NEW SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF AMISULPRIDE IN PHARMACEUTICAL DOSAGE FORMS

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[1]Chief Operating Officer, Veeda CR, Ahmedabad, Gujarat (State)[2]K.V.S.R Siddhartha College of Pharmaceutical Sciences, Vijayawada-520010 ABSTRACT

Three simple and sensitive visible spectrophotometric methods (A, B & C) for the determination of Amisulpride in bulk and pharmaceutical dosage forms are described. Method A is based on the formation of ion-pair complexes of the drug with acidic dye Methyl Orange [MO] (ëmax: 415 nm). Method B is based on molecular salt formation when the drug reacts with picric acid [PA] (ëmax: 400 nm). Method C is based on charge transfer complex formation of the drug with 2, 5- dihydroxy -3, 6- dichloride 1, 4 – benzoquinone[Chloranilic Acid] (ëmax: 545 nm).These methods were extended to the analysis of pharmaceutical formulations and the results are compared with the reference method.

KEY WORDS: Spectrophotometry, Amisulpride, Pharmaceutical formulations.

1.INTRODUCTION

Amisulpride (AMS) (Swetman; Neil, 2006; British Pharmacopoeia, 2006) is a substituted Benzamide, atypical antipsychotic drug. It is official in BP and EP.Chemically it is 4-Amino-N [(1-ethyl-2-pyrrolidinyl) methyl]-5-(ethyl sulphinyl)-2-benzamide. A thorough survey of the literature has revealed that certain analytical methods like Non aqueous titration (European Pharmacopoeia, 1997), RP-HPLC (Skibinski, 2007), Aqueous capillary titration (CE) (Humaire, 2008), Derivative UV Spectrophotometry (Rav, 1978) and UV method (Pelligrino and Segoloni, 2008) have been reported in the literature for the estimation of AMS in bulk and in dosage forms. There is no analytical report for the estimation of AMS using visible spectrophotometry. Therefore, the authors have made a humble attempt in this direction and succeeded in developing three visible Spectrophotometric methods for the determination of AMS. The present paper describes three visible spectrophotometric methods. Method A is based on the formation of ion-pair complexes of the drug with acidic dye MO under specified experimental conditions. Method B is based on formation of picrate salt between PA and free base of the drug. Method C is based on the reaction between free base of the drug and chloranilic acid.

2.MATERIALS AND METHODS

Instrument: A Systronics Model 2201 UV-VIS spectrophotometer was used for the measurements.

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Reagents: All the chemicals used were of analytical grade. Methyl Orange solution (0.2%w/v in distilled water), Acid phthalate buffer P^H-4 (0.2M Potassium hydrogen phthalate in 0.2M HCl), Picric Acid solution (0.4%w/v in chloroform), Chloranilic acid solution (0.1%w/v in 20 ml isopropyl alcohol made upto 100 ml with chloroform).

Standard Drug Solution for Method A:

About 100 mg of the AMS was accurately weighed and dissolved in 30 ml of 0.1N HCl in a 100 ml volumetric flask and sonicated for 10 minutes. The volume was made upto the mark with the methanol to get a stock solution of (1 mg/ml). This stock solution was further diluted with same to get working standard solution.

Standard Drug Solution Method B & C:

About 100 mg of the AMS was accurately weighed and dissolved in 50 ml of chloroform in a 100 ml volumetric flask and sonicated for 10 minutes. The volume was made upto the mark to get a stock solution of (1 mg/ml). This stock solution was further diluted with same to get working standard solution. **Procedures Method A:**

Aliquots of working standard solution of AMS ranging from (0.5-2.5 ml, 100µg/ml) in methanol were transferred in to a series of 125 ml separating funnels equalized with water. To these flasks, 4 ml of buffer P^H-4 and 2 ml of MO (0.2%w/v) dye were added. The total volume of aqueous phase was adjusted to 10 ml with distilled water and 10 ml chloroform was added. The contents were shaken

for 5 minutes. The two phases were allowed to separate and the absorbance of the yellow colored chromogen was measured at 415 nm against reagent blank and the amount of AMS present in the sample was computed from its calibration curve.

Method B:

Aliquots of working standard solution of AMS ranging from (0.5-2.5ml, 100 µg/ml) were transferred into a series of 10 ml volumetric flasks. To this 2 ml of picric acid was added and allowed to stand at room temperature for 5 minutes. The total volume was made up to 10 ml with chloroform. The absorbance of the colored chromogen was measured at 400 nm against reagent blank. The amount of AMS present in the sample solution was computed from its calibration curve.

