Voltammetric Determination of Promethazine by Platinum and Glassy Carbon Electrodes

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The electrochemical oxidation of promethazine was studied by linear sweep and cyclic voltammetry on platinum and glassy carbon electrodes. The dependence of current intensities and potentials on pH, concentration, scan rate and nature of the buffer was examined.

Linear calibration plots were obtained in phosphate buffer (pH 7.0) and acetate buffer (pH 4.7) for platinum and glassy carbon electrode, respectively.

Key words: Promethazine, voltammetry, platinum and glassy carbon electrodes.

Introduction

Promethazine 10-[(2-(dimethylamino) propyl phenothiazine] is a drug widely used in pharmaceutical formulations. It is being used as an antihistaminic and antiemetic drug. But it also has some antiserotoninergic, anticholinergic and marked local anaesthetic properties.

Methods for the determination of promethazine include FIA using fluorimetric detector[1,2] spectrophotometry[3,4], gas chromatography[5] and high-performance liquid chromatography[6-8]. Jarbawi and Heineman studied the electrochemical oxidation of promethazine and various tranquilizers on a wax-impregnated graphite electrode by extraction-adsorption of the drugs through differential pulse voltammetry[9]. The Determination of promethazine and related compounds on carbon paste electrodes modified with fatty acids was studied[10]. The electrochemical behavior of promethazine on lipid-modified carbon paste electrodes was also reported[11]. The electrochemistry of promethazine on a nafion-coated glassy carbon electrode[12,13] and a phospholipid/ cholesterol modified glassy carbon electrode[14] was described.

A common property of all N-substituted phenothiazines is that they are easily oxidized, either chemically or electrolytically. The investigation of the electrooxidation of the drugs gives some information about clinical activities. An explanation of electrode reaction may provide information about drug-receptor interaction. The interaction between the dopamine receptor and phenothiazines is very important in drug activity, and the electrode may be regarded as a simple model of the receptor. In this study, platinum and glassy carbon electrodes were selected, as they are very commonly used in invivo studies and as electrohemical detector for high-pressure liquid chromatography and there is no voltammetric paper using glassy carbon and platinum electrodes related to this substance in the literature.

Experimental

Apparatus

The voltammetric measurements were performed on a PRG-3 polarograph (Tacussel) connected to an EPL-2 recorder (Tacussel). All the potentials were measured *vs.* a saturated calomel electrode (SCE), and the auxiliary electrode was a platinum wire. Two working electrodes were used: a platinum wire (Tacussel, diammeter: 1 mm, length: 15,7 mm) and a glassy carbon electrode (Tacussel XM 540, area 0.47 sq.cm). The cell was covered with aluminium foil to protect it from light.

Reagents

Promethazine hydrochloride (generously provided by GÜNSA Drug Industries Inc. Adana, TURKEY) was used without further purification.

All other reagents were of analytical grade.

Stock solutions were prepared daily by dissolving promethazine in selected supporting electrolyte. Alkaline media were avoided, as promethazine then undergoes a precipitation reaction. Double distilled water was used to prepare the solutions.

Pre-treatment of working electrodes

Pre-treatment of the platinum electrode was performed by anodising the electrode at +1.2 V for five minutes and, after washing it thoroughly with doubly distilled water, allowing it to stand at +0.1 V for fifteen minutes in deaerated 0.5 M sulphuric acid.

Activation of the glassy carbon electrode was obtained by polishing the electrode with alumina for every 10-15 measurements and polarising the electrode for five minutes at +1.5 V, followed by the application of -1.0 V for 2-3 s in 0.1 M potassium nitrate solution before each experiment.

Results and Discussion

Experiments on the platinum electrode

In 0.5 M sulphuric acid, the electrooxidation of promethazine occurs as two well defined steps at about +0.80 V and +1.05 V (Figure 1). A common property of all the N-substituted phenothiazines is that they are easily oxidised, either chemically or electrolytically[15,16]. According to our knowledge about the electrooxidation of phenothiazines, the first oxidation step of promethazine, resulting simply from the loss of an electron from the parent compound, produces the corresponding cation-free radical, which is stable in acidic solutions, but whose life time is shorter in less acidic media. The second step is further 1-electron oxidation of the free radical to the colorless sulfoxide (Scheme 1).

On the cathodic branch, the peak current at about +0.2 V, which corresponds to the reduction of the surface layers of the platinum electrode, was lower than that obtained in supporting elecrolyte. This phenomenon may arise because the formation of the oxidation products hinders surface oxidation to some extent. Moreover, in solutions more concentrated than 8.10^{-4} M, this single cathodic peak split into two overlapping peaks. Cyclic voltammetry demonstrated the total irreversibility of this system at scan rates from 10 m Vs^{-1} to 100 m Vs^{-1}.

