

Semi-Micro Determination of Some Antidepressants in Pure Form and in Their Pharmaceutical Preparations with Ammonium Metavanadate(V) Reagent

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The semi-microdetermination of some antidepressant pure compounds and their pharmaceutical preparations with ammonium metavanadate(V) reagent has been done.

INTRODUCTION

The antidepressives are employed to treat patients suffering from endogenous depressions and certain forms of schizophrenia characterized by apathy. They are sometimes called psychic energizers or thymoleptics and to a considerable extent have replaced electroconvulsive therapy. The antidepressives are not centrally acting depressants. They antagonize some of the central actions of the tranquilizers and are also used primarily to treatmental illness¹. Imipramine hydrochloride, amitriptyline hydrochloride etc. are generally used as anti-depressants.

These drugs show several side effects which include drymouth, tachycardia, blurred vision and constipation which are due to the atropine like properties. In addition, headache, dizziness as well as over-stimulation has also been reported. Due to their antidepressant activity and owing to a great medicinal importance, these drugs were assayed by several workers. Gaur *et al.*² used gravimetric, volumetric and colorimetric methods in the estimation of amitriptyline hydrochloride. Schneider³ developed an improved paper chromatographic procedure for the determination of imipramine and some of its metabolites. Suthamer Craig⁴ improved a liquid chromatography separation of some antidepressants. Magathais *et al.*⁵ spectrophotometrically estimated imipramine hydrochloride using ferric ion.

A survey of literature reveals that vanadium(V) reagent has not been used for the determination of phenols till now. Vanadium(V) reagent has been used as a strong oxidising reagent. This inspired us to undertake present study. Here we have developed a quick and convenient method for microdetermination of some

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drugs like imipramine hydrochloride, amitriptyline hydrochloride and nitroxazepine hydrochloride pure compound and its tablets.

EXPERIMENTAL

Reagents and Solutions

Reagent ammonium metavanadate (B.D.H.) 3.5 gm. accurately weighed was dissolved in 10 ml of concentrated sulphuric acid (AnalaR, sp. gr. 1.84) in a 100 ml volumetric flask and made up to the mark with distilled water. Stock solutions of different compounds (1 mg/1 ml) were prepared by dissolving 50 mg of the pure compound in 50 ml volumetric flask in distilled water.

Apparatus

Micropipettes (least count = 0.05 ml, 0.01 ml), micro burettes (least count = 0.01 ml), Erlenmeyer flasks of 100 ml and 150 ml capacity, volumetric flasks of 25, 50, 100, 250, 500, 1000 and 2000 ml capacity were used.

General Procedure

Aliquots containing 1.5 mg of the sample were taken in a 100 ml. Erlenmeyer flask followed by the addition of 2 ml of 0.3 N vanadium(V) reagent and 5 ml of 8 N sulphuric acid. The reaction contents were shaken gently and kept on a boiling water bath for a prescribed reaction time as 20 minutes for imipramine hydrochloride in pure form and its pharmaceutical preparations and amitriptylene hydrochloride in pure form and its pharmaceutical preparations while 25 minutes for nitroxazepine in pure form and its pharmaceutical preparations. After the reaction was over the reaction mixture was cooled to room temperature. The unconsumed vanadium(V) reagent was titrated against 0.025 N ferrous ammonium sulphate, using N-phenyl anthranilic acid as an indicator.

A blank experiment was also run under identical conditions using all the reagents except the sample. Recovery of the sample was calculated by the following expression

$$\text{mg of the sample} = \frac{M \times N(B - S)}{n}$$

where, M = molecular weight of the sample,

N = molarity of ferrous ammonium sulphate.

S = volume of F.A.S. consumed to titrate the sample experiment,

B = volume of F.A.S. consumed to titrate the blank experiment, and

n = number of moles of vanadium(V) reagent consumed per mole of the sample.

A consolidated Table 1 is given which describes the results obtained with all antidepressant compounds. For evaluating results on an accurate scale and testing the utility of the method, a large number of experiments were carried out and

different variables were calculated. Standard deviation and coefficient of variation was also calculated. For calculating standard deviation in a particular estimation the experiment has to be repeated several times. For each sample size about 10 to 12 estimations are done and the values having less variation in percentage recovery noted. At least 9 such readings are selected and the results are recorded. For each sample size ranging from 1 to 10 mg the same practice is adopted.

