

## Pharmaceutical estimation of aripiprazole to assist in modern research: An upbeat review

Pritam S. Jain<sup>1\*</sup>, Santosh B. Bodkhe<sup>2</sup>, Urmila R. Salunke<sup>3</sup>, Nitin G. Haswani<sup>4</sup>

<sup>1</sup>Professor, <sup>2,3</sup>Student, <sup>4</sup>Principal, Central Instruments Facility (CIF), Dept. of Pharmaceutical Chemistry, R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur, Maharashtra, India

**\*Corresponding Author: Pritam S. Jain**

Email: pritash79@yahoo.com

### Abstract

Aripiprazole is second generation anti-psychotic drug. Numerous investigations that have been published previously; stating analytical methods. The reported investigations for aripiprazole in its medical preparation and biological matrices is in present report. The most widely employed approaches in analysis outlined, such as spectrometric, liquid chromatographic processes, liquid chromatography-mass spectrometry, voltammetry and gas chromatography (GC). Spectrometric methods for ARP alone and in combination are precisely stated. Which includes parameters like  $\lambda$  max, solvent, matrix etc. and HPLC methods for aripiprazole single and in combination are given in tabular form, to parameters like matrix, stationary phase, mobile phase composition detection wavelength etc. HPTLC methods are reported in tabular form contain parameters like mobile phase combination, stationary phase,  $R_f$  etc. LC-MS method of aripiprazole and metabolite including parameter like matrix, stationary phase, mobile phase, internal standard, flow rate, retention time etc. the statistical data regarding the utility of these methods for estimation of aripiprazole published during 2004 to 2019 is precisely presented herein assist in further analytical and formulation research in future.

**Keywords:** Aripiprazole, Pharmaceutical, Analytical methods, Applications, Scope, Review.

### Introduction

ARP is an atypical antipsychotic agent that belongs to derivatives of benzisoxazole and has partial agonistic action on serotonin 5-HT<sub>1A</sub>-receptor as well as antagonist effect of 5-HT<sub>2A</sub>-receptor as a partial agonist at dopamine D<sub>2</sub> receptors and most recent second generation antipsychotic agent.<sup>1-4</sup> ARP is employed for management of schizophrenia, acute manic, bipolar-related mixed episode, and also as an adjunct treatment of depressions. the tablet dosage form of ARP available in the Indian market and dose of ARP in tablet are 2, 5, 10, and 15 mg. moreover, ARP solution is available in the dose of 1 mg/ml, while intramuscular injection of ARP available in the dose of 9.75mg/1.3 ml.<sup>5,6</sup> ARP is practically insoluble into methanol and water, completely soluble into dichloromethane while sparingly soluble in toluene.<sup>7</sup> After oral administration of ARP average half-life elimination is approximately to 75hrs and it reaches to 94hrs for DHA. Peak plasma concentration of ARP is reached within 3-5hrs after tablet administration and steady concentration are achieved within 14 days of dosing.<sup>8,9</sup> Primarily, ARP was metabolized by human cytochrome p450 and its active metabolite. DHA is metabolized by isozymes cyp3a4 and cyp2d6 into different metabolites and the obtained metabolites are removed through urine and faces the excretion profile of ARP is illustrated in Fig. 2.<sup>10</sup> A various analytical approaches like liquid chromatography mass spectrophotometry (LC-MS), high-performance liquid-chromatography (HPLC), ultra-high pressure liquid chromatography (UHPLC), capillary electrophoresis (CE), high-performance thin-chromatography (HPTLC), uv/vis-spectrophotometry, electrochemical methods and many more techniques are systematically used in routine quality control laboratories for analysis of drugs and there degradants in pure forms as well as in biological and pharmaceutical samples. The analytical methodologies play a significant role in understanding the physical and chemical behaviour of drug molecules.

The present review addressed the various analytical methodologies available on literature for estimation of ARP in bulk form, pharmaceutical formulation and biological samples. The review also described the physiochemical properties and pharmacopeial profile of ARP.

