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Original Article

UTILITY OF *N*-BROMOSUCCINIMIDE AS AN ENVIRONMENTAL-FRIENDLY REAGENT FOR SENSITIVE SPECTROPHOTOMETRIC DETERMINATION OF ARIPIPRAZOLE IN TABLETS

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ABSTRACT

Objective: Three sensitive spectrophotometric methods are presented for the assay of aripiprazole in bulk drug and pharmaceutical formulation (tablets) using N-bromosuccinimide (NBS) and three dyes, methyl orange, amaranth and indigo carmine, as reagents.

Methods: The methods involve the addition of a known excess of NBS to drug in acid medium, followed by determination of unreacted oxidant by reacting with a fixed amount of methyl orange and measuring the absorbance at 522 nm (method A), amaranth and measuring the absorbance at 507 nm (method B) or indigo carmine and measuring the absorbance at 610 nm (method C). In all methods, the amount of NBS reacted corresponds to the amount of drug and the measured absorbance is found to increase linearly with the concentration of drug which is corroborated by the correlation coefficients of 0.9993- 0.9997.

Results: The systems obey Beer's law for 0.2-3.0, 0.1-2.4 and 0.2-3.8µg $mL^{-1}$for methods A, B and C, respectively. The limits of detection and quantification are also reported. Intra-day and inter-day precision and accuracy of the methods have been evaluated.

Conclusion: The methods were successfully applied to the assay of aripiprazole in tablets preparations and the results were statistically compared with those of the reference method by applying Student's t-test and F-test. No interference was observed from the common tablet excipients. The accuracy of the methods was further ascertained by performing recovery studies via standard-addition method.

Keywords*:* Spectrophotometry; Aripiprazole; N-bromosuccinimide; Methyl orange; Amaranth; Indigo carmine; Tablets.

INTRODUCTION

Aripiprazole; 7-[4-[4-(2,3-dichlorophenyl)-1-piperazinyl]butoxy] 3,4-dihydro-2 (1H)-quinolinone, (Fig.1) is a novel, atypical antipsychotic drug that is effective for the treatment of patients with schizophrenia or schizoaffective disorder. It has potent partial agonist activity at dopamine (D2) receptors, partial agonist activity at serotonin (5-HT1A) receptors, and antagonist activity at 5HT2A receptors. As a result, aripiprazole can improve both negative and positive symptoms of schizophrenia with lower propensity for extrapyramidal symptoms (EPS). Aripiprazole has moderate affinity for histamine and alpha adrenergic receptors, and no appreciable affinity for cholinergic muscarinic receptors [1-4].

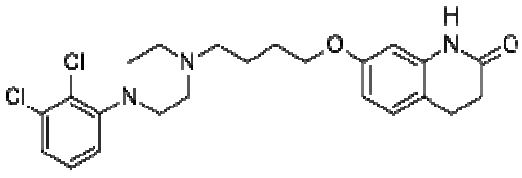


Fig. 1: The chemical structure of aripiprazole

A literature survey has revealed some methods have been described for the analysis of aripiprazole by HPLC with UV detection [5-9] or mass spectrometry detection [10-12], gas-chromatography-mass spectrometry (GC-MS) [13], Liquid chromatography-tandem mass spectrometry (LC-MS/MS) [14, 15] and capillary electrophoresis [6] were also developed. However, these methods are expensive and not available at most quality control laboratories. The spectrophotometric technique continues to be the most preferred method for the assay of different classes of drugs in pure, pharmaceutical formulations and in biological samples, for its simplicity and reasonable sensitivity with significant economic advantages. There are few methods for the estimation of aripiprazole using spectrophotometric technique in pharmaceutical preparations [16-28] (Table 1). These methods were associated with some major drawbacks such as decreased selectivity due to measurement in ultraviolet region and/or decreased simplicity of the assay procedure. For these reasons, it was worthwhile to develop a new simple, cost effective and selective spectrophotometric method for the determination of aripiprazolein its pharmaceutical dosage forms.

MATERIALS AND METHODS

Apparatus

All absorption spectra were made using Kontron Unikon 930 (UV-Visible) spectrophotometer (German) with a scanning speed of 200 nm/min and a band width of 2.0 nm, equipped with 10 mm matched quartz cells.

