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Validated Spectrophotometric Quantification of Aripiprazole in Pharmaceutical Formulations by Using Multivariate Technique

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ABSTRACT

Purpose: An accurate and precise UV spectrophotometric method with multivariate calibration technique for the determination of aripiprazole in pharmaceutical formulations has been described. ***Methods:*** This technique is based on the use of the linear regression equations by using the relationship between concentration and absorbance at five different wavelengths. The aripiprazole shows absorption maxima at 255 nm and obeyed Beer's law in the range of 5-30 µg/mL. ***Results:*** The results were treated statistically and were found highly accurate, precise and reproducible. This statistical approach gives optimum results for the eliminating fluctuations coming from instrumental or experimental conditions. ***Conclusion:*** It was concluded that the proposed method is simple, easy to apply, economical and could be used as an alternative to the existing spectrophotometric and non-spectrophotometric methods for the routine analysis of aripiprazole in pharmaceutical formulations.

Introduction

Aripiprazole is a sixth and a recent second generation anti-psychotic drug with chemical formula 7-[4-[4-(2, 3-dichlorophenyl) -1-piprazinyl] butoxy] -3,4-dihydro-(1H) -quinolinone belonging to the class of benzisoxazole. It is used in the treatment of Schizophrenia and bipolar disorder associated episodes as like acute, manic and mixed.[1,2] It has the partial agonist effect towards 5-HT1A-receptor, dopamine D_2 receptor and antagonistic effect on 5-HT2- receptor.[3]

A survey of pertinent literature revealed that few analytical methods reported for determination of aripiprazole in pharmaceutical dosage forms and biological samples include HPLC[4-11] and spectrophotometric[12,13] methods. Till date no multivariate spectrophotometric method for the estimation of aripiprazole is reported. Multivariate calibration refers to the process of constructing a mathematical model that relates a property such as content or identity to the absorbance of a set of known reference samples at more than one wavelength.[14] If the absorbance of an analyte (Z) is measured at five wavelengths set, straight line equation can be written as; $A_\lambda = aX(Cz+k)$ where A_λ represent the absorbance of the analyte, A is the slope and k is the intercept of the linear regression function of the analyte. C_Z represents the concentration of analyte. At five selected wavelengths, the equation system can also be summed as; $A_T = aX (C_Z + b) X (C_Z + c) X (C_Z + d) X (C_Z + e) X (C_Z + K_T)$, which can be simplified to $A_T = C_Z (a+b+c+d+e) + K_T$ 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 five-wavelength set respectively. The concentration of the Z analyte in a mixture can be calculated by using the Eqn. $C_Z = A_T - K_T /(a+b+c+d+e)$.[15,16] This paper describes the application of UV spectral multivariate calibration technique having simple mathematical content for the quantitative determination of aripiprazole in pharmaceutical formulation.

Materials and Methods

Chemicals

The aripiprazole (Figure 1) reference standard (assigned purity 99.59%) was kindly supplied by Hetero Drugs Limited (Hyderabad). The commercial pharmaceutical formulations were obtained from local Pharmacies.

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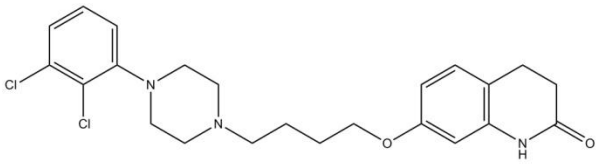

Figure 1. Structure of aripiprazole

Instrumentation

The multivariate technique was performed in 1.0cm quartz cells using T60U UV-Visible spectrophotometer (PG Instruments Ltd., England) with a fixed 2nm spectral bandwidth and UV-Win5 software v5.1.1 was used for all absorbance measurements.

Preparation of Standard Solutions

The standard solution (1000 µg/mL) was prepared by accurately weighed 100 mg of aripiprazole in 100 mL volumetric flask containing 50 mL of ethanol and sonicated for about 5 min, and then the volume was made up to the mark with ethanol. From this 10 mL was pipette out into a 100 mL volumetric flask and volume was made up to the mark with ethanol to get final concentration of 100 µg/mL.

Preparation of sample solution

For analysis of marketing formulations, twenty tablets were weighed accurately and powdered. The powder equivalent to 100mg of the drug weighed accurately and transferred to 100mL volumetric flask containing 50mL of ethanol. The mixture was sonicated to dissolve, make up the volume with ethanol. The above solutions were filtered through Whatmann filter paper and the solution was transferred into volumetric flask, and was made up to the mark with ethanol to obtain a final concentration of 20 µg/mL. All determinations were conducted with six replicates.