### Physiochemical Properties

Aripiprazole (ARP) is structurally 7-[4-[4-(2,3-Dichloro) Phenyl Piprazine-1-Yl] Butoxy]-3, 4-Dihydro-1H-Quinolin-2-One is depicted in Fig. 1 and the molecular formula and molecular weight is C<sub>23</sub>H<sub>27</sub>Cl<sub>2</sub>N<sub>3</sub>O<sub>2</sub> And 448.40 gm/mol. ARP is white to off-white glassy powder.<sup>7-10</sup>

### Present Pharmacopeial Status

Official monograph of ARP is given in Indian pharmacopoeia 2018 [IP]. Which consisted of HPLC assay method. The separation of ARP was done using stainless steel column of octadecylsilane bonded to porous silica (25cm × 4.6mm; with 5  $\mu$ m particle size) At column oven temperature 40°C with mobile phase consisted of buffer solution prepared by dissolving 6.8gm of potassium dihydrogen orthophosphate in 1000 ml of water, add 2 ml of trimethylamine, adjusted to pH 3 with ortho-phosphoric acid 25 volume of methanol and 25 volume of acetonitrile flow rate 1ml/min and was detected at 220 nm.<sup>11</sup>

### Pharmaceutical Estimation Spectrophotometric methods

Till now many uv/vis-spectrophotometry methods have been accounted for the determination of ARP alone and in its combinations. The basic principle, sample matrix,  $\lambda$  max, solvent, linearity range is summarized in Table 1. H. S. Patel et al. Reported a simple, sensitive and reliable uv-spectrophotometric method for estimation of ARP. It shows maximum absorbance at 216 nm and followed linearity in the

range of 4-20 µg/ml. This approach was established for the estimation of ARP in pharmaceutical formulation. The amount of drug was estimated from formulation was found to be 99.70%.<sup>12</sup> R. Kalaichelvia et al. has been developed for the estimate of ARP in bulk material and marketed formulation. It shows maximum absorbance at 219 nm in 95% ethanol. Results of analysis were validated process and by recovery studies. The sandell's sensitivity and apparent molar absorptivity were and  $8.4 \times 10^{-3}$  µgcm<sup>-1</sup>,  $5.2 \times 10^5$  l mol<sup>-1</sup> cm<sup>-1</sup> accordingly. Equation of the regression line give the slop and intercept 0.0035 and 0.1155 respectively. Correlation coefficient obtained 0.999.<sup>13</sup>

Samirandeynew et al. spectrophotometric method for evaluating ARP in bulk and pharmaceutical dosage forms has been developed in the ultraviolet region. Using 95% ethanol as solvent, maximum absorption of 256 nm.<sup>14</sup> Kandikonda Sandeep et al. UV-spectrophotometric method with multivariate measurement methodology for estimation of ARP in pharmaceutical formulations has been determine. This approach is based on the use of the linear regression method by using correlation between concentration and absorbance at five different wavelengths. The ARP shows lambda max at 255 nm and linearity range 5-30 µg/ml.<sup>15</sup> Y. Naga Sri Ramyathe et al. UV method create fast, precise and reliable colorimetric method for estimating ARP, tap using cholornic acid reagent. ARP is in the category of antipsychotics. The procedure is mainly based on charge transfer complexation of these medication with p-chloranilic acid to create magenta purple coloured substance which have been proceed into chloroform. Obtained lambda max at 543 nm for both ARP and TAP. The LOD and LOQ are 5.17 and 15.66; 82.5 and 250 for ARP and TAP respectively. With correlation coefficient has 0.9999 and the % RSD has less than two.<sup>16</sup>

A.V. Subbayamma et al. ARP hydrolyzed product containing primary aromatic amine requires an oxidative binding reaction with MBTH in the presence of Fe(III) culminating in the creation of a colour substance MBTH-Fe(III). In 1910, 3-Methyl-2-Benzothiazolinone-Hydrazone (MBTH) was developed, its experimental applications were only demonstrated in 1957 and published in 1961 as a colorimetric reagent approach is visible spectrophotometric technique adaptive and reproducible, defining ARP in bulk form and pharmaceutical formulation. The  $\Lambda$  max obtained was 480nm with using 0.1n naoh solvent with correlation