Materials and Reagents

All chemicals and reagents used were of analytical or pharmaceutical grade and all solutions were prepared fresh daily. Double distilled water was used throughout the investigation

Materials

Pharmaceutical grade aripiprazole was kindly supplied by Al-Andalus Medical Company, Cairo-Egypt. Aripiprex tablets, labeled to contain 10 mg aripiprazole per tablet (Al- Andalus) were purchased from local commercial markets.

Standard aripiprazolesolution

A stock standard solution of aripiprazole (100 µg mL^{-1}) was prepared by dissolving an exact weight (10 mg) of pure drug in bidistilled water and diluted to 100 mL with bidistilled water in a 100 mL measuring flask. The solution was diluted stepwise to get

working concentration of 10 µg mL^{-1}. The standard solutions were found stable for at least one week without alteration when kept in an amber coloured bottle and stored in a refrigerator when not in use.

Reagents

- N-bromosuccinimide (NBS): An approximately 0.01M NBS solution was prepared by dissolving about 1.8 g of chemical (Sigma-Aldrish) in water with the aid of heat and diluted to one liter with water and standardized iodometrically [36]. The solution was kept in an amber coloured bottle and was diluted appropriately to get 100 µg mL^{-1} NBS for use in all methods. The NBS solution was stored in a refrigerator when not in use.

- Potassium bromide, KBr (1.0% w/v).

- Hydrochloric acid (5.0 M): A 5.0 mol L^{-1} of HCl was prepared by diluting 43 mL of concentrated acid (Merck, Darmstadt, Germany, Sp. gr. 1.18, 37%) to 100 mL with bidistilled water and standardized as recommended previously[37] prior to use.

- Methyl orange (50 µg mL^{-1}): A 500 µg mL^{-1} dye solution was first prepared by dissolving accurately weighed 58.8 mg of dye (Sigma-aldrish, 85 % dye content) in water and diluting to 100 mL in a calibrated flask and filtered using glass wool. It was further diluted to obtain a working concentration of 50 µg mL^{-1}.

- Amaranth (200 µg mL^{-1}): A 1000 µg mL^{-1} stock standard solution was first prepared by dissolving accurately weighed 112 mg of dye (Sigma-aldrish, 90 % dye content) in water and diluting to volume in a 100 mL calibrated flask. The solution was then diluted 5.0-fold to get the working concentration of 200 µg mL^{-1}.

- Indigo carmine (200 µg mL^{-1}): A 1000 µg mL^{-1} stock standard solution was first prepared by dissolving accurately weighed 112 mg of dye (Sigma-aldrish, 90 % dye content) in water and diluting to volume in a 100 mL calibrated flask. The solution was then diluted 5.0-fold to get the working concentration of 200 µg mL^{-1}.

- **Recommended general procedures**

Different aliquots (0.2-3.0 mL), (0.1-2.4 mL) and (0.2-3.8 mL) of a standard 10 µg mL^{-1}aripiprazole solution for methods A, B and C, respectively were transferred into a series of 10 mL calibrated flasks by means of a micro burette and the total volume was adjusted to 5.0 mL by adding adequate quantity of water.

To each flask were added 1.0 mL each of 5.0 MHCl; 1.0 mL of NBS solution (100 µg mL^{-1}) and 1.0 mL of 1.0% KBr were added successively. The flasks were stoppered, content mixed and let stand for 15 min with occasional shaking. Finally, 1.0 mL of was added (accurately measured) and th(100 µg mL^{-1}) methyl orange and (200 µg mL^{-1}) amaranth or indigo carmine solution e volume was diluted to the mark with water and mixed well. The absorbance of each solution was measured at 522, 507 and 610 nm for methods A, B and C respectively after 5.0 min against a reagent blank.

In all methods, a standard graph was prepared by plotting the absorbance versus the concentration of drug. The concentration of the unknown was read from the calibration graph or computed from the regression equation derived using Beer's law data.

