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Spectrophotometric determination of aripiprazole in pharmaceutical formulations with MBTH and ferric chloride

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ABSTRACT

The hydrolyzed product of ARI (HARI) which possess aromatic primary amine involves in oxidative coupling reaction with MBTH in presence of Fe(III) leading to the formation of colored product [MBTH-Fe(III)]. 3-methyl-2-benzothiazolinone-hydrazone (MBTH) was prepared in 1910, its analytical applications[1,2] were evidenced only in 1957 and it was introduced as colorimetric reagent[3] in 1961. The method is sensitive and reproducible visible spectrophotometric, for the determination of ARI in bulk samples and pharmaceutical formulations is described. The λmax exhibited was 480nm within the concentration range of 2-12 µg/ml.

Key words: Aripiprazole, MBTH, spectrophotometric.

INTRODUCTION

Aripiprazole (ARI) is antipsychotic, selective dopamine D_2-receptor antagonist with dopamine auto receptor agoinst activity. It s chemical name is Sec2(IH)-Quinoline,7-[-4-[4-(2,3-dichloro-phenyl)-1- piperazinyl] butoxy]-3,4-dihydro.[129722-12-9] CAS NO .Literature survey reveals that HPLC[4-8],LC-MS[9-11], LC –UV[12] methods involve sophisticated instruments which are expensive and pose problems of maintenance. However analytically important functional groups in ARI have not been exploited properly in developing visible spectrophotometric methods. So the authors have made some attempts in this direction and succeeded in developing this method. The method based on the use of MBTH and $FeCl_3$ .The method was extended for formulations[13-15] and bulk samples.

EXPERIMENTAL

Instruments

An ELICO, UV-visible digital spectrophotometer with 1 cm matched quartz cells were used for the spectral and absorbance measurements. An ELICO L1-120 digital pH meter was used for pH measurements.

Reagents

All the reagents and chemicals used were of analytical or pharmacopoeial grade purity and double distilled water was used throughout aqueous solution of MBTH (Fluka, 8.56×10^{-3}M) and Fe(III) (Wilson labs, 0.9% 1×10^{-2}M) were prepared by dissolving the required amounts in doubly distilled water.

Preparation of standard Drug solution

A 1mg/ml solution was prepared by dissolving 100mg of pure ARI in 100ml of 0.1N sodium hydroxide or isopropanol . To get HARI form, 100mg of ARI was hydrolyzed in a round bottom flask in the presence of 20.0ml of 2.5 M methanolic HCl and refluxed for one hour. Later methanolic HCl was removed under vacuum and the residue was dissolved in distilled water or 5% acetic acid working solution was prepared from stock solution.

For Pharmaceutical formulations

A weighed amount of tablet powder equivalent to100mg of ARI was transferred into a separator with 10ml-distilled water. The separator was shaken to decrease the material and the contents were extracted with 3×25ml portions of chloroform. The total extracts were collected into 100ml volumetric flask and then diluted to the mark with the same solvent to obtain stock solution. This stock solution was further processed as required for analysis.

The UV spectrophotometric method was chosen as reference method for ascertaining the accuracy of the proposed methods.