coefficient has 0.9999.<sup>17</sup> A. M. Eldidamony et al. has employed two spectrophotometric methods are based on the formation of yellow colored ion-pair complexes between the studied drugs and two sulphonphthale in acid dyes, Bromothymol Blue (BTB) And Bromophenol Blue (BPB) with shows maximum absorbance at 406 nm. and at 408nm.<sup>18</sup> Sarma Shreya Balaram et al. ARP has a objective of this works was to associate uv spectrophotometric zero order derivative method for determination of ARP showed maximum absorbance at 217nm.<sup>19</sup> Mohammad Faizan S. Deshmukh et al. UV spectrophotometry methods for the determination of ARP in bulk and pharmaceutical formulation. Four basic UV spectrophotometric methods were calculating for estimation of ARP of maximum absorbance at 255 nm in methanolic HCL as a solvent. The % recovery has been in range 98-100%.<sup>20</sup> R Vijayalakshmi et al. Aim of the present work is to establish two easy, effective colorimetric methods for the determination of ARP and TAP using chloranilic acid reagents. The Methods were based mainly on charge transfer complexation reaction of these drugs with P-Chloranilic acid to bring magenta purple color with lambda max measured at 545nm for ARP and 540 nm for TAP respectively with correlation of 0.999 and % RSD not less than two for the both methods.<sup>21</sup>

### Chromatographic status

Today, several different strategies are used for designing high-performance liquid chromatographic methods and high performance thin layer chromatographic. This review describes a strategy to develop chromatographic (LC) methods in a systematic way. LC is an analytical tool capable of detecting, separating, and quantifying the drug, its different impurities, and the drug-related degradants that may form on synthesis or storage.

Apart from pharmacopoeias methods many HPLC approaches have been reported the determination for ARP alone and in combination. In current review, a sum of total six papers for estimation of ARP alone are presented, while total of four papers are presented for estimation of ARP in combination are presented. The overall of the reported HPLC technique describing the mobile phase used for estimation, sample matrix, FR, RT, detector and column for ARP single is exposed in table 2 and of describing the HPLC technique for ARP in combination is presented in Table 3.

**Table 1:** Analytical conditions for methods by spectrophotometry in ultraviolet and visible range for ARP and its combination

S. No	Drug	Matrix	Solvent	Lambda Max(Nm)	Linearity (µg/Ml)	Coefficient Correlation	Accuracy Study In (%)	Ref
1	ARP	Bulk & Tablet	Methanolic Hcl & Water	216	4-20	1	-	12
2	ARP	Bulk & Tablet	Methanol	219	2-10	0.9998.	100, 150, 200	13
3	ARP	Formulation	95% Ethanol	256	5-30	0.9995	-	14
4	ARP	Tablet	Ethanol	251, 253, 255, 257, 259	5-30	0.999	50, 100, 150	15
5	ARP & TAP	Bulk & Tablet	Chloroform	543	ARP 80-120	0.9999	50, 100, 150	16
					TAP 200-1000	0.9998	50, 100, 150	

6	ARP	Bulk Sample & Formulation	Naoh Or CH <sub>3</sub> -CH <sub>2</sub> OHCH	480	2-12		-	-	17
7	ARP, CLP, SUP	Tablet & Biological Fluid	H <sub>2</sub> SO <sub>4</sub> Dil With Water	408	BPB	ARP	2-20	0.9996	18
						CLP	1-11	0.9996	
						SUP	1-11	0.9996	
				406	BTB	ARP	1-14	0.9996	
						CLP	1-7	0.9996	
8	ARP	Bulk & Formulation	Chloroform	217	1-6		-	-	19
9	ARP (Auc)	Bulk & Tablet	Methanolic Hcl	255, 244-264, 266.50, 259.80-273.40	5-30		0.999	80, 100, 120	20
10	ARP & TAP	Bulk & Tablet	Chloroform	545, 540	80-400, 200-1000		0.999, 0.9998	-	21

