applied statistical method provides considerable resolving power, sensitivity, rapidity and low cost for the quantitative analysis, quality control and routine analysis of subject compounds. The mathematical algorithm of this approach is based on following summation of multivariate to univariate data sets. If the absorbance of an analyte (Z) is measured at six wavelengths set (λ = 224, 226 228, 230, 232 and 234 nm), straight line equation can be written as $A_\lambda = a\times(Cz+k)$… (1) Where A_λ represent the absorbance of the analyte, a is the slope and k is the intercept of linear regression function of the analyte. C_Z represents the concentration of analyte. At six selected wavelengths, the equation system can also be summed as; $A_T = a\times (C_Z + b) \times (C_Z +c) \times (C_Z + d) \times (C_Z +e) \times (C_Z +K_T)$. . (2) which can be simplified to $A_T = C_Z (a+b+c+d+e) +K_T$. . .(3) where a, b, c, d, e are the slopes, A_T and K_T represents the sum of absorbance obtained and sum of intercepts of regression equations at six-wavelength set respectively. The concentration of the Z analyte in a mixture can be calculated by using the Equation $C_Z = A_T - K_T / (a+b+c+d+e)$……. (4)

Preparation of standard solution

Standard stock solution of almotriptan malate reference standard (100 µg/ml) in 100 ml calibrated flask was prepared with distilled water. A validation set consisting of solutions in working range of 2-10 µg/ml were freshly prepared and scanned in the UV region. The absorption maxima observed at 228.8 nm was recorded and plotted against concentration, which followed the Beer and Lambert's law and gave a straight line (r=0.9999). In order to improve this correlation and minimize instrumental fluctuations, absorbance of these solutions was measured over a range surrounding 228.8 nm. The six linear regression functions at the wavelengths of 224, 226, 228, 230, 232 and 234 nm for reference standard was calculated using relationships between the absorbance and concentration

Estimation of almotriptan malate in tablets

Twenty almotriptan malate tablets were powdered in a mortar and an amount equivalent to 10 mg of drug was dissolved in 100 ml distilled water to make a solution (100 µg/ml), which was further diluted in the working range of 2-10 µg/ml. This study showed the applicability of multivariate linear regression approach to the UV data obtained at different wavelengths for the better calibration and tablet analysis. Statistically, the use of infinite number of data measured for a sample analysis makes the results closer to the real result. The unknown concentration of almotriptan malate in tablets was determined by the Eqn. 4 using the sum of absorbance obtained at above wavelengths for samples.

Method validation

The method was validated according to International conference on Harmonization complete reference guidelines in order to determine the linearity, sensitivity, accuracy and precision [6-8].

Accuracy of the method was determined by recovery studies. Different concentrations of pure drug (4.8, 5.0, 5.2 µg/ml) were added to a known pre-analysed formulation sample and the total concentration was determined. The percent recovery of the added pure drug was calculated as follows

% Recovery= [(Cv-Cu)/Ca] ×100,

Whereas, Cv, the total drug concentration measured after standard addition, Cu, drug concentration in the formulation and Ca, drug concentration added to the formulation.

Precision of the method was done by performing Inter-day and Intraday analysis over a period of one week. LOD is the lowest concentration of an analyte that an analytical process can reliably detect; LOQ is defined as the lowest concentration of the standard that can be measured. The LOD and LOQ were calculated according to ICH guidelines as LOD=3.3σ/S and LOQ= 10σ/S where σ is the standard deviation of the lowest standard concentration and S is the slope of the standard curve.

