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ANALYSIS OF AMISULPRIDE IN PHARMACEUTICAL DOSAGE FORMS BY NOVAL SPECTROPHOTOMETRIC METHODS

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ABSTRACT

Two simple, accurate, sensitive, precise and economical spectrophotometric methods have been developed for the determination of amisulpride (AMS) in tablet formulation. The developed methods were based on the formation of a yellow coloured chromogen due to the reaction of amisulpride with methyl orange (method-I) and formation of a blood-red coloured complex resulted from the reaction of amisulpride with 2, 5-dihydroxy, 3, 6-dichloro-1, 4-benzoquinone (method-II). The proposed methods showed the absorption maxima at 420 nm, 545 nm and have good linearity in the concentration range of 5-25 µg/mL and 50-250 µg/mL for method-I and method-II respectively. The results of analysis for the proposed methods were validated statistically by recovery studies.

Key words: Amisulpride, Spectrophotometric method, Pharmaceutical dosage.

INTRODUCTION

Amisulpride[1-3] is a substituted benzamide atypical antipsychotic drug with general properties similar to those of sulpiride. Chemically it is 4-amino-N-[(1-ethyl-2-pyrrolidinyl) methyl]-5-(ethylsulphonyl)-2-methoxy benzamide. It is reported to have a high affinity for dopamine D_2/D_3 receptor antagonist, mainly used in the management of psychoses such as schizophrenia. Amisulpride is absorbed from GIT but the bioavailability is reported to be only about 43 to 48%. Plasma protein binding is reported to be low, metabolism is limited, with most of a dose appearing in the urine and faeces as unchanged drug. The terminal half-life is about 12 hours.

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Amisulpride (AMS) is official in BP and European pharmacopoeia. A literature survey revealed that there are few analytical methods have been reported for the determination of the drug in pharmaceutical dosage forms, which include non-aqueous titration[4], reversed phase high pressure liquid chromatography (RP-HPLC)[5], aqueous capillary electrophoresis (CE), non-aqueous CE, normal phase (NP) and reversed-phase (RP) high performance thin layer chromatography (HPTLC) with densitometry and videodensitometry, and direct and derivative UV spectrophotometry[6]. There are few spectrophotometric[7,8] methods have been developed for the estimation of AMS in dosage forms. There is no analytical report for the estimation of AMS using visible spectrophotometry.

EXPERIMENTAL

Material and methods

A Systronics double beam UV-Visible spectrophotometer 2203 with 1 cm matched quartz cells was used for all spectral and absorbance measurements. The reagents methyl orange (Fluka), 5-dihydroxy, 3,6-dichloro-1,4-benzoquinone (Fluka), isopropyl alcohol, chloroform, potassium hydrogen phthalate, hydrochloric acid (procured from S.D Fine Chem. Pvt. Ltd., Mumbai) and all the chemicals and reagents used were of analytical grade and solutions were prepared in double distilled water. Amisulpride is available as tablets. SULPITAC from Sun Pharma and SOLIAN from Aventis Pharma are the commercial formulations containing 50 mg, 100 mg and 200 mg of amisulpride were procured from the local pharmacy.

Preparation of standard drug solutions

Method-I: About 100 mg of amisulpride pure drug was accurately weighed, transferred into a 100 mL volumetric flask containing 30 mL of 0.1 N hydrochloric acid and sonicated for about 10 minutes. The volume was made up to the mark with methanol to get the stock solution (1 mg/mL). This stock solution was further diluted with same to get the working standard solution

Method-II: 100 mg of amisulpride pure drug was accurately weighed, transferred into a 100 mL volumetric flask containing 50 mL of chloroform and sonicated for about 10 minutes. The volume was made upto the mark with chloroform to get the stock solution (1 mg/mL). The solution was further diluted with same solvent to get the working standard solution.

Recommended procedure

A. For bulk samples

Method-1: Aliquots of standard drug (0.5 to 2.5 mL, 100 µg/mL) solution in methanol was transferred into a series of 125 mL separating funnels and equalized with water. To these flasks added 4 mL of buffer pH 4.0 and 2 mL of methyl orange (0.2% w/v) and the solution was saturated with aqueous phase upto 10 mL. The reaction mixture was shaken for 5 min. The drug-dye complex was then extracted with 10 mL chloroform. The yellow colour organic layer was taken for absorbance measurements and it was estimated at 420 nm against the reagent blank. The amount of AMS was computed from its calibration plot.

Method-II: Aliquots of standard AMS solution (1000 µg/mL) ranging from 0.5 to 2.5 mL were transferred into a series of 10 mL volumetric flasks. To each flask 2.0 mL of chloranilic acid solution was added and allowed to stand at room temperature for 5 min. The final volume was adjusted to 10.0 mL with chloroform and the absorbance was measured at 545 nm against a reagent blank. The amount of AMS in sample was calculated from the Beer-Lambert's plot.

