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New spectrophotometric methods for the determination of amisulpride in pharmaceutical dosage forms

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ABSTRACT

Three simple and sensitive visible spectrophotometric methods (A, B, & C) for the determination of Amisulpride in bulk and pharmaceutical dosage forms are described. They are based on the formation of coolred species by treatig its diazotized product with Bratton-Marshall (B.M.) reagent (method A; λ_{max} 525 nm) or pure drug with 3-methyl-2-benzothiazolinone hydraze hydrochloride (MBTH) in the presence of Ferric chloride (method B; λ_{max} 580 nm) or with Folin-Ciocalteau phenol's reagent under alkaline conditions (method C; λ_{max} 625 nm) . These methods were extended to the analysis of pharmaceutical formulation and result compared with the reference method.

Key words: Spectrophotometry, amisulpride, pharmaceutical formulations.

INTRODUCTION

Amisulpride[1-3] (AMS) is a substituted Benzamide atpyical antipsychotic drug. It is official in BP and EP/Chemically it is 4-Amino-N [(1-ethyl-2-pyrolidinyl) methyl]-5-(ethyl sulphinyl)-2-benzamide. A through survey of the literature has revealed that certain analytical methods like Non aqueous titration[4]. RP-HPLC[5]. Aqueous capillary titration (CE)[6]. Derivative UV Spectrophotometry[7] and UV method[8] 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 spectophotometry. Therefore, the authors have a humble attempt in this direction and suceeded in developing their visible spectrophotometric methods for the determination of AMS.

The present paper described three visible spectrophotometric methods based on primary aromatic amino group present in the drug. Method is based on the coupling of the diazotized drug with B.M. reagent to form a pink colored species. Huning and Fritsch described oxidative coupling of MBTH with amines in presence of an oxidant. Method B utilizes this reaction for the estimation of AMS to form a colored chromogen. In method C FC reagent reacts with AMS under alkaline conditions to form a blue colored species.

MATERIAL AND METHODS

Instrument

A systronics Model 2201 UV-VIS spectrophotometer was used for the measurements.

Reagents

All the chemicals used were of analytical grade. Aqueous solutions of Sodium Nitrite (0.1% w/v), HCl (5 N), Amonium Sulfamate (0.5% w/v), B.M. reagent (0.1% w/v), MBTH (0.2% w/v), Ferric chloride (0.1 w/v) and Sodium Carbonate (20% w/v) were perpared. The commerically available FC reagent (2N) was taken and diluted suitably with distilled water.

Standard drug solution

About 10 mg of the AMs was accurately

weighed and dissolved in 20 ml of 0.1 N HCL in a 100ml volumetric flask and sonicated for 15 minutes. The volume was made the mark with the same and diluted to get required working standard solution.

Procedures

Method A

Aliquots of standard drug solution (0.2-1.0 ml, 100µg/ml) were transferred into a series of 10 ml volumetric flasks. To each flask added 1ml of 5N Hydrocholoric acid and 1ml of Sodium Nitrite, mixed well and kept aside for 5 minutes. To this then added 1 ml of Ammonium sulfa mate with shaking to neutralize excess nitrous acid. Finally added 1 ml of B.M. reagent mixed well and kept aside for 20 minutes to carry out the reaction. The purple red coloured chromogen thus formed was measured at 525 nm against reagent blank. The AMS was computed from its calibration plot.

Method B

Aliquots of standard drug solution (0.2-1.0ml, 100µg/ml) were trasferred into a series of 10ml volumetric flask. A 1.5 ml portion of Ferric Chloride solution was added to each flask and kept aside for 2 minutes at room temperature. The absorbances were measured at 580 nm against a reagent blank. The concentration of AMS was compound from its calibration graph.

Method C

Aliqouts of standard drug solution (0.2-1.0 ml, 100µg/ml) were transferred into a series of 10 ml volumetric flasks. To this added 1 ml of FC reagent and 2ml of Sodium Carbonate solution, shaken well and kept aside for 15 minutes. The blue coloured chromogen thus formed was measured at 625 nm against reagent blank. The amount of AMS was computed from its calibration plot.

Analysis of pharmaceutical formulations

Twenty tablets of AMS were weighed and powdered. A quantity of tablet power 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 0.1N HCl. This

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)	525	280	625
Beer's law limit (µg/ml)	1-5	2-12	10-50
Molar absorptivity (L mol^{-1} cm^{-1})	3.731×10^{5}	2.725×10^{4}	1.112×10^{4}
Detection limits (µg/ml)	0.028938	0.433523	0.17633
Sand ell's sensitivity (µg/cm^2/0.001 abs. unit)	0.009901	0.01342	0.03322
Optimum photometric range (µg/ml)	1.0-8.0	1.5-15	5-60
Regression equation (Y=a+b+c) slope (b)	0.1022	0.036479	0.0098
Standard Deviation of slope (S_b)	1.39×10^{-5}	3.96×10^{-3}	3.96×10^{-3}
Intercept (a)	0.000333	0.00029	0.0014
Standard deviation of intercept (S_a)	2.298×10^{-3}	0.004792	4.792×10^{-2}
Standard error of estimation (S_e)	4.94×10^{-3}	3.33×10^{-3}	4.77×10^{-3}
Correlation coefficient (r)	0.99996	0.9995	0.9999
% Relative standard deviation*	0.5976	0.2743	0.9247
% Range of Error (Confidence limits)*			
0.05 level	0.627	0.2879	0.699
0.01 level	0.983	1.4515	01.5210
% Error in bulk samples**	0.33	-0.51	0.25

*Average of six determinations

**Average of three determinations

solution was further diluted to obtain 100µg/ml solution.

Recovery studies

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

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 cailbration plots. The pecision 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 and between 98%-102% and values of coefficient variation are sufficiently low indicating that the proposed methods are free to interferences from any excipients like starch, talc etc, and results are reproducible. The systematic study revealed that the proposed methods for the determination of AMS are simple,

Table 2: Assay and Recovery of AMS in Tablet forms

Methods	Pharmace utical formulation	Labelled amount	Proposed method			Found by reference method± S.d.	% Recovery by propsed method± S.D.
			Amount found* (mg)±S.D.	T value	F value		
a	Tablet - 1	50	50.02+0.018	0.588	1.212	50.3+0.012	100.05+0.21
	Tablet - 2	100	99.8+0.012	0.826	1.457	100.4+0.008	99.89+0.18
	Tablet - 3	150	1.49.9+0.011	1.023	2.043	150.1+0.005	101.15+0.31
B	Tablet - 1	50	49.4+0.0.013	0.543	1.452	49.7+0.015	100.12+0.09
	Tablet - 2	100	100.2+0.015	1.327	1.978	100.8+0.011	99.89+0.96
	Tablet - 3	150	150.9+0.021	0.562	1.758	149.05+0.016	100.11+0.14
C	Tablet - 1	50	49.8+0.012	0.719	2.531	49.9+0.011	99.26+0.55
	Tablet - 2	100	100.8+0.009	0.541	1.233	100.4+0.084	100.04+0.12
	Tablet - 3	150	150.6+0.017	10.23	1.651	148.99+0.022	99.95+0.11

*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

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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