RESULTS AND DISCUSSION

The proposed method for the estimation of almotriptan malate in pharmaceutical dosage form was found to be simple, economic, accurate and more precise. The absorption spectrum of almotriptan malate in distilled water was scanned over the range of 190-380 nm, which shows an absorption maximum at 228.8 nm (Fig.1) and obeyed Beer's law in the range of 2-10µg/ml with a correlation coefficient of 0.9999. The calibration curves of almotriptan malate at different wavelengths are shown in Fig-2. The regression characteristic of the proposed method for standard drug is incorporated in Table-1. The amount of almotriptan malate present in the sample solutions were calculated by using multivariate technique. The results are shown in Table- 2 & 3. The method was validated in terms of accuracy and precision. The accuracy of the proposed method was determined by performing recovery studies in sample solution. The % recovery was found to be 99.2-102.0 indicates that the method is accurate. The results are given in Table-4. Precision of the method was checked by intra and inter day studies. The calculated % RSD for precision was found to be less than 2%. The results are presented in Table-5.

Figure 1. The Absorption Spectrum of Almotriptan Malate

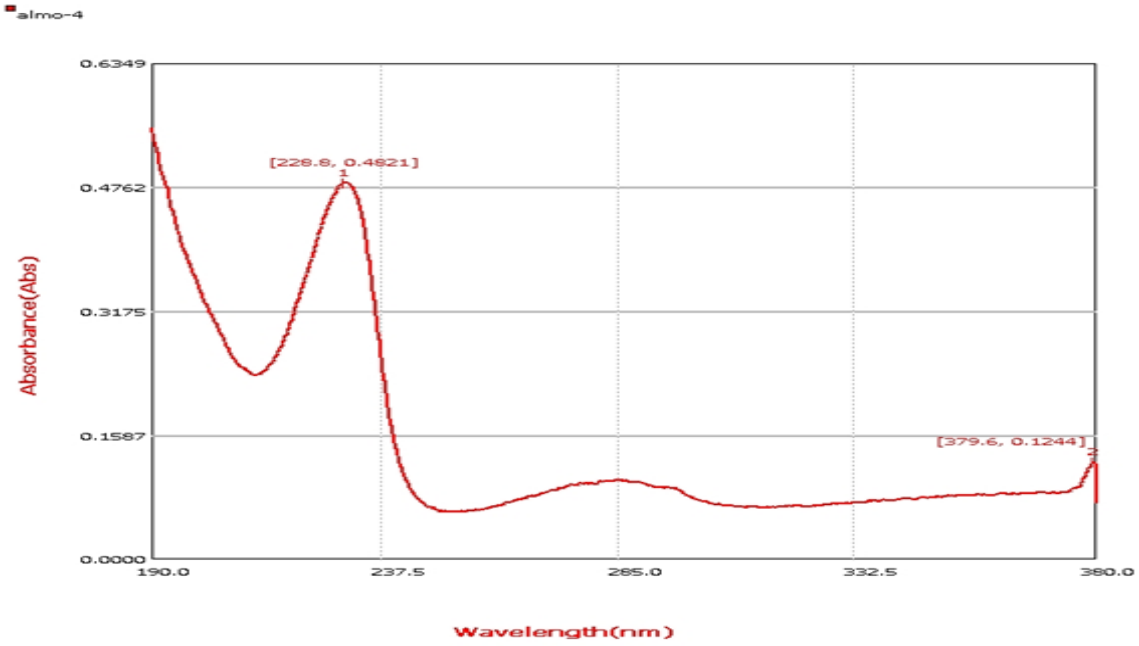
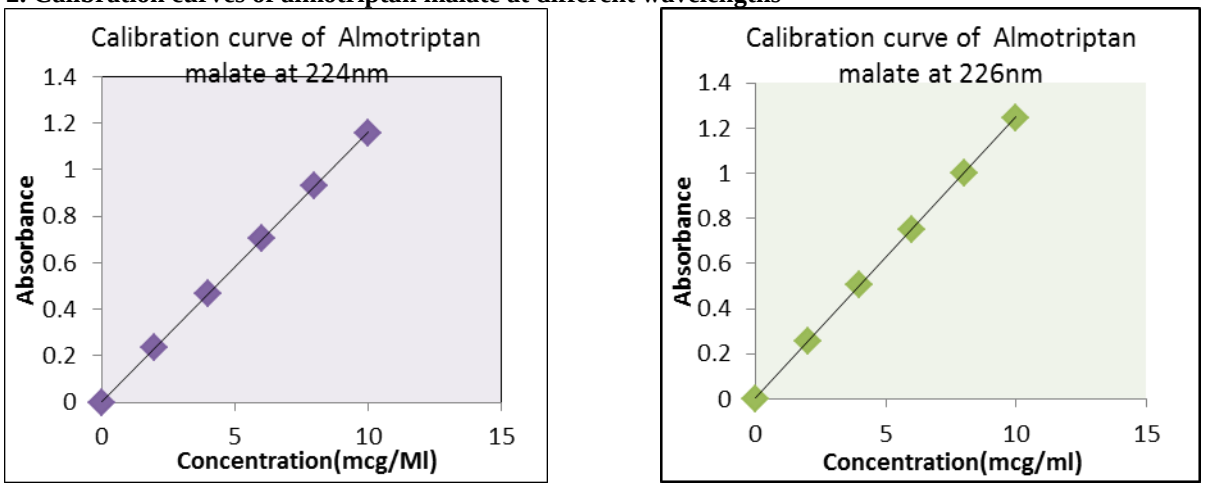
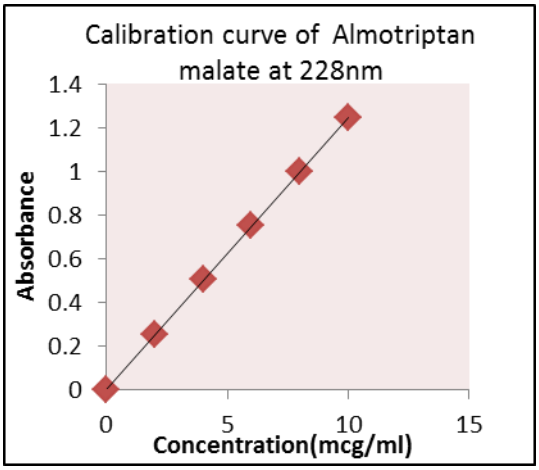
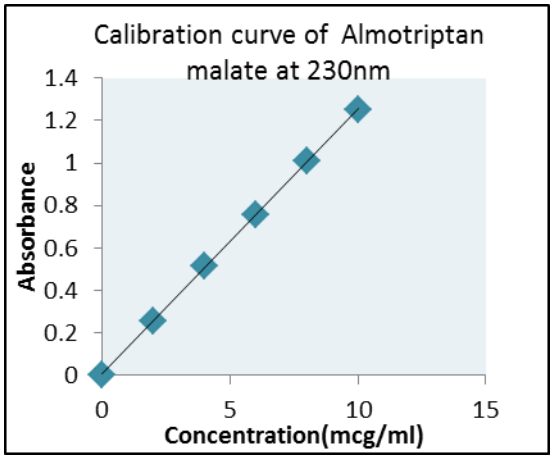
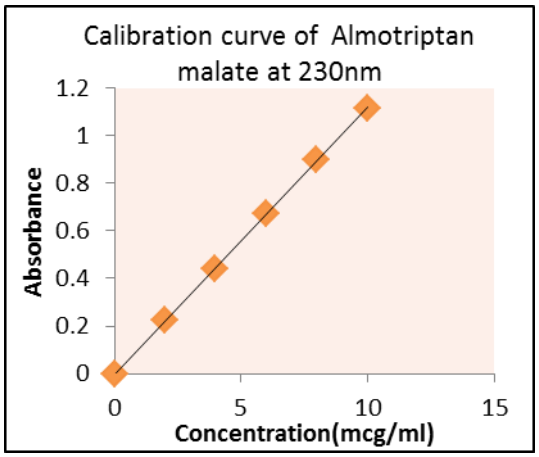