B. For pharmaceutical formulations

For methods-I: Twenty tablets of AMS were weighed and powdered. A quantity of tablet powder equivalent to 50 mg of AMS was accurately weighed and transferred into a 100 mL volumetric flask containing 50 mL of 0.1 N HCl. The solution was sonicated for extracting the drug for about 15 minutes, filtered through a cotton wool and the filtrate was made upto volume with 0.1 N HCl. Then it was appropriately diluted with methanol. Working sample solution was prepared and the procedure described under bulk samples was followed.

For method-II: Twenty tablets of AMS were weighed and powdered. A quantity of tablet powder equivalent to 50 mg of AMS was accurately weighed and transferred into a 100 mL volumetric flask containing 50 mL of chloroform. The solution was sonicated for extracting the drug for about 15 minutes, filtered through a cotton wool and the filtrate was made upto volume with chloroform. The solution was further diluted with chloroform to get the strength of 1000 µg/mL solution. Working sample solution was prepared and the procedure described under bulk samples was followed.

RESULTS AND DISCUSSION

The proposed methods I and II obeyed Beer's law in the concentration range of 5-25

µg/mL with methyl orange and 50-250 µg/mL with chloranilic acid respectively. The optical characteristics and the data concerning to the proposed method is represented in Table 1. Recovery studies were carried out for both the developed methods by addition of known amount of standard drug solution of amisulpride to pre-analysed tablet sample solution at three different concentration levels. The resulting solutions were analyzed by the proposed methods. The recovery (Table 2) was in the range of 99.85 to 101.15 percentages.

Table 1: Optical characteristics, regression data, precision and accuracy of the proposed methods for AMS

Parameter	Method-I	Method-II
λ_{max} (nm)	420	545
Beer's law limits (µg/mL)	5-25	50-250
Molar absorptivity (L. mole^{-1} cm^{-1})	1.112 x 10^3	7.278 x 10^3
Detection limits (µg /mL)	0.17633	2.6116
Sandell's sensitivity (µg /cm ^{2}/0.001 absorbance unit)	0.03322	0.3472
Optimum photometric range (µg /mL)	4-30	45-300
Regression equation (Y = a+ bc):		
Slope (b)	0.0303	0.029
Standard deviation of slope (S_b)	1.674 x 10^{-3}	1.39 x 10^{-5}
Intercept (a)	-0.000357	-0.0018
Standard deviation of intercept (S_a)	1.62 x 10^{-2}	2.29 x 10^{-2}
Standard error of estimation (S_e)	4.28 x 10^{-3}	0.12835
Correlation coefficient (r)	0.9998	0.9999
% Relative standard deviation*	0.953	0.6407
% Range of error (Confidence limits)*		
0.05 level	0.48817	0.5187
0.01 level	0.7655	0.8513
% Error in bulk samples**	0.44	0.75

*Average of six determinations

**Average of three determinations

Table 2: Assay and recovery of AMS in dosage forms

Method	Pharmaceutical formulation	Labelled amount (mg)	Proposed method			Found by reference[45] method ± S.D	% recovery by proposed methods** ± S.D
			Amount found* (mg) ± S.D	t (value)	F (value)		
Method-I	Tablet-I	50	49.8 ± 0.009	0.672	1.249	50.1 ± 0.011	100.29 ± 0.13
	Tablet-II	100	100.6 ± 0.018	0.811	1.204	100.8 ± 0.026	99.98 ± 0.37
	Tablet-III	150	149.5 ± 0.013	0.624	2.117	149.9 ± 0.021	99.86 ± 0.46
Method-II	Tablet-I	50	49.91 ± 0.011	0.628	1.257	50.1 ± 0.012	100.12 ± 0.81
	Tablet-II	100	100.6 ± 0.013	0.735	2.584	100.9 ± 0.014	100.22 ± 0.11
	Tablet-III	150	150.5 ± 0.015	1.114	1.951	150.6 ± 0.012	98.95 ± 0.17

* Average ± standard deviation of six determinations, the t and F- values refer to comparison of the proposed method with reference method; Theoretical values at 95 % confidence limits t = 2.571 and F = 5.05.