Method C:

Aliquots of working standard solution of AMS ranging from (0.5-2.5 ml, 100µg/ml) were transferred into a series of 10 ml volumetric flasks. To these 2 ml of chloranilic acid was added and allowed to stand at room temperature for 5 minutes. Finally the volume was made upto 10 ml with chloroform. The absorbance of the colored chromogen was measured at 545 nm against reagent blank and the amount of AMS present in the sample solution was computed from its calibration curve.

Analysis of Pharmaceutical Formulations

Method A :

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 0.1N HCl. The solution was sonicated for 15 minutes, filtered through cotton wool and the filtrate was made upto volume with methanol. This solution was further diluted to obtain 100 µg/ml solution and analysed as per above procedures.

Methods B & C:

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 15 minutes, filtered through cotton wool and the filtrate was made upto volume with chloroform. This solution was further diluted to obtain 100 µg/ml, 1000 µg/ml solution and analysed as per above procedures. **Recovery Studies**

To study the accuracy, reproducibility and precision of the proposed methods, recovery studies were carried out. Recovery of the added standard was studied at three different levels.

3.RESULTS AND DISCUSSION

The optimum conditions for each method were established by varying one parameter at a time and keeping the others fixed and observing the effect of the product on the absorbance of the colored species and incorporated in the procedure. The optical characteristics and figures of merit are given in Table 1, together with the regression equations obtained by linear least square treatment for the calibration plots. The precision and accuracy were formed by analyzing six replicate samples and containing known amount of drug and their results were summarized in Table 1. Table 2 shows that the values of percentage recovery are between 98%-101% and values of coefficient variation are sufficiently low indicating that the proposed methods are free of interferences from any excipients like starch, talc etc; and the results are reproducible. The systematic study revealed that the proposed methods for the determination of AMS are simple, selective and sensitive with reasonable precision and accuracy. They can be used as alternative methods to reported ones for the routine determination of AMS in pure and in pharmaceutical formulations.

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Table-1: Optical Characteristics, Regression Data, Precision and Accuracy of the Proposed Methods for AMS

Parameter	Method A	Method B	Method C
λ_{max}(nm)	415	400	545
Beer's law limit(µg/ml)	5-25	5-25	50-250
Molar absorptivity (L mol^{-1} cm^{-1})	1.112×10^{3}	8.645×10^{3}	7.278×10^{3}
Detection limits(µg/ml)	0.17633	0.8178	2.6116
sandell's sensitivity (µg/cm^2/0.001 abs. unit)	0.03322	0.04273	0.3472
Optimum Photometric range(µg/ml)	4-30	8-24	45-300
Regression equation(Y=a+bc) Slope(b)	0.0303	0.0233	0.029
Standard Deviation of Slope (S_b)	1.674×10^{-3}	3.82×10^{-3}	1.39×10^{-5}
Intercept(a)	-0.000357	-0.00262	-0.0018
Standard deviation of intercept(S_a)	1.62×10^{-2}	5.77×10^{-2}	2.29×10^{-2}
Standard error of estimation(S_e)	4.28×10^{-3}	0.04633	0.12835
Correlation coefficient(r)	0.9998	0.9990	0.9999
%Relative standard deviation*	0.953	0.756	0.6407
%Range of Error (Confidence limits)* 0.05 level 0.01 level	0.48817 0.7655	0.9699 1.5210	0.5187 0.8513
%Error in bulk samples**	0.44	-0.19	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/Tablet)	Proposed Method			Found by Brotton (1939) method ± S.D	% Recovery by proposed methods**± S.D
			Amount found*(mg)± S.D	T (value)	F (value)		
A	Tablet-1	50	49.8±0.012	0.672	1.249	50.1±0.011	100.29±0.013
	Tablet-2	100	100.6±0.018	0.811	1.204	100.8±0.026	99.98±0.37
	Tablet-3	150	149.5±0.013	0.624	2.117	149.9±0.021	99.86±0.46
B	Tablet-1	50	50.4±0.013	1.271	1.401	49.8±0.009	99.88±0.25
	Tablet-2	100	100.3±0.015	0.532	1.345	99.89±0.014	99.12±0.19
	Tablet-3	150	150.8±0.014	0.571	0.994	150.3±0.011	98.72±0.25
C	Tablet-1	50	49.91±0.011	0.628	1.257	50.1±0.012	100.12±0.81
	Tablet-2	100	100.6±0.013	0.735	2.584	100.9±0.014	100.22±0.11
	Tablet-3	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 with reference method. Theoretical values at 95% confidence limits t = 2.571 and F = 5.05.

** Average of five determinations.

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