Available online at www.pharmaresearchlibrary.com/ijrpls

ISSN: 2321-5038
IJRPLS, 2013,1(2):77-80
Research Article

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND LIFE SCIENCES
www.pharmaresearchlibrary.com/ijrpls

Colorimetric Assay of Atomoxetine Hydrochloride by Simple Aurum Coupling Reaction in Bulk and Tablet Dosage Form

B. Mohammed Ishaq*, Dr. Hindustan Abdul Ahad, Shaik Muneer, Praveena B
Department of Pharmaceutical Analysis, Balaji College of Pharmacy, Anantapur, A.P India
*E-mail: bmdishaq@yahoo.com

Abstract

Simple, rapid and sensitive spectrophotometric procedure was developed for the analysis of atomoxetine hydrochloride (ATH) in pure form as well as in pharmaceutical formulations. The method was based on the reaction of ATH with gold (III) chloride in the pH range 3.5-4.5 forming violet colored complex solution, showing absorption maxima at 550 nm. The linear plot indicates that Beer's law is obeyed in the range of 5 – 80 µg/ml of atomoxetine hydrochloride. The molar absorptivity and Sandell's sensitivity are 3.77 x 10^3M and 0.0774 µg cm^{-2} respectively. The standard deviation of the method for ten determinations ATH is 9.9827 x 10^3. The correlation coefficient (r^2) of the experimental data of the calibration plot is 0.9997. The effective range of concentration for accurate determination of ATH as ascertained from Ringbom's plot and it is 10 – 80 µg/ml.

Key words: Atomoxetine hydrochloride, Spectrophotometric, Ringbom's plot, Pharmaceutical formulations

Introduction

(-)-N-Methyl-3-phenyl-3-(o-tolyloxy)-propylamine hydrochloride is atomoxetine hydrochloride (ATH). The molecular formula is $C_{17}H_{21}NO{\cdot}HCl$, Its molecular weight is 291.82. The structure of automoxetin is as follows

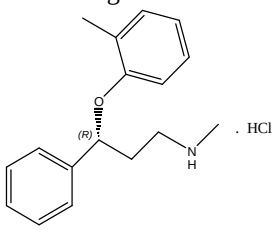

Fig 1: Chemical Structure of atomoxetine hydrochloride

It is practically a white solid and has a solubility of 27.8 mg ml^{-1} in water. It is the first nonstimulant drug approved by the FDA for the treatment of attention-deficit hyperactivity disorder (ADHD) in children, adolescents and adults. ADHD is the most common neurobehavioral disorder among children with an estimated worldwide prevalence of 8–12% [1]. ATH is not official in IP, BP, USP and EP. AMX is available commercially as capsules under brand name Straterra, Eli Lilly and company capsules. AMX capsules are intended for oral administration only. The capsules are available with strengths of 10, 18, 25, 40, 60 and 80 mg of ATH base. The capsules also contain pregelatinized starch and dimethicone.

A number of analytical methods based on liquid chromatography with fluorescence detection [2], liquid chromatography/mass spectrometry/mass spectrometry [3-6] (LC/MS/MS) have been developed for the determination of atomoxetine in human plasma and urine. A chiral analytical method by using HPLC with UV[7] has been reported for the determination of AMX impurities [7, 8]. To the best of our knowledge, there is no work in the literature reported about the colorimetric method for the analysis of ATH in pharmaceutical formulations. Hence the author has made an attempt to develop simple and sensitive spectrophotometric method for the estimation of ATH in bulk drugs and in pharmaceutical formulations. The method was based on the reaction with gold (III) to form a violet colored complex in the pH range 3.5 – 4.5.

Materials and Methods

All chemicals used were of analytical reagent grade and double distilled water was used for preparing the reagent solutions [9, 10]. ATH was obtained from Dr. Reddy's labs Hyderabad. Stock solution of ATH was freshly prepared by dissolving 100mg of ATH in 100mL of distilled water and then this was further diluted with distilled water so as to obtain working standard solution of 100 µg/ml.

Apparatus

All spectral and absorbance measurements were made on a Shimadzu UV-Visible digital Spectrophotometer (UV-160A) with 10mm matched quartz cells

Pharmaceutical dosage form

Tablet label claim of 10 mg ATH (Straterra, Eli Lilly) was procured from local market.

Preparation of Atomoxetine hydrochloride solution

100 mg of ATH was weighed accurately and transferred into a 100ml standard flask, dissolved and made up to the mark with methanol. This solution is diluted as required.

Preparation of Gold (III) solution

1g of chloroauric acid (Johnson Mathews, materials technology, U.K.) is dissolved in distilled water after adding few drops dilute HCl. The solution is made upto the mark in 100 ml volumetric flask. The gold content of the solution is determined by rhodamine B method[8]. The working solutions are prepared by diluting the stock solution.