** Average of five determinations.

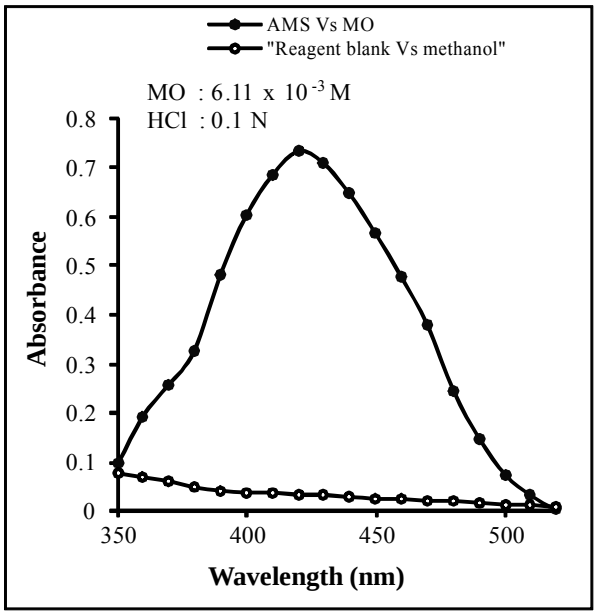


Fig. 1: Absorption spectra of AMS with methyl orange system and its reagent blank

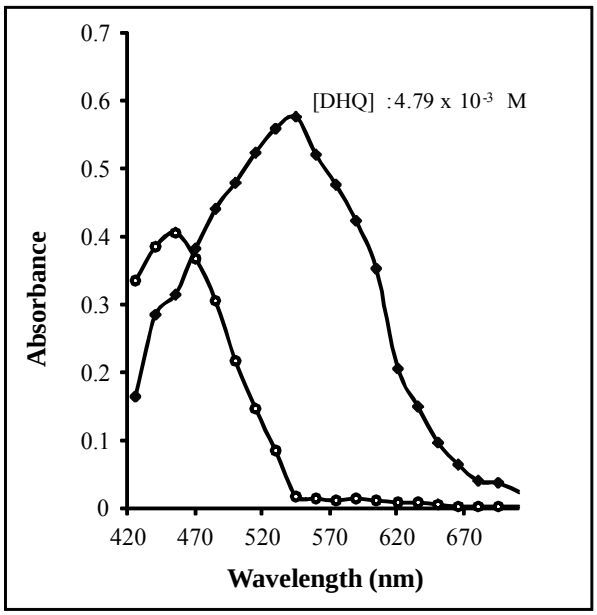


Fig. 1.1: Absorption spectra of AMS with chloranilic acid system and its reagent blank