Table 1: **Comparison between the reported spectrophotometric methods for determination of aripiprazole**

	Method	λ_{max}(nm)	Beer's law (µg mL^{-1})	LOD (µg mL^{-1})	Molar absorptivity (L mol^{-1} cm^{-1})	References
1.	UV	218	2.5-20	0.01	2.2 x 10^5	[16]
2.	UV	216	4-20			[17]
3.	UV	219	2- 10		5.2 x 10^5	[18]
4.	UV	256	5. 30		0.74023 x 10^4	[19]
5.	a- sodium nitro prusside	430	2-10		1.83 x 10^4	[20]
	b- cobalt thiocyanate	625	50-200		1.61 x 10^4	
6.	Citric acid- acetic anhydride	590	2-12	0.37	0.3374 × 10^5	[21]
7.	a- 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ)	457	10-120	2.44	2.87 x 10^3	[22]
	b- Iodine (I_2)	364	2-28	0.39	1.36 x 10^4	
	c- Bromocresol green (BCG)	413	2-24	0.50	1.70 x 10^4	
	d- Bromocresol purple (BCP)	400	2-20	0.30	2.20 x 10^4	
8.	a- 2, 6- dichloroquinone-4-chlorimide (DCQC)	620	2.5-12.5			[23]
	b- 1, 2-napthoquinone-4-sulphonic acid (NQS)	485	2.5-12.5			
	c- sodium nitroprusside (SNP) / hydroxyl amine and alkali	515	5-40			
9.	a- Rosaniline hydrochloride	560	50-300			[24]
	b- Bromocresol purple	412	5-25			
10.	a- Fe (III)/ o-phenanthroline	508	0.5-7.0	0.098	8.88 x10^4	[25]
	b- Fe (III)/ bipyridyl	519	0.5-7.0	0.17	7.21 x10^4	
	c- Fe (III)/ ferricyanide	796	0.5-9.0	0.18	7.74 x10^4	
11.	a- N-Bromosuccinimide	520	1-20			[26]
	b- Chloramine-T	540	0.2-0.8			
12.	Bromocresol green	414	10-60		6.5018 x 10^4	[27]

From the foregoing paragraphs, it is clear that N-bromosuccinimide (NBS) despite its strong oxidizing power, versatility, high oxidation potential and high stability in solution has not been applied for the assay of aripiprazole in pure form and tablets. This paper describes for the first time the application of acidic N-bromosuccinimide (NBS) to the spectrophotometric determination of aripiprazoleusing methyl orange, amaranth and indigo carmine as chromogenic agents. N-bromosuccinimide (NBS) has earlier been widely applied for the assay of a variety of pharmaceuticals [29–35]. The proposed methods have the advantages of speed and simplicity besides being accurate and precise, and can be adopted by the pharmaceutical laboratories for industrialquality control.

Procedure for pharmaceutical formulations (tablets)

The contents of twenty aripiprex tablets (10 mg aripiprazole per tablet) were weighed accurately and ground into a fine powder. An accurate weight equivalent to 10 mg aripiprazole was dissolved in 20 mL of 0.2 M HCl with shaking for 5.0 min and filtered using a Whatman No. 42 filter paper.. The filtrate was diluted to the mark with 0.1 M HCl in a 50 mL measuring flask to give and 10 µg mL^{-1} stock solution of aripiprazole for analysis by spectrophotometric methods. A convenient aliquot was then subjected to analysis by the spectrophotometric procedures described above. Determine the nominal content of the tablets either from a previously plotted calibration graph or using the corresponding regression equation.

RESULTS

A close examination of the literature search presented in the introduction reveals that NBS has not yet been used for the spectrophotometric determination of aripiprazole. NBS is a strong oxidizing agent and perhaps the most important positive bromine containing organic compound; it is used for the specific purpose of brominating alkenes at the allylic position [38]. The present work involves the bromination of aripiprazoleby NBS followed by determination of surplus NBS after allowing the bromination reaction to complete. The ability of NBS to oxidize aripiprazoleand bleach the colors of methyl orange, amaranth and indigo carmine dyes has been used for the indirect spectrophotometric assay of the drug. In the three methods, aripiprazole was reacted with a known excess of NBS in acid medium and the unreacted oxidant is determined by reacting with a fixed amount of dyes and measuring the absorbance at 522, 507 and 610 nm for methods A, B and C, respectively(Fig. 2). In the three methods, the absorbance increased linearly with increasing concentration of drug.

