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# RP-HPLC Determination of Aripiprazole in Pharmaceutical Formulations

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A rapid, sensitive and specific reverse phase-high performance liquid chromatography (RP-HPLC) method was developed for the estimation of aripiprazole in pharmaceutical formulations. The RP-HPLC analysis was performed isocratically on a Phenomenex Luna $C_{18}$ column (250 mm length, 4.6 mm internal diameter and 5 µm particle size) using mobile phase having a composition of acetonitrile and sodium acetate buffer (20 mM sodium acetate, pH adjusted to 4.50 with acetic acid after addition of 0.4 % triethyl amine) in 55:45 v/v proportion with a flow rate of 1.0 mL/min. The analyte was monitored with UV detector at 254 nm. In the developed method aripiprazole elutes at a typical retention time of 6.84 min. The proposed method is having linearity in the concentration ranging from 2-12 µg/mL of aripiprazole. The method was statistically validated and had been applied to analysis of the drug in tablet dosage forms.

**Key Words: Aripiprazole, RP-HPLC, $C_{18}$ column.**

## INTRODUCTION

Aripiprazole[1] is an atypical antipsychotic agent. Aripiprazole appears to mediate its antipsychotic effects primarily by partial agonism at the $D_2$ receptor. In addition to partial agonist activity at the $D_2$ receptor, aripiprazole is also a partial agonist at the $5HT_{1A}$ receptor and like the other atypical antipsychotics, aripiprazole displays an antagonist profile at the $5HT_{2A}$ receptor.

Aripiprazole is chemically known as 7-[4-[4-(2,3-dichlorophenyl)-1-piperazinyl]-butoxy]-3,4-dihydrocarbostyril. Literature survey reveals the availability of few analytical methods such as UV[2], HPLC[2-4] and LC-MS[5,6] for estimation of aripiprazole in biological fluids and in pharmaceutical formulations. In the present investigation, a new RP-HPLC method was developed for the estimation of aripiprazole in bulk and in its pharmaceutical formulations using UV detector at 254 nm. The developed method is simple, sensitive, reproducible and rapid.

## EXPERIMENTAL

Aripiprazole was procured as a gift sample from Sun Pharmaceuticals Limited, Baroda, India. HPLC grade acetonitrile and triethyl amine were obtained from

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Merck, Mumbai, India. Water for HPLC was produced from Millipore apparatus. All other chemicals and reagents used were of Analytical reagent grade. A 50:50 v/v mixture of water and acetonitrile was used as diluent. All the standard and sample solutions were prepared in diluent.

**Chromatographic conditions:** Shimadzu HPLC (class VP series, high pressure gradient system) with LC10 AT VP pumps and SPD 10AVP UV detector was employed for the present study. Chromatography was performed by using a mobile phase having a fixed composition of acetate buffer (to 20 mM sodium acetate, 0.4 % of triethyl amine was added and final pH adjusted to 4.50 ± 0.01 with acetic acid) and acetonitrile in the proportion of 55:45 v/v and a stationary phase of Phenomenex Luna $C_{18}$ column (250 mm length, 4.6 mm internal diameter and 5 µm particle size). The chromatographic run time was maintained up to 12 min. The drug was monitored with UV detector at 254 nm.

**Preparation of standard solutions:** About 100 mg of aripiprazole was accurately weighed and dissolved in 100 mL of diluent to get a working standard concentration of 1 mg/mL. The working standard is further diluted with the diluent to get standard solutions of 2, 4, 6, 8, 10 and 12 µg/mL of aripiprazole.

**Preparation of sample solution:** Tablet powder equivalent to 100 mg of aripiprazole was taken and transferred to 100 mL volumetric flask. About 70 mL of diluent was added and sonicated for 0.5 h with intermittent shaking. It was filtered through Whatman filter paper (No. 1) into another 100 mL volumetric flask and was diluted up to the mark with the same solvent. The solution was further diluted with the diluent to the working concentration range of calibration curve.

**Estimation of drug from pharmaceutical formulations:** Each standard solution of aripiprazole in the concentration range of 2, 4, 6, 8, 10 and 12 µg/mL was injected thrice into the system and the calibration curve was constructed by plotting concentration of aripiprazole on X-axis and corresponding peak area on Y-axis. The sample solution was injected twice into the system and the chromatograms were recorded. The amount of drug present in the sample was computed from the calibration curve.

## RESULTS AND DISCUSSION

**Specificity:** The blank prepared from the formulation excipients was injected into the system. No peaks were detected in the retention time corresponding to analyte peak, which indicates no interference of excipients of the formulation. So the developed method is having the specificity. The sample chromatogram is given in Fig. 1.

