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RP-HPLC Method Development and Validation for Estimation of Aripiprazole in Bulk and Dosage Form

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Abstract
A simple, rapid, sensitive, reverse phase high performance liquid chromatographic method was developed for estimation of aripiprazole in bulk & dosage form. The method was validated as per ICH guidelines. Aphenomenex C18 (250mm X 4.6mm,5µm).The mobile phase for estimation is phosphate buffer (PH 4.2)70: Methanol 30 and detection was carried out 255nm.The analysis was performed runtime 7min at a flow rate 1ml/min. Linearity was obtained in concentration range of 10 to 60 µg/ml with correlation coefficient 0.9997 respectively. The method was validated for precision. Limit of detection, limit of quantitation, linearity, robustness and ruggedness. The limit of quantitation and limit of detection was found to be 3.72µg/ml to 1.23µg/ml respectively. Proposed HPLC method was sensitive and reproducible for the analysis of aripiprazole in pharmaceutical dosage form (tablet) with short analysis time.
Keywords:
Keywords
Aripiprazole, bulk dosage form**,** RP-HPLC, Validation.

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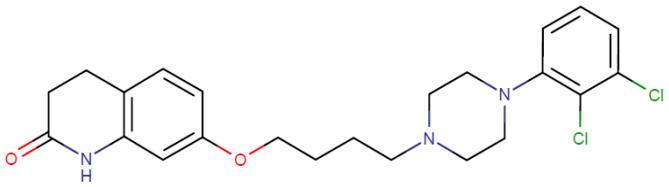
INTRODUCTION
Aripiprazole is chemically 7-(4-(4-(2,3-Dichlorophenyl) - 1- piperainyl) butoxy) - 3, 4-dihydro-2(lH) quinolinone. Aripiprazole is a psychotropic agent belonging to the chemical class of benzisoxazole derivatives and is indicated for the treatment of schizophrenia. It acts as a D_2 partial agonist. Aripiprazole is also a partial agonist at the 5-HT_{1A} receptor, and like the other atypical antipsychotics displays an antagonist profile at the 5-HT_{2A} receptor. Literature survey reveals that few spectroscopic and chromatographic methods have been reported for the quantitative estimation of Aripiprazole in bulk drug and pharmaceutical formulation. Therefore, here is an attempt to develop simple, specific and cost-effective method for determination of Aripiprazole as drug substance as well drug product.



MATERIALS AND METHODS

Instrumentation

Quantitative HPLC was performed on high performance liquid chromatography equipped water™486 with UV detector.

Chromatographic condition

Column: Phenomenex C18 (250mm X 4.6mm,5µm).
Mobile phase: phosphate buffer (PH 4.2): Methanol (70:30)
Flow rate: 1ml/min
Wavelength: 255nm
Run time: 7min
Injected volume: 10µl
Preparation of standard stock solution
Accurately weighed 10mg of ARPZ and transferred to 10ml volumetric flask containing a mixture of Phosphate buffer (pH 4.2): Methanol (30:70). The volume was made up to the mark using same mixture of mobile phase. The resulting stock solution (1000µg/ml) was filtered through 0.45µ membrane filter and sonicated for three cycles each of 10 min.

Preparation of working solution

Aliquot solution of 0.1ml was pipetted out from the above standard stock solution and transferred to 10ml volumetric flask. It was then diluted up to 10ml using mobile phase to obtain resultant solution of 10µg/ml. This working solution was sonicated for three cycles each of 10 min.

System suitability

The same standard solution was injected in following optimized chromatographic conditions and the chromatogram was recorded. The resulting chromatogram was integrated to determine retention time, peak area, number of theoretical plates, tailing factor etc. The obtained results were assessed for criteria prescribed in ICH guidelines Q2R1.

Method validation

Linearity

Aliquots of 0.1, 0.2, 0.3, 0.4, 0.5 and 0.6ml standard stock solution (1000µg/ml) were pipetted out and transferred to 10 ml volumetric flask and diluted up to 10ml using mobile phaseto obtain resultant solution of 10, 20, 30, 40, 50, 60µg/ml.