Recommended procedure

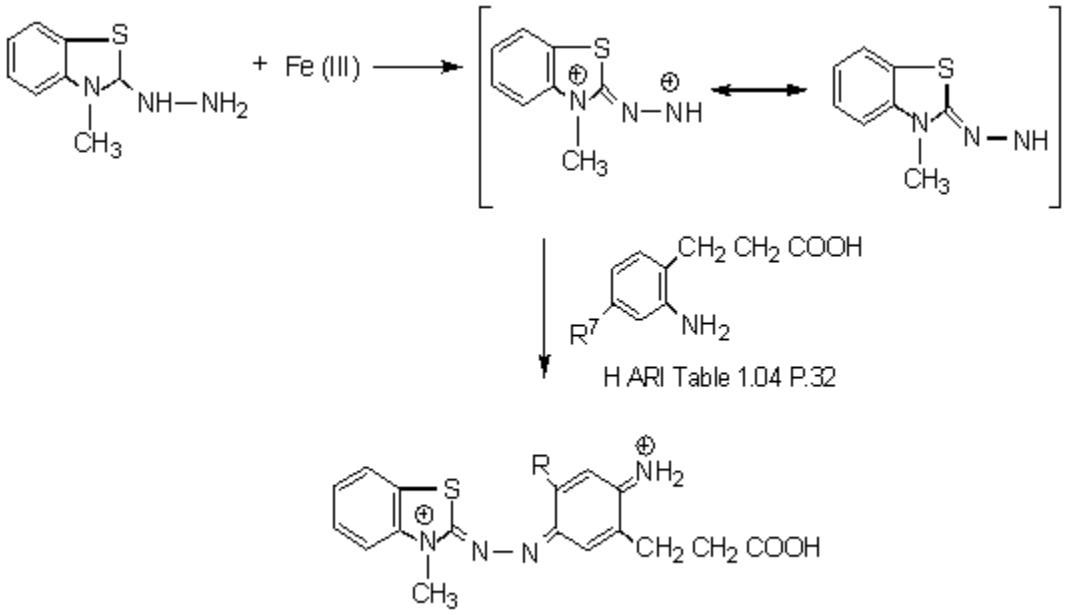
Aliquots of standard HARI (1.0-3.0 ml; 100 µg/ml) were transferred into a series of 25 ml volumetric flasks. To that 1.0 ml MBTH (1.711×10^{-4}M) solution was added and allowed to stand for 2 min at room temperature. Then 1.0 ml of Fe (III) (5.0×10^{-4}M) solution was added and allowed to react for 5 min. The solutions in each flask were made up to the mark with distilled water and the absorbance was measured immediately at 480 nm against reagent blank. Within 30 min. and the amount of the drug in the sample was computed from a calibration curve.

RESULTS AND DISCUSSION

The optimum conditions for the development of the method were established by varying the parameters one at a time and keeping the others fixed and observing the effect produced on the absorbance of the colored species. As the drug molecule possess aromatic primary amine after hydrolysis, the suitability of MBTH reagent fro its determination was examined. The applicability of MBTH in conjunction with various oxidizing agents (potassium dichromate, sodium meta periodate, chloramines-T, iodine, ferric chloride) for the determination of HARI was examined and Fe(III) was found to be the best. The effects of reagent concentration, temperature, H_2SO_4 strength, waiting time prior to dilution and order of addition of reagents were studied and the optimum conditions were fixed. The spectrum of the colored species produced by the suggested procedure was found to possess maximum absorbance at 480nm.

Table 1

Parameter	MBTH- Fe(III)
λ_{max} (nm)	490nm
Beer's law limits (µg/ml)	2 - 12
Detection limits (µg/ml)	0.5835
Molar absorptivity ($1.mol^{-1}cm^{-1}$)	$0.3419x10^5$
Sandell's sensitivity ($\mu g.cm^{-2}$/0.001 absorbance unit)	0.0131
Optimum photometric range (µg/ml)	4-10
Regression equation (Y=a+bx) i) Slope (b)	0.0764
ii) Standard deviation on slope (S_b)	$1x25^{-4}$
iii) Intercept (a)	-0.0008
iv) Standard deviation on intercept (S_a)	$1.486x10^{-2}$
v) Standard Error of Estimation (S_e)	$8.37x10^{-4}$
vi) Correlation co-efficient (r)	0.9999
vii) Relative standard deviation (%)*	0.3064
% Range of error (confidence limits)*	
i) 0.05 level	0.3216
ii) 0.01 level	0.5044
% Error in bulk samples**	-0.0148



Scheme 1

Analytical data

The Beer's law limits, molar absorption, Sandell's sensitivity, detection limits, regression equation and correlation coefficient obtained by least squares treatment of these results are given in Table 1. The precision of the method was tested by analyzing six replicate samples.

Chemistry of the colored species

In this method, MBTH on oxidation with Fe(III) loses two electrons and one proton forming an electrophilic intermediate which is the active coupling species which then condenses with aldehyde to give a brilliant blue colored cationic dye.

CONCLUSION

The method is simple, accurate and constitute better alternative to the reported ones in the assay of ARI in bulk form and pharmaceutical formulations.

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