Method Validation

The method was validated according to International Conference on Harmonization (ICH) Q2B guidelines[17] for validation of analytical procedure to determine the linearity, limit of detection, limit of quantitation, accuracy and precisions.

Results and Discussion

Aripiprazole was estimated by proposed multivariate UV spectrophotometric method in tablets. It was completely soluble in ethanol and hence ethanol was selected as the solvent for aripiprazole to obtain UV spectrum in the range of 220-400 nm. After the evaluation of the spectrum, aripiprazole presented maximum absorbance at 255 nm (Figure 2).

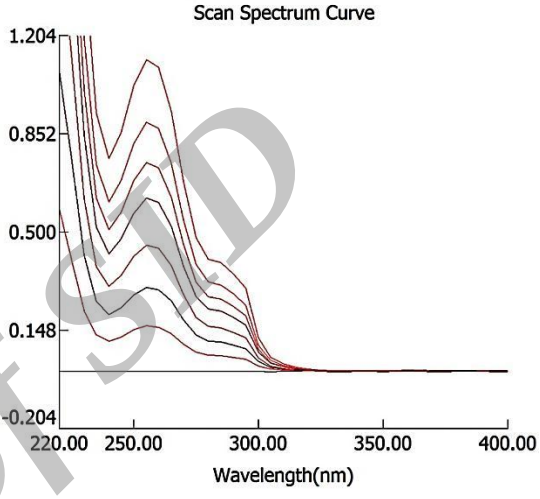

Figure 2. Absorbance spectrum of aripiprazole

A validation sets consisting of six solutions in working range of 5-30 µg/mL were freshly prepared and scanned in the UV region. The absorbance was recorded and plotted calibration curve against concentration, which followed the Beer's law and gave a straight line (Table 1). In order to improve this correlation and minimize instrumental fluctuations, absorbances of these solutions were measured over a range surrounding 255 nm i.e., 251, 253, 257,259 nm. The calibration curves of aripiprazole at different wavelengths is shown in Figure 3.

Table 1. Calibration data of the proposed method

Parameters		Results				
		At 251nm	At 253nm	At 255nm	At 257nm	At 259nm
Beer's law range (µg/mL)		5-30	5-30	5-30	5-30	5-30
Molar extinction coefficient (1/mol/cm)		0.0313	0.0304	0.0299	0.0297	0.0289
Sandell's sensitivity (µg/cm^2)		0.032	0.0329	0.0334	0.0337	0.0347
Limit of detection (µg/mL)		0.29	0.22	0.3	0.23	0.2
Limit of quantitation (µg/mL)		0.87	0.68	0.91	0.69	0.61
Regression equation	Intercept (a)	0.0059	0.0067	0.0071	0.0072	0.0047
	Slope (b)	0.0305	0.0296	0.0292	0.0288	0.0283
	Correlation coefficient (r^2)	0.9993	0.9994	0.9992	0.9996	0.9992