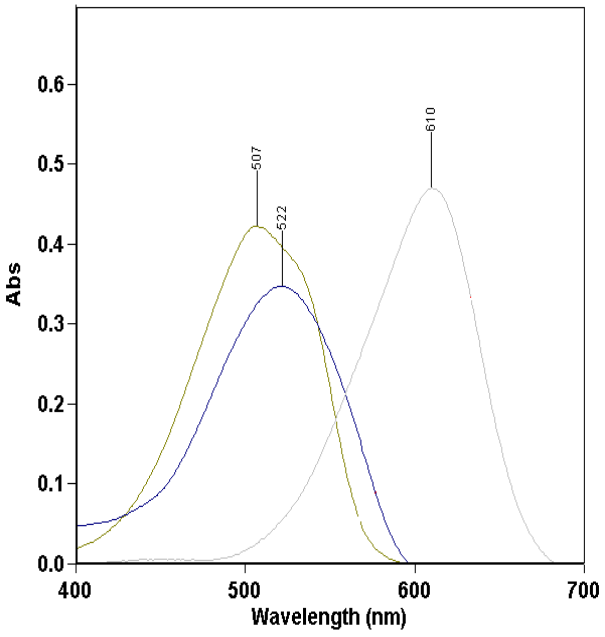


Fig. 2: Absorption spectra for the unreacted oxidant that determined by reacting with a fixed amount of dyes and measuring the absorbance at 522, 507 and 610 nm for methods A, B and C, respectively.

Effect of acid concentration

The hydrochloric acid was found most appropriate. The effect of HCl was studied and 0.25-3.0 mL of 5.0 M HCl in a total volume of 5.0 mL was found to have constant effect on both reactions (i.e. Drug with NBS, and residual NBS with dyes). The results presented in Table 2. indicated that, at 1.0-3.0 mL of 5.0 M HCl, there was almost same absorbance values were obtained in the presence of aripiprazole, the absorbance values obtained were constant and were almost the same as those of the reagent blank. At the acid volumes less than 1.0 mL, reaction led to go slower and incomplete. Therefore, 1.0 mL of 5.0 M HCl was used though out the study (Fig. 3).

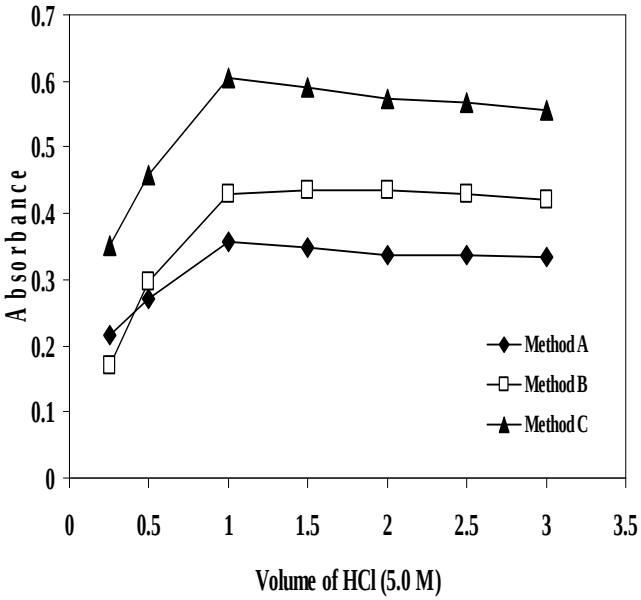


Fig. 3: Effect of volume of HCl (5.0 M) of the oxidation product of aripiprazole with NBS and dyes.

Effect of reagents

Preliminary experiments were performed to determine the maximum concentrations of the dyes spectrophotometrically in acid medium, and these were found to be 10 and 20 µg mL^{-1} for methyl orange and (amaranth or indigo carmine), respectively. A NBS concentration of 10 µg mL^{-1} was found to irreversibly destroy the colours of dyes in HCl medium. Hence, different concentrations of drug were reacted with 1.0 mL of 100 µg mL^{-1} NBS in all methods before determining the residual NBS as described under the respective procedures.1.0 mL of KBr (1.0%) was chosen as optimum volume in 10 mL total volume to accelerate the oxidation process.

Effect of time and temperature

The reaction time between aripiprazoleand NBS was studied by standing the drug solution after mixing with NBS for different intervals of time in the presence of 1.0 mL of 5.0 M HCl and the results indicated that time of 5.0-10 min was required to complete of the reaction. Therefore, a 10 min reaction time was fixed as optimum after the addition of NBS. A sufficient time to completely bleach dyes due to unreacted NBS was found to be 5.0 min, and the same was fixed in all subsequent studies. Raising the temperature does not accelerate the oxidation process and does not give reproducible results, so the optimum temperature is the ambient (25±2 °C). The measured colour was found to be stable for several hours in the presence of the reaction product/s in the three methods.

Effect of sequence of addition

Drug–acid–NBS–KBr-(dye) is the optimum sequence of addition; other sequences gave lower absorbance values under the same experimental conditions.