Experimental Method

Determination of Atomoxetine hydrochloride

To explore the possibility of employing the colour reaction for the determination of ATH, the absorbance of the experimental solution containing different amounts of ATH, keeping the Au (III) concentration constant is measured in the wavelength range 400 – 700 nm.

Determination of gold (III)

To explore the possibility of employing the colour reaction for the determination of gold (III) in trace level, the absorbance of the experimental solutions containing different amounts of gold (III), keeping the ATH concentration in excess, is measured in the wavelength range 400 – 700 nm.

Assay of Pharmaceutical dosage form of Atomoxetine hydrochloride

The present method for the determination Atomoxetine hydrochloride is applied for its determination in a pharmaceutical sample. A know aliquot of pharmaceutical sample solution of atomoxetine hydrochloride is added to a 10 ml volumetric flask containing 5ml of buffer solution of pH 4.0 and 0.5 ml of gold(III) (5.0×10^{-3}M) solution 1.5 ml of 2% SDS solution. The contents are made upto the mark with distilled water. After heating for 60 minutes at 65^0C and cooling the solution to room temperature. The absorbance of the resulting solution is measured at 550 nm against the buffer blank. The amount of atomoxetine hydrochloride is computed from the predetermined calibration plot at 550 nm.

Results and Discussion

The spectra presented in fig 2 show that the complex has an absorption maximum at 550 nm. Neither gold (III) nor atomoxetine hydrochloride has absorbance at 550 nm. Hence, analytical studies are made at 550 nm. However, in presence of excess atomoxetine hydrochloride the complex shows maximum absorbance at 550 nm.

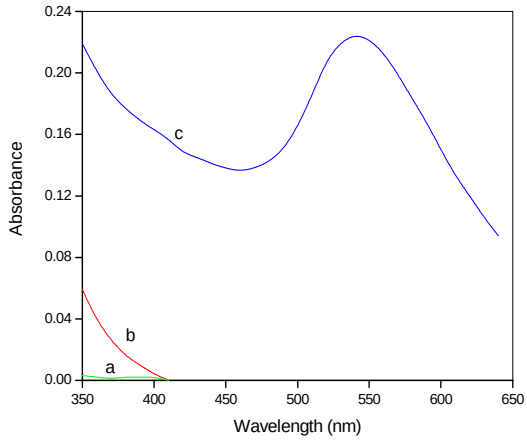

Fig. 2 Absorption spectra of AMX – Au (III) system

a. AMX Vs buffer blank
b. Au(III) Vs buffer blank
c. AMX – Au(III) Vs buffer blank

[Au(III)] = 5.0 x 10^{-3}; [AMX] = 3.42 x 10^{-3}M

Linearity

A plot of absorbance Vs amount of atomoxetine hydrochloride is presented in fig. 3 the straight line plot obtained obeys the equation A = 0.129C – 0.0009. The linear plot indicates that Beer's law is obeyed in the range of 5.0 – 80.0 µg/ml of atomoxetine hydrochloride. The molar absorptivity and Sandell's sensitivity are 3.77 x 10^3 l mol^{-1} cm^{-1} and 0.0774 µg/cm^2 respectively.The standard deviation of the method for ten determinations of 10 µg/ml of atomoxetine hydrochloride is 9.9826 x 10^{-4}. The correlation coefficient (γ) of the experimental data of the calibration plot is 0.9997. The effective range of concentration for accurate determination of atomoxetine hydrochloride as ascertained from Ringbom's plot and it is 10.0 – 70.0 µg/ml.

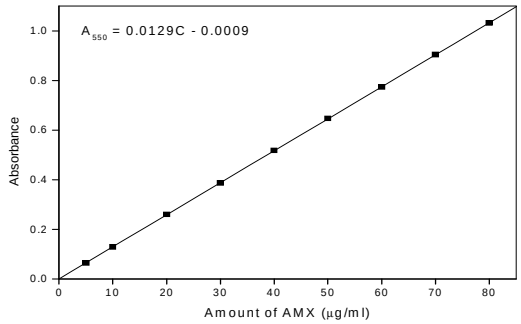

Fig. 3 Absorbance Vs amount of AMX (µg/ml)

[Au(III)] = 5.0 x 10^{-3}M ; pH = 4.0 ; λ = 550 nm

Effect of excipients

Various amounts of excipients that are generally associated with the atomoxetine hydrochloride in its pharmaceutical formulations are added to a fixed amount of atomoxetine hydrochloride (10 µg/ml) solution and the absorbance measurements are carried out under optimal conditions. The concentration (µg/ml) at which various ions do not cause an error of more than ± 4% in the absorbance is taken as the tolerance limit and the results are given in table 1.