The second peak, at about 1.1 V, which became sharper as the concentration increased, was used for analytical evaluations.
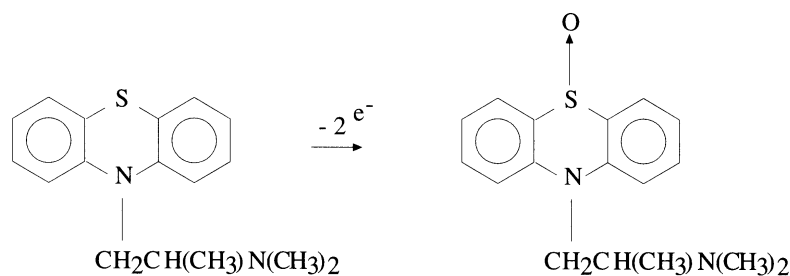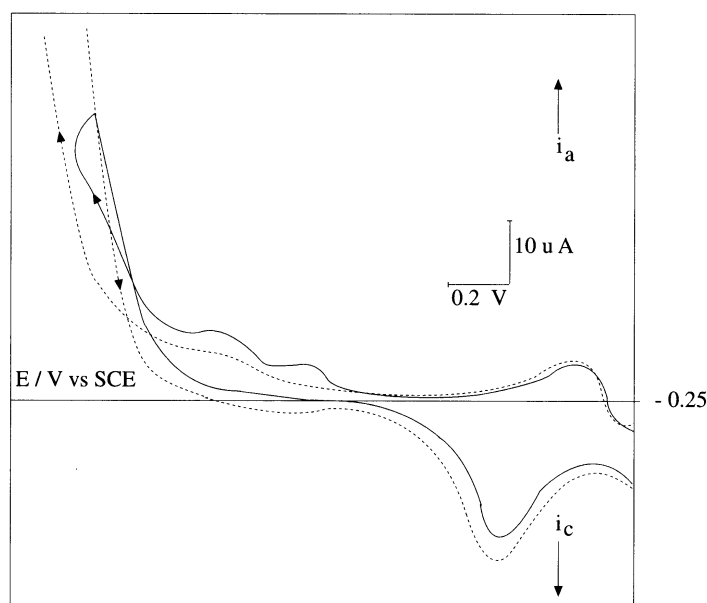

Scheme 1. Oxidation pathway of promethazine

Figure 1. Cyclic voltammogram of 8.10^{-4} M promethazine in 0.5 M H_2SO_4 at platinum electrode. Scan rate: 100 mVs^{-1}. Dotted line represents the residual current

The effect of potential scan rate on the peak current and the peak potential for promethazine was evaluated. The linear increase of the oxidation peak current with the square root of the scan rate over the 10-100 mVs^{-1} range, with a slope of 1.68 (correlation coefficient 0.9999), showed the diffusion control of the process. The peak potentials shifted to more positive values by increasing the scan rate. The plot of peak potential versus the square root of the scan rate, with a slope of 12.36 (correlation coefficient 0.9996), was also linear.

The effect of the solution pH on the peak current and peak potential was evaluated (Figure 2). By increasing the pH, the peak intensity reached a maximum at pH 7.0 and decreased again; hence this pH value was chosen to carry out the electroanalytical study. The peak potential showed the behavior depicted in Figure 2b. The influence of pH on the second peak current can be interpreted as a general increase with pH in the pH range of 1.5-7.0, except pH values 4.7 and 6.2 with the radical disappearence with increasing pH. At higher pH's (pH 7.6, 8.5), the reaction rate of the free radical decreases.
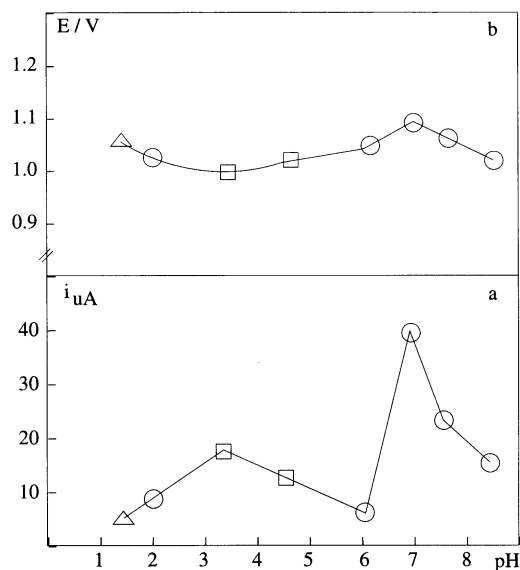
Figure 2. Effect of the pH on the promethazine peak current (a) and peak potential (b). Promethazine concentration, 4.10^{-4} M; Scan rate; 100 mVs^{-1}; Electrode Pt; (Δ)H_2SO_4, ($\square$) acetate buffer; ($\circ$) phosphate buffer

Experiments on the glassy carbon electrode

In the case of the glassy carbon electrode, we observed three oxidation steps. The third step at +1.55 V in 0.5 M H_2SO_4 is related to the further oxidation of promethazine 5-sulphoxide[17]. This step disappeared when the platinum electrode was used, due to its overlap with background electrolyte discharge.