Method of validation

The proposed methods have been validated for linearity, sensitivity, precision, accuracy, selectivity and recovery.

Linearity and sensitivity

Under the optimum conditions a linear correlation was found between absorbance λmax and concentration of aripiprazolein the range of (0.1-3.8 µg mL^{-1}). The calibration graph is described by the equation:

A = a + b C (1)

(where A = absorbance, a = intercept, b = slope and C = concentration in µg mL^{-1}) obtained by the method of least squares. Correlation coefficient, intercept and slope for the calibration data are summarized in Table 2. For accurate determination, Ringbom concentration range [40] was calculated by plotting log concentration of drug in µg mL^{-1} against transimittance % from which the linear portion of the curve gives accurate range of microdetermination of aripiprazoleand represented in Table 2. Sensitivity parameters such as apparent molar absorptivity andSandell's sensitivity values, as well as the limits of detection and quantification, were calculated as per the current ICH guidelines [41] and illustrated in Table 2. The high molar absorptivity and lower Sandell sensitivity values reflect the good and high sensitivity of the proposed methods. The validity of the proposed methods was evaluated by statistical analysis [42] between the results achieved from the proposed methods and that of the reported method. Regarding the calculated Student's *t*-test and variance ratio *F*-test (Table 2), there is no significant difference between the proposed and reported method [41] regarding accuracy and precision. The limits of detection (LOD) and quantification (LOQ) were calculated according to the same guidelines using the formulas [41, 42]:

LOD=3.3σ/s and LOQ=10σ/s (2)

where σ is the standard deviation of five reagent blank determinations, and s is the slope of the calibration curve.

Accuracy and precision

In order to evaluate the precision of the proposed methods, solutions containing three different concentrations of aripiprazolewere prepared and analyzed in six replicates. The analytical results obtained from this investigation are summarized in Table 3. The low values of the relative standard deviation (% R.S.D) and percentage relative error (% R.E) indicate the precision and accuracy of the proposed methods. The percentage relative error is calculated using the following equation:

$$\% \, R.E. = \left[\frac{found - taken}{taken} \right] \times 100 \quad (3.)\ldots..$$

The assay procedure was repeated six times, and percentage relative standard deviation (% R.S.D) values were obtained within the same day to evaluate repeatability (intra-day precision), and over five different days to evaluate intermediate precision (inter-day precision).

For the same concentrations of drugs inter- and intra-day accuracy of the methods were also evaluated. The percentage recovery values with respect to found concentrations of each drug were evaluated to ascertain the accuracy of the methods. The recovery values close to 100% as compiled in Table 3 shows that the proposed methods are very accurate.

Table 2: Analytical and regression parameters of proposed oxidation spectrophotometric methods for determination of aripiprazole.

Parameters	Method A	Method B	Method C
Beer's law limits, µg mL^{-1}	0.2-3.0	0.1-2.4	0.2-3.8
Ringboom limits, µg mL^{-1}	0.4-2.6	0.4-2.0	0.4-3.4
Molar absorptivity, x 10^4 L mol^{-1} cm^{-1}	5.1255	8.1111	6.9898
Sandell sensitivity, ng cm^{-2}	8.75	5.53	6.42
Regression equation,[a]			
Intercept (a)	- 0.0005	0.0019	0.005
Standard deviation of intercept (S_a)	0.0018	0.0068	0.0048
Slope (b)	0.1167	0.1735	0.1622
Standard deviation of slope (S_b)	0.0057	0.0073	0.0068
Correlation coefficient, (r)	0.9997	0.9995	0.9993
Mean ± SD	100.09 ± 0.87	100.30 ± 0.98	100.04 ± 0.75
RSD%	0.87	0.98	0.75
RE%	0.89	1.03	0.79
Limit of detection, µg mL^{-1}	0.061	0.028	0.056
Limit of quantification, µg mL^{-1}	0.184	0.093	0.183
Calculated *t*-value [b]	0.13	0.39	0.64
Calculated *F*-value [b]	1.06	1.37	1.16

[a] $A = a + bC$, where C is the concentration in µg mL^{-1}, A is the absorbance units, a is the intercept, b is the slope., [b] The theoretical values of t and F are 2.57 and 5.05, respectively at confidence limit at 95% confidence level and five degrees of freedom (p= 0.05).

