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Determination of tetraethyl thiuram disulphide in commercial drugs and rubber accelerators by pulse polarography

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A simple and accurate pulse polarographic method has been described for the determination of tetraethyl thiuram disulphide, based on its reduction at DME in dimethylformamide medium in the presence of pyridinium perchlorate. The analysis has been carried out by normal pulse and differential pulse polarography using linear calibration plots. The method has been successfully applied to the analysis of a commercial drug (antabuse) and rubber accelerators (tuad and thiurad) for the purpose of quality control.

Tetraethyl thiuram disulphide(TETD) is a compound of pharmaceutical and industrial importance. It is an active ingredient of a drug, antabuse[1], used for the treatment of alcoholism. Ethyl tuad and ethyl thiurad are commercial formulations of TETD used as vulcanisation accelerators in rubber industry[2]. The method commonly employed for analysing TETD in its formulated products is based on its acid hydrolysis followed by measuring the evolved carbon disulphide titrimetrically, colorimetrically or by derivative spectrometry[3-6]. These methods are tedious, time-consuming and require special apparatus. In view of the difficulty of dispersing TETD, a water-insoluble material, the analysis is required to be repeated several times in order to obtain consistent results. Therefore, considerable experimental skill is required in order to obtain good results. Further, the stoichiometry of the hydrolysis reaction of TETD is not yet clear. This, therefore, creates need for a method which besides being simple and accurate should be rapid.

TETD is easily reducible to the corresponding diethyl dithiocarbamate,

$$(C_2H_5)_2\ N.CS.S.S.CS.N(C_2H_5)_2 + 2e \rightarrow 2(C_2H_5)_2\ N.CS.S^-$$

thus enabling its determination by polarography. However, TETD is not only insoluble in water but the compound as well as its reduction oduct, i.e., diethyl dithiocarbamate, tend to react with acids and bases commonly used as supporting electrolytes in polarography. The determination of this compound by non-aqueous polarography (through the use of a suitable solvent-electrolyte system) would, therefore, be advantageous[7]. The present investigation demonstrates the application of non-aqueous pulse-polarography for the determination of TETD in commercial products. The observation that TETD is smoothly reduced at dropping mercury electrode (DME) in dimethylformamide medium in the presence of pyridinium perchlorate as supporting electrolyte, giving a well-defined, diffusion-controlled reduction wave at −0.39 V(vs SCE) has

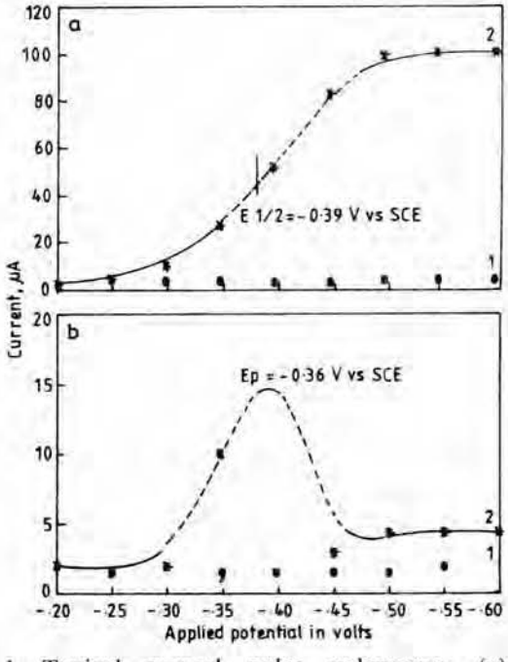

Fig 1—Typical normal pulse polarogram (a) and differential pulse polarogram (b) of TETD in 0.01*M* Pyridinium perchlorate at 23±1°C. [1, Py, ClO_4; 2, TETD, Initial applied voltage =-50 mV vs SCE; Height of Hg pool =3.5 cm; H_{eff} Value =150 cm; CC compensation =5.0; IR compensation =0; Time constant =20 ms; Sensitivity =100μA/V for NPP, 10μA/V for DPP; Pulse amplitude = 50mV; Drop time = 0.5 s; Acquisition = Fast; O/P zero = 485; Scan = Normal. On polarocord X-axis = 100 mV/cm; Y-axis =500 mV/cm