Standard deviation (S.D.) is calculated by the following expression:

$$\text{S.D.} = \frac{(X_1 - X)^2 + (X_2 - X)^2 + (X_3 - X)^2 + \dots + (X_n - X)^2}{(n - 1)}$$

where, X = mean value or average value of the amount obtained by calculation and X_1, X_2 and X_3 = Amount obtained by calculation. After getting S.D. values the coefficient of variation is also calculated by the following expression.

$$\text{Coefficient of variation} = \frac{\text{S.D.} \times 100}{X^-}$$

where X^- = mean value or average value of the amount obtained by calculation.

RESULTS AND DISCUSSION

The effect of variables such as reaction time, reagent concentration, volume of sulphuric acid and temperature were studied. It was noticed that imipramine hydrochloride and amitriptylene hydrochloride need 20 minutes while nitroxazepine hydrochloride needs 25 minutes for complete reaction. Further increase in reaction time does not give any improvement in the stoichiometry as well as the recovery of the sample. To enhance the reactivity of the reagent and to get quick reaction the ionic reaction medium was tested. It was found that the presence of 5 ml of 8 N sulphuric acid is essential to provide ionic medium to vanadium(V) 0.3 N reagent. A low concentration of sulphuric acid although helps in reaction but gives inaccurate results. Incomplete reaction may be due to incomplete ionisation of vanadium(V) reagent. A higher concentration of sulphuric acid is a wastage and unnecessary. Moreover, a higher concentration of sulphuric acid tends to give inconsistent results. After studying the variation in the concentration of vanadium(V) reagent it was found that 0.3 N concentration of vanadium(V) reagent is sufficient for quantitative results. A lower concentration tends to give lower results because of incomplete results while higher concentration is a wastage of the reagent. A large difference in the titre values of the blank and of the actual experiment because of higher concentration of vanadium(V) may also add to inaccuracy.

Stoichiometric determination shows that imipramine hydrochloride and amitriptylene hydrochloride consume four equivalents of vanadium(V) reagent while nitroxazepine hydrochloride consumes six equivalents of vanadium(V) reagent.

TABLE 1
MICRODETERMINATION OF SOME ANTIDEPRESSANT COMPOUNDS WITH VANADIUM(V) (0.3) REAGENT

Sample Name	Amount taken (ml)	Amount present (mg)	Reaction time (min)	Amount obtained by calculation (mg)	Molarity	Error	Standard deviation	Coefficient of variation
1. Imipramine hydrochloride	5	5.015	20	5.0641	4	+0.98	.0548	1.0890
				5.0626		+0.95		
				4.9684		-0.93		
(a) Antidep (tab)	5	5.015	20	5.0616	4	+0.93	.0548	1.0894
				5.0621		+0.94		
				4.9669		-0.96		
(b) Deprodiaz (tab)	5	5.015	20	4.9669	4	-0.96	.0471	0.9364
				5.0616		+0.93		
				5.0611		+0.92		
(c) Depsonil (tab)	5	5.015	20	5.0606	4	+0.91	.0463	0.9203
				4.9689		-0.92		
				5.0621		+0.94		
(d) Tancodep (tab)	5	5.015	20	4.9665	4	-0.93	.0486	0.9661
				5.0631		+0.96		
				5.0626		+0.95		
2. Amitriptyline hydrochloride	5	5.015	20	5.0561	4	+0.82	.0420	0.8352
				4.9724		-0.85		
				5.0566		+0.83		

Table 1 Contd.

Sample Name	Amount taken (ml)	Amount present (mg)	Reaction time (min)	Amount obtained by calculation (mg)	Molarity	Error	Standard deviation	Coefficient of variation
(a) Amitral (tab)	5	5.015	20	5.0641	4	+0.98	0.0556	1.1051
				5.0626		+0.95		
				4.9669		-0.96		
(b) Amiline (tab)	5	5.015	20	5.0636	4	+0.97	0.0546	1.0851
				5.0626		+0.95		
				4.9884		-0.93		
(c) Tryptomer (tab)	5	5.015	20	5.0626	4	+0.95	0.0539	1.0714
				5.0611		+0.92		
				4.9684		-0.93		
(d) Quietal (tab)	5	5.015	20	5.0611	4	+0.93	0.0533	1.0594
				5.0626		+0.95		
				4.9694		-0.91		
3. Nitroxazepine hydrochloride	5	5.010	25	5.0590	6	+0.98	0.0547	1.0882
				5.0575		+0.95		
				4.9635		-0.93		
(a) Sintamil (tab)	5	5.010	25	5.0555	6	+0.91	0.0539	1.0726
				5.0565		+0.95		
				4.9625		-0.93		

In each case three determinations were done.

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