**Table 2:** HPLC methods for pharmaceutical estimation of ARP

S. No.	Matrix	Mobile Phase	Flow Rate (ml/min)	Detector	Ph	Rt (Min)	Ref
1	Tab	ACN: Sodium Acetate Buffer (55:45 V/V)	1	UV	4.5	6.8	22
2	Tab	ACN: Triethanolamine Buffer (40:60 V/V)	1.5	UV	3.5	3.8	23
3	Tab	Phosphate Buffer & Acetonitrile	1	DAD	3	28.2	24
4	Tab	ACN: Meoh: Sodium Sulphate: Acetic Acid (27:25:48:1 V/V/V/V)	1	UV	-	-	25
5	Bulk & Formulation	ACN: Meoh: Buffer(20:40:40 V/V/V)	1	UV	-	7.7	26
6	Bulk & Formulation	Buffer: ACN: THF(30:60:10, V/V/V)	1.5	UV	-	3.91	27

**Table 3:** Bio-analytical methods for ARP and its combinations

S. No.	Drug(S)	Sample Matrix	Mobile Phase	Detector	IS	Ref
1	ARP & DHAR	Human Plasma	Ammonium Buffer: ACN	DAD	Chlorohaoperidol	28
2	ARP & CLO	Human Plasma	ACN: Potassium Dihydrogen Orthophosphate (40: 60 V/V)	UV	Citalopram	29
3	ARP & DHAR	Blood Serum	ACN: H <sub>2</sub> O (30 : 70 V/V)	UV	-	30
4	ARP & OLP	Human Plasma	Phosphate Buffer : ACN	UV	Carbamazepine	31
5	ARP	Human Plasma	Phosphate Buffer: ACN (50:50 V/V)	UV	-	32

**Table 4:** HPTLC methods for analysis of ARP in combination

S. No.	Drugs	Method	Stationary Phase	Mobile Phase	Detection (nm)	R <sub>F</sub>	Ref.
1	ARP	HPTLC	Silica Gel 60F254	Carbon Tetrachloride: Methanol: Trimethylamine (2.5:2.4:0.1 V/V/V)	255	0.58 ± 0.02	33
2	ARP & OXD (STABILITY)	UV & HPTLC	Silica Gel 60 F254	Ethyl Acetate: Methanol (11:4 V/V)	.	ARP - 0.73 OXD - 0.29	34

**Table 5:** LC-MS/MS methods for analysis of ARP in combination

S. No.	Drug	Matrix	Stationary Phase	Mobile Phase	Method	IS	Linearity (ng/ml)	Ref
1	ARP & Metabolite, OPC-14857,	Human Plasma	RP- Chem Co Bond ODS -W(150mm×2.1mm Id., 5-μm;	0.1% Acetic Acid: Acetonitrile (65:35 V/V)	LC-MS/MS	-	-	35
2	ARP, Risperidone, Pipamperone & Its Metabolite	Blood	C18 RP Column (2.1 - 50 Mm, 1.7 Mm)	Ammonium Acetate/Formic Acid In water or Methanol. (0.1% / 2 Mmol/L)	UHPLC MS/MS	-	-	36

3	ARP & DHARP	Human Plasma	RP- BDS Phenyl Column (250 - 4.6 Mm, 5 Lm,)	Methanol: Ammonium Acetate Buffer (70: 30)	LC-MS/MS	Papaverine	ARP 0.1 - 600 DHARP 0.01-60	37
4	ARP & DHAR	Serum	C18 (50 Mm ×2.0 Mm)	0.1% Formic Acid: 100% ACN	LC-MS/MS	-	ARP 2–1000, DHARP 3.5–500	38
5	ARP	Human Plasma	Grace Smart RP 18 4.6 3 100 Mm, 3 M Column	Methanol: Ammonium Acetate Buffer (95:5 V/V)	LC-ESI-MS	-	0.20 - 60	39
6	ARP,	Human Plasma	C18 (2.1×100 Mm; 3.5m)	Ammonium Acetate :ACN (84:16 V/V)	LC-MS	Emoxipride	2–200	40