The shape of the anodic step at less positive potential was markedly dependent on pH (Figure 3). In strongly acidic solutions, this step split into two or three peaks. As pH increased only a single peak appeared. Nearly the same pH-peak current dependence can be seen on the curve in Figure 3. In alkaline media, peak height decreased. For this reason, the peak in an acetate buffer of pH 4.7 was chosen for analytical purposes.
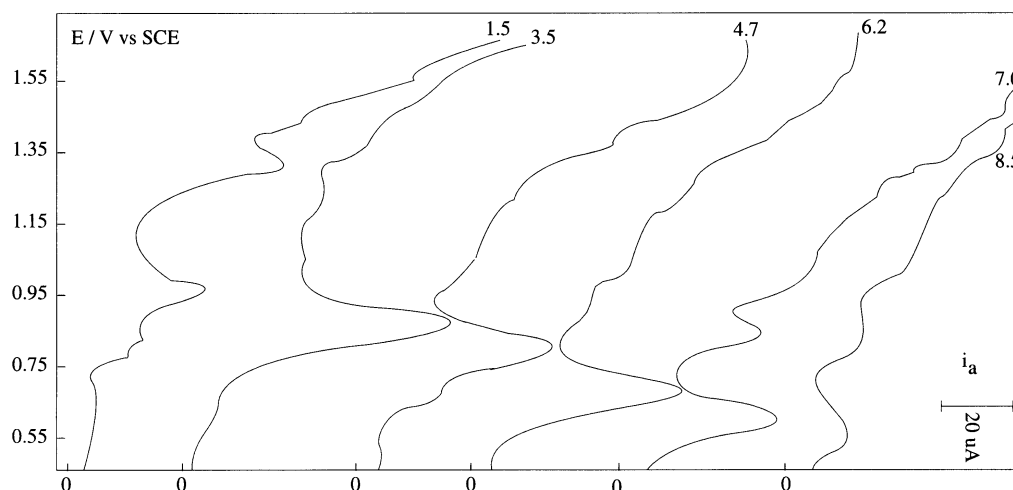

Figure 3. Influence of pH on the anodic voltammograms of 4.10^{-4} M promethazine on the glassy carbon electrode Scan rate: 100 mVs^{-1}

The linear relationship existing between peak current and the square root of scan rate over the 10-100 mVs^{-1} range, with a slope of 7.17 (correlation coefficient 0.9999) showed the diffusion control of process. A

plot of peak potential versus the square root of the scan rate gave a straight line with a the slope of 24.51 (correlation coefficient 0.9985).

Quantitative Determination

Various electrolytes, e.g., 0.5 M sulphuric acid, acetate buffer (0.2 M, pH 3.5-4.7) and phosphate buffer (0.2 M, pH 2, 4.7-8.5), were evaluated as suitable media for the quantitative determination of promethazine. Best results (with respect to peak current enhancement and peak shape) were obtained at a scan rate of 100 mVs^{-1} with a phosphate buffer of pH 7.0 and an acetate buffer of pH 4.7 for a platinum and a glassy carbon elecrode, respectively. The peak current at about 1.1 V at the platinum and 0.8 V on the glassy carbon electrode were linearly dependent on concentrations.

The detection limits were 8.10^{-5} M for the platinum electrode and $2. \ 10^{-5}$ M for the glassy carbon electrode. The reproducibility of peak potential and peak current was tested by repeating 4 experiments for 4.10^{-4} M promethazine. The relative standard deviations were calculated to be 0.91% and 0.63 % for peak potential and, 1.78% and 1.98% for peak current at platinum (in phosphate buffer of pH 7.0) and at glassy carbon (in acetate buffer of pH 4.7) electrodes, respectively. By choosing the optimum conditions mentioned above, calibration plots were drawn by spiking different amounts of the drug individually, to the blank solution. The characteristics of these plots are listed in Table 1.

Table 1. Statistical analysis of current-potential dependence. For the platinum electrode the peak currents were measured for the peak at 1.1 V and For the glassy carbon electrode the peak currents were measured for the peak at 0.8 V

Electrode	Medium	Concentration Ranges/M	Slope μA/M	Intercept μA	Correl. Coeff.	SE of Slope μA/M	SE of Intercept μA
Platinum	Phosphate Buffer (pH 7.0)	1.10^{-4}-1.10^{-3} (n=6)	$5,97.10^4$	-6.92	0.998	$1,8.10^3$	1.11
Glassy Carbon	Acetate Buffer (pH 4.7)	6.10^{-5}-8.10^4 (n=7)	$6,50.10^4$	-1.23	0.999	$1,4.10^3$	0.58

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