Precision

From the established range three QC standard were decided viz. 15, 35 and 55µg/ml as LQC, MQC and NQC respectively. The solutions for QC standards were prepared by diluting main stock standard solution of 0.15, 0.35, and 0.55ml up to 10ml. These three solutions were injected to given chromatographic conditions in triplicate and mean area was then determined. Results were recorded to calculate mean, SD, %RSD.

Accuracy

% Accuracy was determined from the observations of precision study using following formula. Limit for % accuracy is NMT 5% RSD.

% Accuracy = (Mean measured concentration/Nominal Concentration) x 100

%Recovery

$$\% \text{ Recovery} = \frac{Sample\ Area}{Standard\ Area} \times \frac{Standard\ Concentration}{Sample\ Concentration} \times 100$$

LOD and LOQ

Limit of detection (LOD) and Limit of quantitation (LOQ) was determined from the following formulae.

$$LOD = \frac{3.3 * STEYX}{Slope}$$

$$LOQ = \frac{10 * STEYX}{Slope}$$

Where, STEYX = Standard error of Y and X axis.

RESULTS AND DISCUSSION

System suitability testing

Table 1: Results of system suitability experiment and their correlation with standards

Sr. No.	Parameter	Mean observations	SD	%RSD	Acceptance criteria	Inference
1	Peak Area	93354.33	746.73	0.80	< 2	Pass
2	Retention time	3.77	0.02	0.46	< 0.5	Pass
3	Number of Theoretical plates	3794	--		> 2000	Pass
4	Tailing factor	1.31	--		< 2	Pass

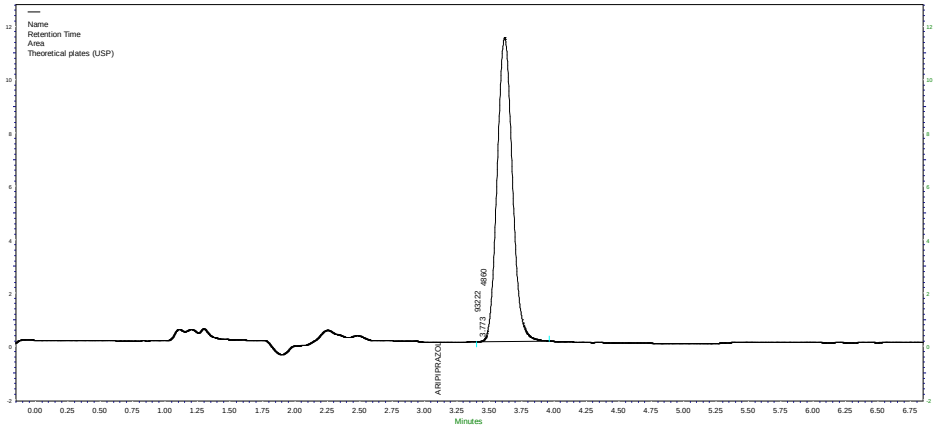


Figure 1: ARPZ chromatogram obtained for system suitability testing

Linearity

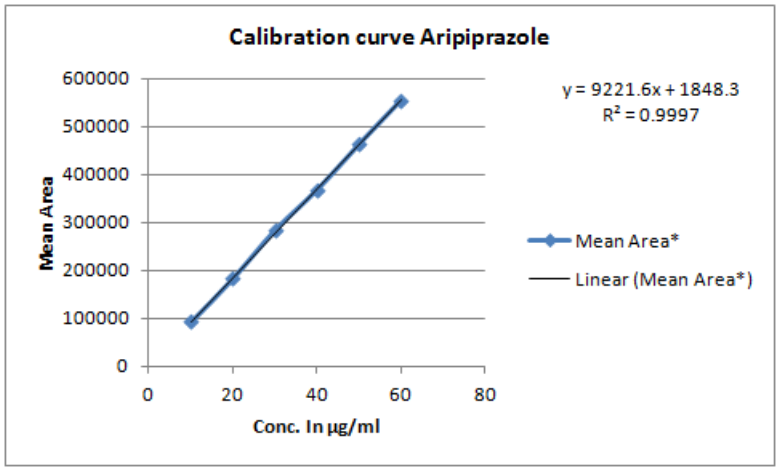


Figure 2: Calibration curve of Aripiprazole

Precision

Table 2: Observation table for Repeatability and Intermediate precision experiment