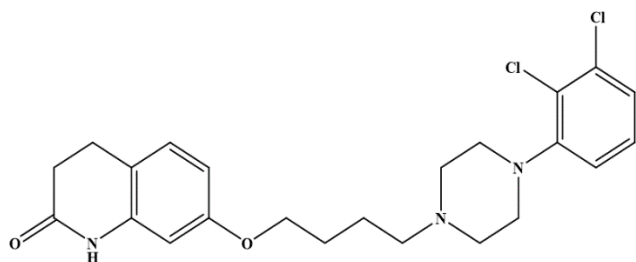


Fig. 1: Chemical structure of aripiprazole

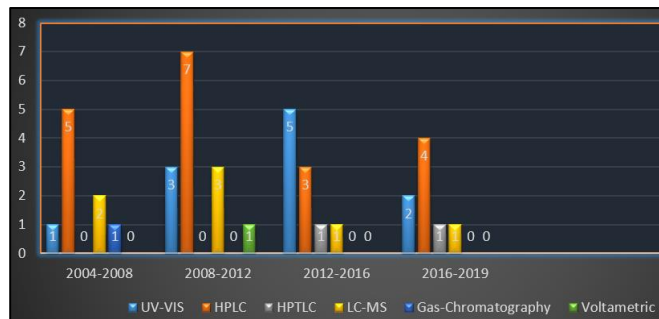


Fig. 4: Literature survey year wise distribution of publication

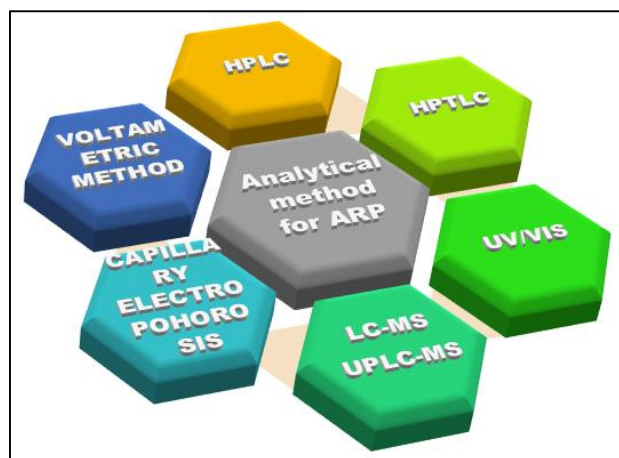


Fig. 2: Analytical account of aripiprazole

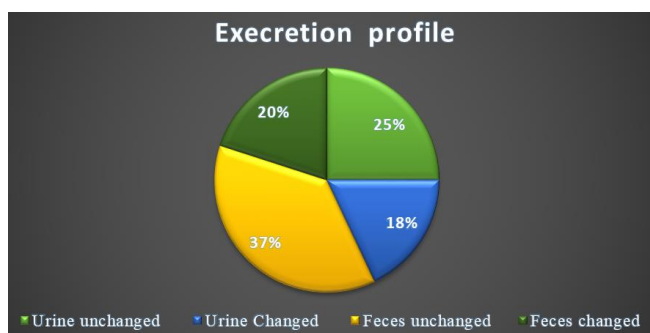


Fig. 3: Summary of the excretion profiles of the ARP

#### HPLC methods

Gananadhamu Samanthula et al. has of RP-HPLC technique was accepted for the estimation of ARP in marketed product. Using isocratic system, mobile phase using a composition of sodium acetate buffer and acetonitrile (20 mm sodium acetate, pH adjusted to 4.5 with acetic acid after addition of 0.4 % Triethyl Amine) in 45:55 V/V proportion with a flow rate of 1.0 ml/min. The analyte was checked with UV detector at 254 nm. In the determine technique ARP elutes at a RT of 6.84 min. The technique was statistically confirmed and was been applied to examination of the tablet dosage form.<sup>22</sup> R. Kalaichelvi et al. Technique has been established for determination of ARP in dosage of tablet. ARP use for an ODS analytical column for separation with a 60:40 (V/V) Mixture of triethanolamine buffer and acetonitrile (5 mm, Ph 3.5 ± 0.05 modified by introduction of 85% phosphoric Acid) as movable phase at a FT of 1.5 ml min<sup>-1</sup>. The effluent was examined by UV detection at 254 nm. Concentration of linearity 20–60 µg/ml and the LOQ and LOD were 1.248 and 0.411 µgml<sup>-1</sup>.<sup>23</sup> N. Djordjević Filijović et al. established a validated simple and sensitive method for determination of ARP. Showing maximum absorbance at 215nm using detector DAD. Ph 3 with OPA. The FT was 1.0 ml/min. The projected this technique was convenient and dependable for the purity control in equally dosage form and raw material.<sup>24</sup> Yoshihiko Shimokawa et al. has determination of ARP (OPC-14597, Abilify TM) in rat plasma and brain. Flow rate 1.0ml/min by using nova pack phenyl column and mobile phase, methanol: acetonitrile: sodium sulfate: acetic acid (25:27:48:1, V/V/V/V); Detection of UV at 254 nm. Uniform in plasma and brain give better precision and linearity range 10.0–2000 ng/ml and 30.0–6000 ng/g, with accuracy (96.0–102.4% and 99.0–108.7%) accordingly. determination HPLC methods Were successfully utilized to study of