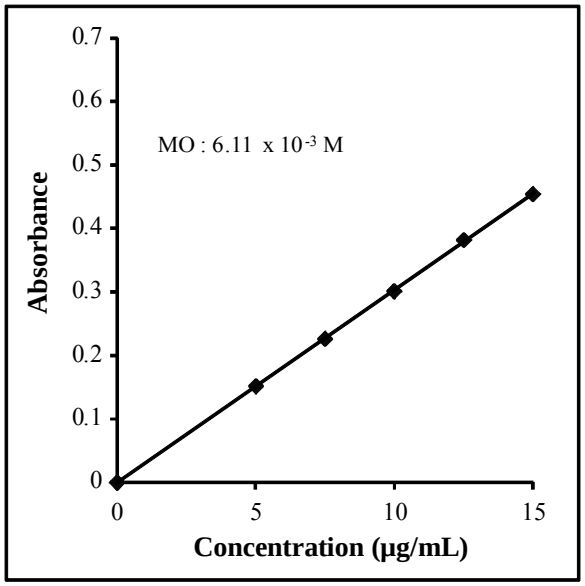


Fig. 1.2: Beer's law plot of AMS with methyl orange system

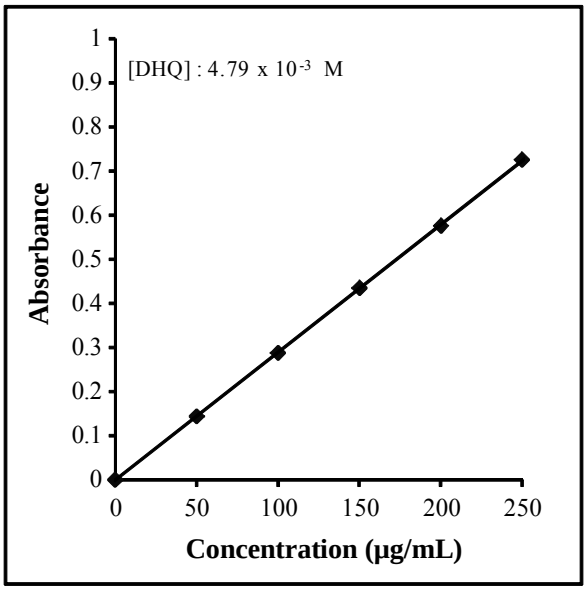
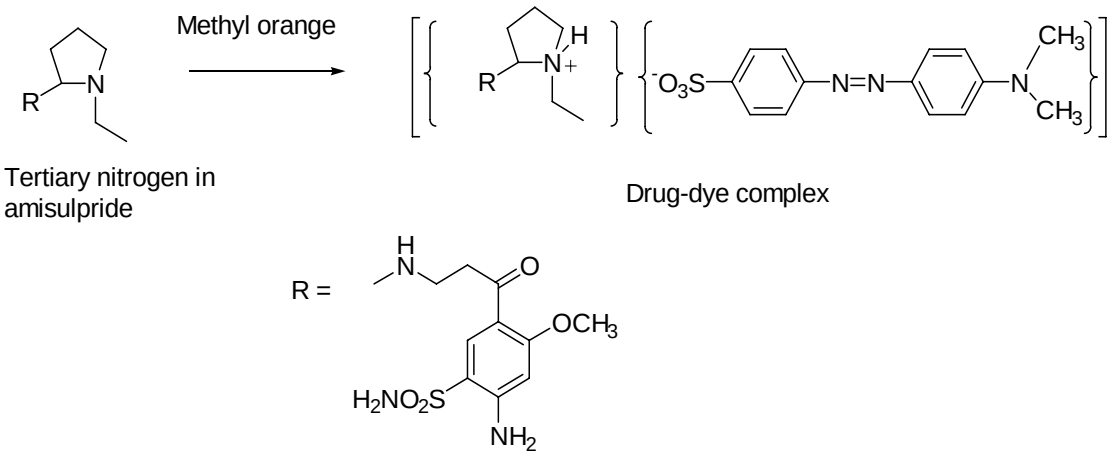
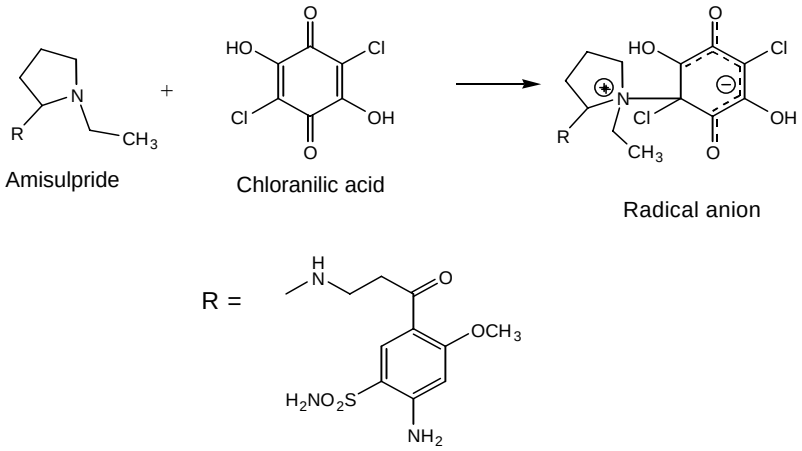


Fig. 1.3: Beer's law plot of AMS With chloranilic acid syste

The chemistry involved in the above proposed methods to give various colored chromogens can be explained by the following Scheme 1 and Scheme 2 for method-I and method-II, respectively.



Scheme 1: Proposed reaction scheme for method-I



Scheme 2: Proposed reaction scheme for method-II

Method-I: As AMS possesses cyclic tertiary nitrogen, it forms ion association complex with acidic dyes [MO], which is extractable into chloroform from the aqueous phase. The protonated nitrogen (positive charge) of AMS molecule in acid medium is expected to attract the oppositely charged part (negative charge) of the dye and behave as a single unit being held together by electrostatic attraction. The slope ratio method of study revealed that the drug to dye mole ratio as 1 : 1. Based on analogy the structure of ion association complex is shown in Scheme 1.

Method-II: AMS possesses cyclic tertiary nitrogen of aliphatic nature and function as electron donor and participates in charge transfer interaction with substituted quinones

like chloranilic acid (CAA). The colored species formed due to formation of radical cation. Based on analogy, the sequence of reactions was given in Scheme 2.

CONCLUSION

There was only few spectrophotometric method reported in the literature for the determination of AMS. The author developed two visible spectrophotometric methods based on the reactivity of different structural units such as primary aromatic amine and aliphatic tertiary amine in AMS. Each method uses a specific reagent and the ε_{max} (molar extinction coefficient) values of each method are different. The sensitivity order of the proposed methods is $M_1 > M_2$.

Statistical analysis of the results shows that the proposed procedures have good precision and accuracy. Results of analysis of pharmaceutical formulations reveal that the proposed methods are suitable for their analysis with virtually no interference of the usual additives presented in pharmaceutical formulations. These methods can be adopted for routine quality control of AMS in bulk and pharmaceutical preparations.

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Abbreviations

AMS = Amisulpride, RP-HPLC = Reversed phase high performance liquid chromatography, CE = Capillary electrophoresis, HPTLC = High performance thin layer chromatography UV = Ultra Violet, CAA = Chloranilic acid.

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