Amount of AMX = 10 µg/ml; pH = 4.0

Table 1. Tolerance limit of excipients

Excipient	Tolerance limit (µg/ml)
Fructose	1257
Glucose	901
Sucrose	1369
Lactose	1704
Gelatin	1811
Starch	1424
Sodium Alginate	1324
Boric acid	1891
Magnesium stearate	1576

The data in table1 indicate that the excipients that are associated with atomoxetine hydrochloride do not interfere even in large quantities in the determination of atomoxetine hydrochloride making the method highly selective and direct.

Assay of atomoxetine hydrochloride

The present method for the determination atomoxetine hydrochloride is applied for its determination in the tablet dosage form. The amount of atomoxetine hydrochloride is computed from the predetermined calibration plot at 550 nm. The results are presented in table 2.

Table 2. Assay of atomoxetine hydrochloride in pharmaceutical formulation

Sample (manufacturer formulation)	Label claim (mg)	Amount found * (mg)	Error (%)
Straterra, Eli Lilly and company	10.00	9.91	-0.90

* Average of seven determinations

Optimal characteristics, accuracy and precession, data of the determinations of atomoxetine hydrochloride and gold (III) are presented in table. 3.

[AMX] = 3.42 x 10^{-3}M ; pH = 4.0
[Au(III)]= 5.0 x 10^{-3}M; λ = 550 nm

Table.3 Optimal and regression characteristics, precession and accuracy of the proposed method for atomoxetine hydrochloride and gold(III)

Parameter	Atomoxetine hydrochloride	Gold(III)
Analytical wavelength (nm)	550	530
Beer's law limits (µg/ml)	5.0 - 80.0	9.84 – 157.42
Limits of detection (µg/ml)	2.2837	10.3723
Limits of quantization (µg/ml)	7.6170	34.7446
Molar absorptivity ($lmol^{-1}$ cm^{-1})	3.77 x 10^3M	0.75 x 10^3M
Sandell's sensitivity (µg cm^{-2})	0.0774	0.2625
Regression equation (y = a + bx)		
Slope (b)	0.0129	0.0047
Intercept (a)	-0.0009	0.0104
Correlation coefficient (γ)	0.9997	0.9981
Standard Deviation (SD)	9.9827 x 10^3	0.0163

Conclusions

Atomoxetine hydrochloride reacts with gold (III) to form stable violet colored 1: 1 complex at pH 4.0. Spectrophotometric and derivative spectrophotometric methods are developed based on this reaction. They are sensitive for the assay of both atomoxetine hydrochloride and gold (III). The tolerance limit of the excipients and the foreign ions in derivative methods is found to be generally 10 – 20% greater than that of the zero order method. The present spectrophotometric methods are direct, simple and highly selective for the determination of gold (III) or atomoxetine hydrochloride. Further, the methods can easily be employed by ordinary clinical laboratories as the methods can be carried out using a simple colorimeter.

References

1. Faraone SV; Sergeant J; Gillberg C; Biederman J. *World Psychiatry*, **2003**; 2: 104.
2. Mullen JH; Shugert RL; Ponsler GD; Qimin Li; Sundaram B; Coales HL et al. *J. Pharm. Biomed. Anal*., **2005** ; 38 (4) : 720.
3. Hao-Jie Z ; Jun-Sheng W ; Donovan JL ; DeVane CL ; Gibson BB ; Markowitz JS. *J. Chromatogr. B*, **2007**;846(1-2);351.
4. Sauer JM ; Ponsler GD ; Mattiuz EL ; Long AJ ; Witcher JW ; Thomasson HR *et al*, *Drug Metab. Dispos*., **2003**; 31: 98.
5. Witcher JW; Long A; Smith B; Sauer JM; Heilgenstein J; Wilens T *et al*, *J. Child Adolesc. Psychopharmacol*., **2003**;13**:**53.
6. Mattiuz EL; Ponsler GD; Barbuch RJ; Wood PG; Mullen JH; Shugert RL et al. *Drug Metab. Dispos*.,**2003**; 31: 88.
7. Sellers JA; Olsen BA; Owens PK; Gavin PF. *J. Pharm. Biomed. Anal*., **2006**; 41(4): 1088.
8. Mohammed Ishaq B, Vanitha Prakash K, Hari Kumar C, Usha Rani G, Ramakrishna P, *Journal of Pharmacy Research*, **2011**; 4(1), 226-228.
9. Hindustan Abdul Ahad; Mallapu Rani E; Rani M; Mandava Giri; Kishore Kumar Reddy B; Kranthi. *Journal of Pharmacy Research*, **2011**, 4(3), 730-731
10. Ahad HA, Rani M; Kishore Kumar Reddy B; Mahendra Kumar P; Kranthi G; Ramya Sree P. *Journal of Pharmacy Research*, **2011**,4(3),735-736.