pharmacokinetic in rat, five times more than plasma concentrations after oral administration of demonstrating brain.<sup>25</sup> Naved Ahmed et al. Accurate, simple, sensitive, fast and inexpensive (RP-HPLC) technique was developed for the quantifiable detection of ARP in API and marketed formulation. The separation and measurement by using of C18 (Waters Spherisorb 5 $\mu$  ODS 24.6mm X 250mm) column and used mobile phase of methanol: Acetonitrile: Buffer (40:20:40 V/V/V) and adjusting Ph 3.5 at FR of 1.0 ml/min with detection UV at 254nm. The separation was occurred between 7.7 $\pm$ 0.1 min for ARP. The process shows excellent linearity between the ranges of 5-25 $\mu$ g/ml. The % recovery of drug has been 103.67%.<sup>26</sup> Ashu Mittal et al the estimation of ARP and separation, quantification was occurred on waters spherisorb 5 $\mu$  ODS 24.6mm X 250mm column and using a mobile phase of ACN: Buffer: THF (60:30:10 V/V/V) At A FR of 1.5 ml/min with maximum absorbance at 255 nm. The separation was obtained between 3.91 $\pm$  0.1 min for ARP sample. The technique excellent linearity 1-100  $\mu$ g/ml. and precision parameter in intraday and interday % RSD is obtained 0.83-1.18%. The % recovery (Mean  $\pm$  S.D.) of high, middle and low concentrations were, 100.44  $\pm$  0.75, 100.00  $\pm$  1.05, 102  $\pm$  0.82 accordingly.<sup>27</sup>

#### HPTLC Methods

Md. Faizandeshmukh et al. Determination of ARP was achieved on thin layered of 200  $\mu$ m layer of silica Gel60f254 (10cm $\times$ 10cm) aluminium packed plates coated using mobile phase Ccl4: MEON: C<sub>6</sub>H<sub>15</sub>N (2.5:2.4:0.1 V/V/V). Photographic detection of ARP was done at 255 nm. Aripiprazole showed linearity over the required linearity range 300-1800 ng with correlation coefficient of 0.998. The retention factor of ARP was found to be 0.58  $\pm$  0.02. The proved technique was employed for marketed formulation and label claim for ARP was recovered to be in range of 98-100% and the % recovery found in range from tablet formulation show that there is no interference from excipients available in pharmaceutical formulation.<sup>33</sup> Kareem M. younes and research Team et al. The derivative spectrophotometric technique was depending on calculating the peak maximum amplitude of second derivative spectra of ARP at 217.2 and 229 nm where zero crossing points obtained with its oxidation product, linearity range of 1.0 – 6.0 $\mu$ g/ml for aripiprazole. The derivative spectra method was constructed on measuring the peak max amplitude for aripiprazole at 209.8, 222, 246.8 and 283.2 nm using 5.0 $\mu$ g/ml the oxidation product as a divisor, then concentration range of 1.0-6.0  $\mu$ g.ml<sup>-1</sup>. Bivariate method is used for determination of aripiprazole in presence of oxidation product over a concentration range of 1.0 – 6.0 $\mu$ g/ml<sup>-1</sup> for aripiprazole. The technique was depending on measuring the absorbance at the detected wavelengths. A TLC separation with densitometry detection of ARP was succeeding using ethyl acetate: methanol [11:4 v/v] as solvent. This technique accepted estimation of ARP in linearity ranges of 1.0-4.0  $\mu$ g/spot.<sup>34</sup>