Conc. (µg/ml)	Intra-day precision			Inter-day precsion		
	Mean area ± SD	% RSD	Inference	Mean area ± SD	% RSD	Inference
15	131028.67 ± 684.83	0.52	Pass	132857.89 ± 1328.03	1.00	Pass
35	308218.67 ± 5700.07	1.85	Pass	319585.22 ± 4703.50	1.47	Pass
55	514688.33 ± 10350.67	2.01	Pass	513538.33 ± 8596.03	1.67	Pass

Robustness

Table3: Results obtained in Robustness experiment for organic concentration variation

Methanol Concentration (%)	Standard Conc. (µg/ml)	Mean peak area*	Mean measured conc. (µg/ml)	% Assay	Inference (Compendial standard 90-110 %w/w)
30	10	93222	9.91	99.09	Pass
32	10	95899	10.20	101.99	Pass
28	10	91638	9.74	97.37	Pass

Table 4: Observation table for Flow rate variation for Robustness assessment

Flow Rate (ml/min)	Standard Conc. (µ)	Mean peak area*	Mean measured conc. (µg/ml)	% Assay	Inference (Compendial standard 90-110 %w/w)
1	10	93222	9.91	99.09	Pass
1.1	10	90528	9.62	96.00	Pass
0.9	10	97229	10.34	103.43	Pass

% Recovery

Table 5: Results obtained for percent recovery experiment of ARPZ in tablet dosage form

% Recovery Level	Conc. of standard spiked (µg/ml)	Conc. of sample (µg/ml)	Mean peak Area of sample conc.*	Amount recovered (µg/ml)	% Recovery	Inference (Standards 95-105%w/w)
80	10	8	73527	7.78	97.69	Pass
100	10	10	95067	10.11	101.05	Pass
120	10	12	116771	12.46	103.43	Pass

LOD and LOQ

Table 6: Results obtained for LOD and LOQ

Standard Drug Solution	LOD (µg/ml)	LOQ (µg/ml)
Aripiprazole	1.23	3.72

CONCLUSION

The experiments were started with trial run in order to optimize the chromatographic conditions to get best possible results. Therefore, it was optimized, and final conditions were set as mobile phase composition, flow rate, wavelength, injection volume and temperature as phosphate buffer at pH 4.2 70: Methanol 30 percent, 1ml/min, 255nm, 10µl and ambient temperature respectively. Therefore, eventually it was concluded that we have attained our objectives by successful development and validation of RP HPLC method for quantification of Aripiprazole. Moreover, the applicability of the method was also proved for schedule analysis of aripiprazole in tablet dosage form.

REFERENCES:

1. Chatwal, G. R.; Anand, S. K. Instrumental Methods of Chemical Analysis, 5th ed.; Himalaya Publishing House: New Delhi, 2004; pp. 2.599-2.605, 2.112, 2.570-2.582, 2.652-2.630.
2. Khopkar S. M. Basic concepts of analytical chemistry, New age International Ltd. Publishers, New Delhi, 1998,2, pp. 178-179.
3. Kasture A.V.; Wadodkar S. G. Pharmaceutical Analysis 7thedition vol.2, Nirali Prakashan pp.7
4. Beckett A. H.; Stenlake J. B. Practical Pharmaceutical Chemistry 4th edition Vol. 2, CBS Publishers and Distributors, New Delhi, 2007, pp. 95-96, 96, 92-93, 99-100, 275.
5. Thakkar R. S. et al., *Indian J Pharm Sci.* 2011, 73(4), pp. 439–443.
6. Sastry B. S. et al., Asian J. Chem. 21(9), 2009, pp. 6643-6646.
7. Pai N. R. et al., *Der Pharmacia Lettre*, 2010, 2(4), pp. 1-10.
8. Vijayabharathi et al., *Asian J Pharm Clin Res*, 2017, 10(5), pp. 379-382.
9. Kalaichelvi R. et al., E-Journal of Chemistry, 2010, 7(3), pp. 827-832.
10. Kumari et al., World Journal of Pharmacy and Pharmaceutical Sciences, 2016, 5(6), pp. 1168-1179.