Robustness and ruggedness

For the evaluation of method robustness, volume of HCl and reaction time (between NBS and drug) were slightly varied deliberately. The analysis was performed with altered conditions by taking three different concentrations of drug and the methods were found to remain unaffected as shown by the RSD values in the ranges of 0.81-2.45%. Methods ruggedness was expressed as the RSD of the same procedure applied by three different analysts as well as using three different instruments (spectrophotometers). The inter-analysts RSD were in the ranges 0.94-2.28% whereas the inter-instruments RSD ranged from 0.72-1.96% suggesting that the developed methods were rugged. The results are shown in Table 4.

Recovery studies: To study the reliability and accuracy of the proposed methods, a standard addition technique was followed. This study was performed by spiking a fixed amount of tablet preparation to three different levels of pure drug. The total concentration was found by the proposed methods. The determination with each level was repeated three times and the percent recovery of the added standard (pure drug) was calculated from:

$$\% \text{ Recovery} = \frac{[C_F - C_T]}{C_p} \times 100 \quad (4)$$

where $C_F$is the total concentration of the analyte found, C_T is a concentration of the analyte present in the tablet preparation, C_P is a concentration of analyte (pure drug) added to tablet preparation. Results of this study presented in Table 5 revealed that the accuracy of the proposed methods was unaffected by the various excipients present in tablets.

Table 3: Results of intra-day and inter-day accuracy and precision study for aripiprazole obtained by the proposed methods.

Method	Taken (µg mL^{-1})	Recovery %	Precision RSD % [a]	Accuracy RE %	Confidence Limit [b]
	Intra-day				
Method A	0.5	99.50	0.78	-0.50	0.498 ± 0.004
	1.5	100.33	1.20	0.33	1.505± 0.019
	2.5	99.70	0.90	-0.30	2.493± 0.024
Method B	0.5	99.60	0.94	-0.40	0.498 ± 0.005
	1.0	99.80	1.25	-0.20	0.998 ± 0.013
	2.0	99.80	1.30	-0.20	1.996 ± 0.027
Method C	1.0	100.20	0.89	0.2	1.002 ± 0.009
	2.0	99.70	1.16	-0.30	1.994 ± 0.024
	3.0	99.90	1.28	-0.10	2.997 ± 0.054
	Inter-day				
Method A	0.5	99.30	0.87	-0.70	0.497± 0.005
	1.5	100.60	1.86	0.60	1.509 ± 0.029
	2.5	100.20	1.59	0.20	2.505 ± 0.042
Method B	0.5	100.40	0.88	0.40	0.502 ± 0.005
	1.0	99.90	1.36	-0.10	0.999 ± 0.014
	2.0	100.70	1.90	0.70	2.014 ± 0.040
Method C	1.0	100.20	1.05	0.20	1.002 ± 0.011
	2.0	100.10	1.39	0.10	2.002 ± 0.029
	3.0	99.70	1.86	-0.30	2.988 ± 0.078

[a] RSD%, percentage relative standard deviation; RE%, percentage relative error. [b] Mean ± standard error.

Table 4: Results of method robustness and ruggedness (all values in RSD%) studies.

Methods	Nominal amount concentration (µg mL^{-1})	RSD%			
		Robustness		Ruggedness	
		Variable alerted [a]			
		Acid volume (n=3)	Reaction time (n=3)	Different analysts (n=3)	Different instruments (n=3)
Method A	0.5	0.81	1.40	1.26	0.92
	1.5	1.16	1.90	2.28	1.30
	2.5	2.30	2.40	0.94	0.72
Method B	0.5	1.20	1.38	0.99	1.03
	1.0	1.75	1.70	1.22	1.40
	2.0	2.24	1.50	1.76	1.90
Method C	1.0	1.30	1.10	1.05	1.55
	2.0	1.60	1.60	1.70	1.60
	3.0	2.45	1.05	2.15	1.96

[a] Volume of 5.0 M HCl is (1.0±0.2 mL) and reaction time is (10±2.0 min) (after adding NBS) were used.

Table 5: Results of recovery experiments for aripiprex tablets by standard addition method.