#### Hyphenated determinations

LC-MS It is adaptable analytical tool which blends liquid chromatography resolving strength with mass spectrometry's detection specificity. Sample components are isolated By Liquid Chromatography (LC) and then added to Mass Spectrometer (MS). The MS generate the charged ions and determine them.

Masanori Kuboprecise et al. Efficient, reproducible and accurate liquid chromatography/tendon mass spectrometry (LC-MS/MS) method for determination of ARP and its metabolite, OPC-14857, produced and tested in human plasma. On reversed phase column C18 within 7.5 min chromatographic separation was accomplished isocratic.<sup>35</sup> Min Song et al. The simultaneous estimation of ARP and its active metabolite DHARP in human plasma a specific responsive and precise liquid chromatography – Mass Spectrometry (LC-MS/MS) approach was developed using papaverine as an IS. Study of LC-MS/MS on finnigan LC-TSQ quantum mass spectrometer was conducted utilizing positive electrospray ionization (ESI+) and chosen reaction monitoring. The ARP and DHARP assay are linearity in the range in the 0.1-600ng/ml and 0.01- 60ng/ml ranges respectively. The total recovers are greater than 85% in plasma specimen to the regulation of the U.S. food and drug administration, the intra and inter run precision and reliability values were considered to be in criteria the research variance criterion limit. Oral administration of a 5 mg ARP tablet in safe Chinese participants, the procedure produce was shown to be appropriate for use in a clinical pharmacokinetics test.<sup>37</sup>

D. S. Patel et al. A rapid, selective, and sensitive liquid chromatography-tandem mass spectrometer (LC-MS/MS) assay has been proposed for the determination of aripiprazole in human plasma. The analyte and propranolol as Internal Standard (IS) were extracted from 200 $\mu$ l of human plasma via liquid-liquid extraction using methyl *Tert*-Butyl ether under alkaline conditions. The best chromatographic separation was achieved on an aquasil C18 (100  $\times$  2.1 mm, 5 $\mu$ m) column using methanol-deionized water containing 2 mm ammonium trifluoroacetate and 0.02% formic acid (65:35, v/v) as the mobile phase under isocratic conditions. Detection of analyte and is was done by tandem mass spectrometry, operating in positive ion and multiple reaction monitoring (MRM) acquisition mode. The method was fully validated for its selectivity, interference check, sensitivity, carryover check, linearity, precision and accuracy, reinjection reproducibility, recovery, matrix effect, ion suppression/enhancement, stability, ruggedness, and dilution integrity. The assay was linear over the concentration range of 0.10–100ng ml<sup>-1</sup> for aripiprazole. The intra-batch and inter-batch precision (% CV) was  $\leq$ 4.8%, while the mean extraction recovery was >96% for aripiprazole across quality control levels. The method was successfully applied to a bioequivalence study of 10 mg aripiprazole orally disintegrating tablet formulation in 27 healthy Indian subjects under fasting and fed condition. The reproducibility in the measurement of study data was demonstrated by reanalysis of 260 incurred samples.<sup>41</sup>

## Methods of unique importance

### **Voltametry Method for estimation of ARP**

Anodic activity of ARP was analysed using electrochemical methods. Charge transfer, diffusion and surface distribution parameter of absorbed molecule and the amount of electrons transported to electrode structure are determined for reversible and adsorption-controlled electrochemical oxidation of ARP at 1.15 V Versus Ag/AgCl at Ph 4. Britton Robinson buffer (BR) on glassy carbon electrode. Voltammetric technique for direct estimation of ARP in dosage forms and biological samples were developed. The linearity spectrum is between 11.4mm (5.11 mg/l) to 157mm (70.41 mg/l) without stripping mode is located in a stripping mode from 0.221mm (0.10 mg/l) to 13.6mm (6.10 mg/l). Limit of detection (LOD) was established to be 0.11mm (0.05 mg/l) in voltammetry. Methods were positively applied to assay the formulation in tablets and human serum and well recovered human urine with good recoveries between 95.0% and 104.6% with RSD less than 10%.<sup>42</sup>