Table 1—Determination of tetraethylthiuram disulphide by pulse polarography

Am of TETD taken, μg	NPP		DPP	
	Mean diffusion current I_d, μA	TETD found± μg	Mean peak current I_p, μA	TETD found± μg
3	46.80	3.02±0.02	7.87	2.97±0.02
6	92.70	5.98±0.04	15.88	5.99±0.03
12	187.55	12.10±0.08	31.54	11.90±0.06
15	230.65	14.88±0.08	40.02	15.10±0.06
20	307.20	19.82±0.08	53.32	20.12±0.07

±Values are mean of three determinations with standard deviation

been made the basis of the present method. The analysis has been accomplished by normal pulse polarography (NPP) and differential pulse polarography (DPP) using linear calibration plots. The method has been successfully adapted to the analysis of antabuse (drug) and ethyl tuad and ethyl thiurad (rubber accelerators).

Experimental

The voltammetric measurements were made on an Elico(India) pulse polarograph (model CL-90) coupled with an X-Y polarocord (model LR-108). The electrode system consisted of a dropping mercury electrode (DME) as the working electrode, a modified saturated calomel electrode (methanolic potassium chloride instead of aqueous) as a reference electrode and platinum electrode as an auxillary electrode. Dimethylformamide(BDH) was purified by storing it over anhydrous sodium carbonate (AR) for two days. The solvent was decanted off, distilled and the fraction distilling at 148.5-149.5° was collected in coloured bottles. All chemicals used in this study were of AR grade. Tetraethyl thiuram disulphide (Fluka) was recrystallised before use. All polarograms were recorded in an inert atmosphere of nitrogen at room temperature (23±1°C).

Procedure

A solution of pyridinium perchlorate in DMF (90 ml, 0.01 *M*) was taken in the polarographic cell. To this, aliquots (0.1-1.0 ml) of standard solution of tetraethyl thiuram disulphide (0.01 m*M* in DMF) and 2 ml of Triton-X in DMF (0.002%) as suppressor were added and the final volume was made up to 100 ml with DMF. Nitrogen gas was bubbled through this solution for five min. The polarograms (both NPP and DPP) of this solution were recorded (Fig. 1). A blank polarogram was also recorded.

Table 2—Assay of some formulated products based on TETD

Formulation	Active ingredient	TETD, μg			
		Taken	Added	Found	
				NPP	DPP
Antabuse tablets	500 mg per tablet	2.5	–	2.45	2.48
		15	–	14.85	14.90
		10	10	20.05	19.80
		10	15	24.78	25.06
Ethyl tuad	100%	3	–	2.97	3.01
		6	–	6.03	5.95
		8	7	14.80	16.06
		10	15	24.80	25.02
Ethyl Thiurad	100%	5	–	5.01	4.96
		10	–	9.92	9.95
		15	5	20.08	19.85
		20	5	24.80	25.05

Results and discussion

The voltammograms of TETD, showed that the wave/peak height was proportional to the amount of compound taken; the concentration relationship using NPP and DPP was linear up to 48 μg/ml and 5 μg/ml of TETD respectively (Table 1).

Analysis of real samples

Samples of the drug formulation, antabuse, containing 500 mg active ingredient per tablet and two technical formulations of rubber accelerators, viz., ethyl tuad and ethyl thiurad, each containing 100% active ingredient, were analysed. A single large sample of each was weighed, shaken with dimethylformamide at –23°C and filtered through a Whatman (No. 40) filter paper. The residue (if any) was washed 2-3 times with dimethylformamide. The filtrate and washings were diluted to a known volume with the same solvent. Suitable aliquots of the solution were taken in the polarographic cell and processed for analysis as described above. In order to check the accuracy of the method, known amounts of pure TETD were also added to the test solutions of each formulation and processed similarly. The results are given in Table 2.

The proposed pulse-polarographic method is simple, rapid and more sensitive. The minimum amount of TETD which can be determined under the

given experimental conditions is 0.4 μg ml^{-1} by NPP and 0.04 μg ml^{-1} by DPP. TETD in the range 3-20 μg can be determined with maximum relative standard deviation (RSD) of 0.7% (Table 1). The method when applied to the assay of commercial products based on TETD, gave recoveries in the range of 98.0-100.3%, in the analysis of antabuse tablets of the nominal content and in the range of 98.7-100.5% in the analysis of rubber accelerators with RSD's in the ranges 0.4-0.8% and 0.3-0.8% respectively (Table 2). The manufacturer's specification of each formulated product has separately been established by an independent method[3].

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