**Linearity:** Aliquots of standard aripiprazole stock solution (100 µg/mL) in the concentration range of 0.2 to 1.2 mL were transferred in 10 mL volumetric flask and made up to the mark with the diluent. Each standard solution was injected thrice into the HPLC system. The linearity graph was plotted by taking the concentration of aripiprazole (µg/mL) on X-axis and the mean area of the corresponding peak on Y-axis. The method is having good linearity (r = 0.9995). The linearity graph was given in Fig. 2.

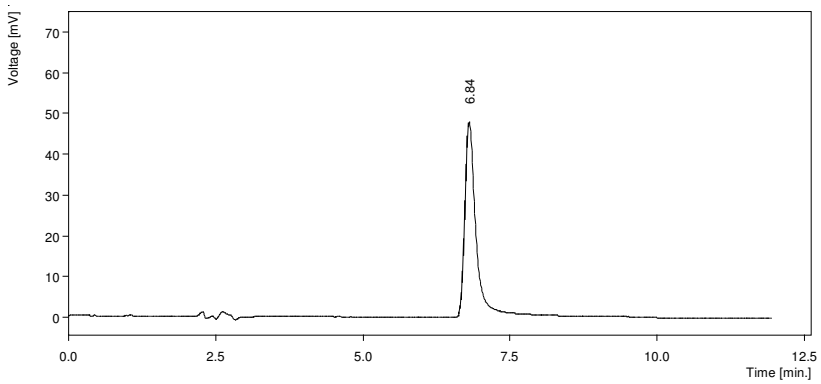


Fig. 1. Representative sample chromatogram showing aripiprazole peak at 6.84 min

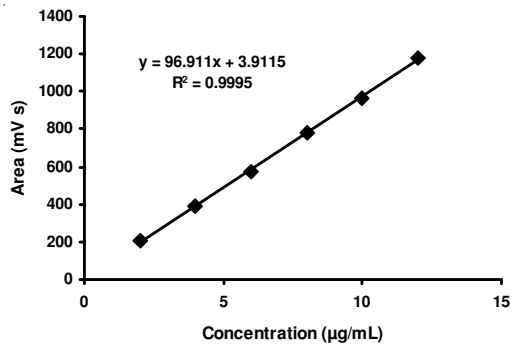


Fig. 2. Linearity of aripiprazole

**Precision:** To study the effect of day-to-day variations on the proposed method, 5 and 10 µg/mL standard solutions were subjected to intra-day and inter-day precision. The low % RSD values indicate that this method is having good precision and is not affected by day-to-day variations. The results were given in Table-1.

TABLE-1
PRECISION OF THE METHOD

| Aripiprazole concentration (µg/mL) | Concentration of aripiprazole (µg/mL) found | | | |
|---|---|---|---|---|
| | Intra-day | | Inter-day | |
| | Mean (n = 5) | CV (%) | Mean (n = 5) | CV (%) |
| 5 | 5.03 | 1.17 | 4.99 | 1.28 |
| 10 | 10.01 | 1.05 | 10.02 | 1.31 |

**Accuracy:** Accuracy of the method can be established by performing recovery studies and also by comparing the results of the developed method with the already reported methods.

Previously analyzed samples were spiked with known amounts of drug and reanalyzed by the proposed method. Recovery results were presented in Table-2.

The developed method is accurate as high recovery values were obtained. Some of the commercially available tablet formulations were analyzed by the proposed method and compared with already reported HPLC method[2]. The obtained results are in good agreement with each other as evidenced by low 't' and 'F' values than the theoretical values. The analytical results are given in Table-2.

TABLE-2
ASSAY OF ARIPIPRAZOLE IN PHARMACEUTICAL FORMULATIONS

| Formulation | Labeled amount (mg) | Amount obtained (mg) (n = 5) | Reference method[2] (n = 5) | % Recovery | |
|---|---|---|---|---|---|
| | | | | Proposed method | Reference method |
| Tablet 1 | 5 | 4.99 ± 0.02<br>t = 1.02<br>F = 2.15 | 5.01 ± 0.01<br>t = 1.08<br>F = 2.28 | 99.98 | 99.99 |
| Tablet 2 | 10 | 10.11 ± 0.08<br>t = 0.92<br>F = 3.13 | 10.05 ± 0.04<br>t = 0.85<br>F = 2.58 | 101.21 | 100.78 |
| Tablet 3 | 15 | 16.02 ± 0.06<br>t = 0.89<br>F = 2.93 | 16.05 ± 0.08<br>t = 0.93<br>F = 3.27 | 100.51 | 100.22 |

Note: The 't' and 'F' values refer to the comparison of the proposed RP-HPLC method with the reference HPLC method[2]. Theoretical values of 't' and 'F' for 5 measurements at 95 % level are 2.776 and 6.39, respectively.

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