Methods	Taken Conc. from tablet (µg mL^{-1})	Pure drug added (µg mL^{-1})	Total found (µg mL^{-1})	Recovery% [a] ± SD
Method A	0.5	0.5	0.994	99.40 ± 0.92
		1.5	1.984	99.20 ± 1.0
		2.5	2.994	99.80 ± 1.20
Method B	0.5	0.5	0.998	99.80 ± 0.76
		1.0	1.502	100.10 ± 1.22
		1.5	1.982	99.10 ± 1.19
Method C	0.5	0.5	1.001	100.10±0.70
		2.0	2.513	100.50±1.20
		3.5	3.972	99.30±1.30

[a] Mean value of three determinations

Application to formulations

The proposed methods were applied to the determination of aripiprazolein tablets. The results in Table 6 showed that the methods are successful for the determination of aripiprazoleand that the excipients in the dosage forms do not interfere. The results obtained from the assay of aripiprazoleby the proposed methods and reference method [22] for the same batch of material is presented in Table 6. The results agreed well with the label claim and also were in agreement with the results obtained by the reference methods. When the results were statistically compared with those of the reference methods by applying the Student's t-test for accuracy and F-test for precision, the calculated t-value and F-value at 95% confidence level did not exceed the tabulated values of 2.57 and 5.05, respectively, for five degrees of freedom [42].

Hence, no significant difference existed between the proposed methods and the reference methods with respect to accuracy and precision.

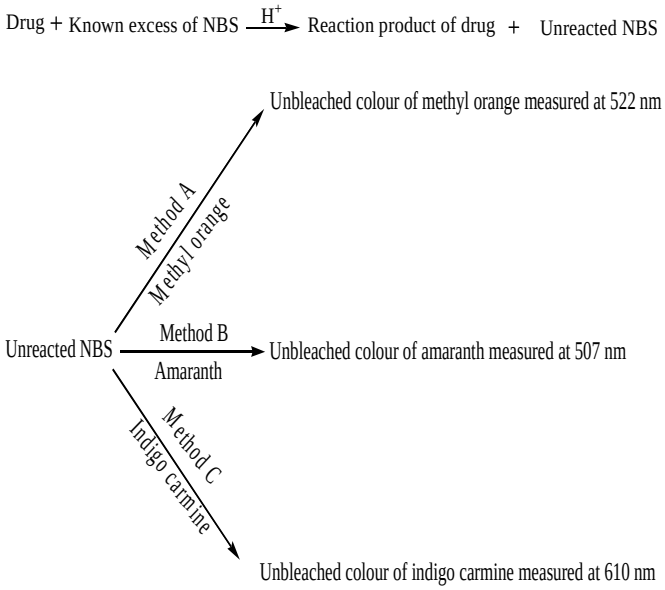
Table 6: Application of the proposed methods for the determination of aripiprazole in aripiprex tablets

	Proposed methods			Reported method [22]
	Method A	Method B	Method C	
Recovery ± RSD [a]	99.63 ± 0.62	99.10 ± 0.74	99.45 ± 0.58	99.21 ± 0.54
t-Value [b]	1.14	0.27	0.68	
F-Value [b]	1.32	1.88	1.15	

[a] Mean for six independent analyses. [b] The theoretical values of *t* and *F* are 2.57 and 5.05, respectively at confidence limit at 95% confidence level and five degrees of freedom (*p*= 0.05).

DISCUSSION

Aripiprazole, when added in increasing amounts to a fixed amount of NBS, consumes the latter and there will be a concomitant fall in its concentration. When a fixed amount of each dye is added to decreasing amounts of NBS, a concomitant increase in the concentration of dye results. This is observed as a proportional increase in the absorbance at the respective wavelengths of maximum absorption with increasing concentration of aripiprazole as indicated by the correlation coefficients ranged from of 0.9993-0.9997. The tentative reaction scheme of spectrophotometric methods is shown in Scheme 1. The bromination of aripiprazole will take place in position α to the carbonyl group [39].



Scheme 1: Tentative reaction scheme for the proposed spectrophotometric methods.

CONCLUSION

Three methods have been developed for determination of aripiprazolein bulk drug and in its tablets and validated as per the current ICH guidelines. The present spectrophotometric methods are characterized by simplicity since they do not involve any critical experimental variable and are free from tedious and time-consuming extraction steps and use of organic solvents unlike many previous methods. The proposed methods have additional advantages of ease of operation and possibility of carrying them out with a common laboratory instrument unlike many other instrumental methods reported for aripiprazole. They are characterized by high selectivity and comparablesensitivity with respect to the existing methods. The accuracy, reproducibility, simplicity, and cost-effectiveness of the methods suggest their application in the quality control laboratories where the modern and expensive instruments are not available.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests with the company name used in the paper.

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