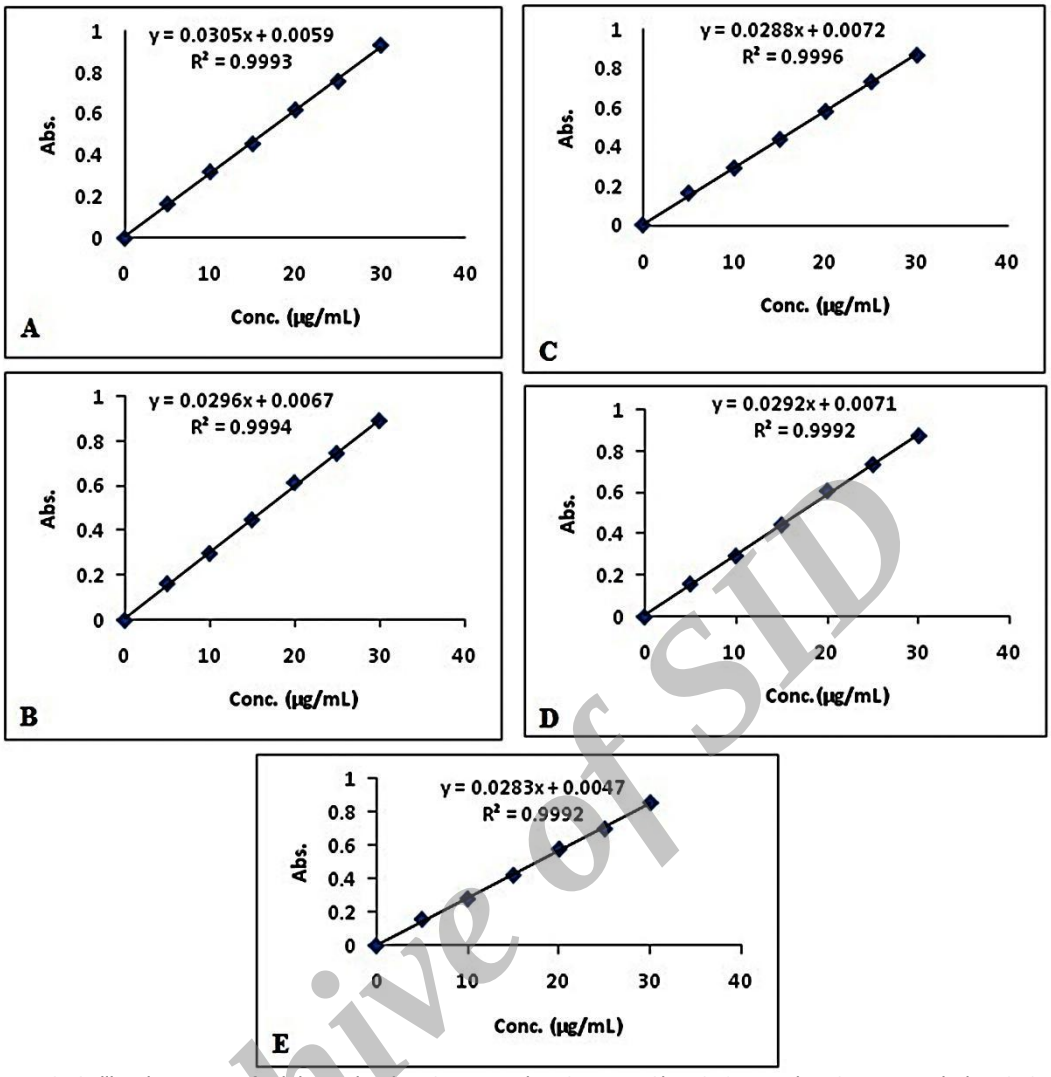

Figure 3. Calibration curve of aripiprazole A) at 255 nm, B) at 257 nm, C) at 259 nm, D) at 251 nm and E) at 253 nm

The accuracy of the method was evaluated through the recovery studies. Recovery studies were carried out by addition of a known quantity of pure drug solution to pre analyzed sample solution at three different concentration levels (50, 100 and 150%). The percentage recovery values were found to be 98.27-102.01 with %RSD of <2% (Table 2), which indicates that the proposed method was accurate.

Table 2. Accuracy of the proposed method (standard addition technique)

Amount (%) of drug added to analyte	Theoretical content (µg/mL)	Conc. found (Mean± SD)*	%RSD	% Recovery range
50	5	5.02±0.8	0.8	99.6-101.2
100	10	10.19±0.2082	0.2	101.7-102.01
150	15	14.76±0.13	0.14	98.27-98.53

Precision was determined as intra-assay and inter-assay, in accordance with ICH guidelines. The intra-day and inter-day precision were determined by analyzing the samples of aripiprazole at a concentration of 10, 20 and 30µg/mL. The results of intra-day and inter-day precision studies were shown in Table 3. The low %RSD values obtained from the analysis of tablets indicated that the method was highly precise.

Table 3. Precision data of proposed method

Analyte Conc. (µg/mL)	Intra-assay precision		Inter-assay precision	
	*Mean ±SD	%RSD	*Mean ±SD	%RSD
10	100.26±0.5565	0.56	99.21±0.6906	0.7
20	99.94±0.1704	0.17	99.41±0.1852	0.19
30	100.32±0.83	0.83	100.43±1.3009	1.3
*Triplicate results				

The developed methods were applied to the quantification of aripiprazole in tablet dosage forms available in the local market. The results were tabulated in Table 4. It can be seen that, the results obtained by proposed method was very much similar to that of established methods.

Table 4. Assay results of aripiprazole in tablet dosage forms

Brand Name	Label Claim (mg)	Assay	SD	%RSD
ARIP MT	10	99.75	0.2833	0.28
APICORD	10	99.44	1.0192	1.02
ARIA	10	99.36	0.6526	0.66
ARIPAT	10	100.01	0.3562	0.36
* Average of six determinations				

Conclusion

The proposed method is rapid, accurate, precise and sensitive for the quantification of aripiprazole from its pharmaceutical dosage forms by the multivariate spectrophotometric method. The method relies on the use of simple working procedure comparable to that achieved by sophisticated and expensive technique like HPLC, and hence this method can be routinely employed in quality control for analysis of aripiprazole in tablets.

Conflict of Interest

The authors report no conflicts of interest.

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