### **Unique determination of ARP and Its Metabolite GC**

In this research a new method for detecting ARP and its major metabolite DHA, throughout plasma was established and validating using gas-chromatography-mass spectrometry (GC-MS). Blood samples from seven psychiatric patients treating with ARP (10–20 Mg/Day) A solid-phase extraction (SPE) and *n*-methyl-*n*-trimethyl silyl trifluoro acetamide (MSTFA) derivatization. The characteristic ions of mass spectra for ARP and DHARP were *m/z* 306, 292, 218 and 304, 290, 218, accordingly. Extraction recoveries from this technique were 75.4% (*n* = 5) for aripiprazole and 102.3% (*N* = 5) for DHAR. The calibration curves of aripiprazole and DHA were linearity from 16 to 500 ng/ml ( $r^2 = 0.999$ ) and 8–250 ng/ml ( $r^2 = 0.999$ ), accordingly. The particular (log<sub>s</sub>) for ARP and DHA revaluated in 0.5 ml of serum were 14.4 ng/ml and 6.9 ng/ml. intra-assay and inter-assay precision and accuracy were within acceptable ranges. In this study, we also discovered that the mean trough concentrations in plasma at steady-state were 128.9 µg /L for ARP and 30.1 µg/L for DHA.<sup>43</sup>

## Discussion and Conclusion

The analysis highlights the various method used to examination ARP. There have been various studies, including HPLC, HPTLC, UV/Vis spectroscopy, LC-MS/MS, UPLC-MS/MS, voltametric method, and gas chromatography etc. For determination of ARP in loose and in its collective pharmaceutical preparations and in plasma. Liquid chromatography with UV detection was found to be most careful for evaluating of ARP in bulk as well as drug dosage forms, while hyphenated UPLC-MS/MS, LC-MS/MS approaches were expressed in plasma and biological fluid for deciding ARP and its metabolite. Method for the both pharmacokinetics and bioequivalence studies have been documented.

## Abbreviation

**ARP**- Aripiprazole

**DHA** - Dihydroaripiprazole

**TAP** - Tapentadol

**CLP** - Clozapine

**SUP** - Sulpiride

**OLP** - Olanzapine

**ATO** - Atomoxetine

**DUL** - Duloxetine

**CLO** - Clozapine

**STN** - Sertindole

**VEN** - Venlafaxine

**NCLO** - Norclozapine

**DSTN** - Dehydrosertindole

**λ Max** - Wavelength Maxima

**LIN** - Linearity

**FR** - Flow Rate

**RT** - Retention Time

**RF** - Retention Factor

**UV-VIS** - UV/Visible Spectrophotometry

**HPLC** - High Performance Liquid Chromatography

**RP-HPLC** - Reverse Phase Liquid Chromatography

**HPTLC** - High Performance Thin Layer Chromatography

**LC-MS/MS** - Liquid Chromatography Mass Spectrometry/  
Mass Spectrometry

**UPLC-MS/MS** - Ultra Pressure Liquid Chromatography-  
Mass Spectrometry-Mass Spectrometry

**AUC** - Area under Curve

**ODS** - Octadecyl Silane

**KH<sub>2</sub>PO<sub>4</sub>** - Potassium Dihydrogen Phosphate

**IUPAC** - International Union of Pure and Applied Chemistry

**IP** - Indian Pharmacopoeia

**Cm** - Centimetre

**Mm** - Millimetre

**Nm** - Nanometre

**µl** - Micro Litter

**µg** - Microgram

**ml** - Millilitre

**DMF** - Dimethylformamide

**NaOH** - Sodium Hydroxide

**KOH** - Potassium Hydroxide

**ACN** - Acetonitrile

**MeOH** - Methanol

**EtOH** - Ethanol

**LOD** - Limit of Detection

**LOQ** - Limit of Quantification

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