Figure 2. Calibration curves of almotriptan malate at different wavelengths









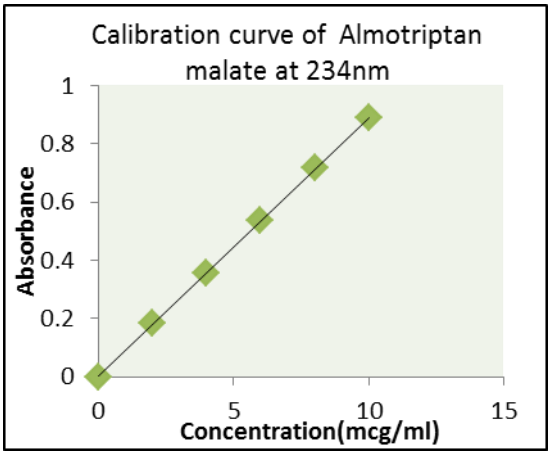


Table 1. Regression Characteristics of Proposed Method

Wavelength (nm)	Regression equation	r	LOD	LOQ	%RSD
224nm	A=0.115734286 X + 0.003528571	0.99994	0.570	1.710	0.73
226nm	A=0.124601429 X + 0.00327619	0.99998	0.529	1.587	0.67
228m	A=0.127087143 X + 0.006180952	0.99999	0.519	1.557	0.83
230nm	A=0.125024286 X + 0.006295238	0.99993	0.527	1.581	0.75
232nm	A=0.111854286 X + 0.000261905	0.99994	0.590	1.770	0.69
234nm	A=0.088778571 X + 0.003090476	0.99995	0.743	2.229	0.83

r is correlation coefficient; LOD is Limit of Detection; LOQ is Limit of Quantitation;
RSD is Relative Standard Deviation

Table 2. Concentration of Almotriptan Malate Found in Sample Solutions

Approximate Concentration (µg/ml)	224nm	226nm	228nm	230nm	232nm	234nm	Multi UV[a]
2	1.89	1.92	2.05	2.09	1.85	1.70	2.02
4	3.85	3.90	4.07	4.19	5.79	5.69	4.05
6	5.83	5.96	6.09	6.12	5.89	5.85	5.98
8	7.90	7.95	8.10	8.13	7.87	7.76	8.09
10	9.85	9.89	10.03	10.12	9.88	9.78	10.02

[a] multivariate UV data, concentration in µg/ml

Table 3. Assay Results of Almotriptan in Tablets

S.NO	Brand name	Label claim	Amount* found in mg	% purity
1	Axert	12.5	12.494	99.95 %

* Means value of six determination

Table 4. Intra and Inter Day Precision of the Developed Method

Drug concentration (µg/ml)	Intra day		Inter day	
	Concentration found	%R.S.D	Concentration found	%R.S.D
4	4.01	0.758	3.99	0.222
6	6.66	0.196	6.82	0.459
8	8.27	0.939	8.03	0.884

***** Average of three determinations

Table 5. Accuracy of the Proposed Method

Concentration of drug in formulation (µg/ml)	Concentration of Pure drug added (µg/ml)	Total concentration of drug found (µg/ml)	%Analytical recovery(± SD)
5	4.8	9.65	98.46±0.041
5	5.0	9.89	98.90±0.035
5	5.2	10.12	99.21±0.050

CONCLUSION

Concept behind this effort was to minimize the uncertain hindrances caused during the observation. In this Paper, statistical analysis with multivariate spectral technique was used. The data obtained for the estimation of almotriptan malate in bulk and drug formulation evidenced the high level accuracy and precision after multivariate calibration. Percent recovery and found concentration of active ingredient in pharmaceutical formulations showed that the amount of drug present is consistent with the label claim. Hence, this method is very useful with very simple mathematical contents, is more reliable than the other spectrophotometric methods and strongly recommends the application in calibration models for a routine analysis.

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