

Electrochemical analysis of some phenothiazine derivatives — I. Chlorpromazine HCl*

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Abstract: In this study the electrochemical behaviour of chlorpromazine hydrochloride in sulphuric acid solutions has been examined by cyclic and linear sweep voltammetry using oxidised and non-oxidised ruthenium wire electrodes. Although a stable and permanent RuO₂ coating on the electrode took a long time to prepare, the resulting curves were highly reproducible. It was possible to study solutions in a wide concentration range only by use of scan rates lower than 20 mVs⁻¹. The cyclic voltammograms of chlorpromazine hydrochloride in solutions of different concentrations of sulphuric acid and the behaviour of oxidised and non-oxidised ruthenium electrodes have been compared.

Keywords: *Chlorpromazine hydrochloride; anodic oxidation; voltammetry; RuO₂ electrode.*

Introduction

Chlorpromazine is a member of the phenothiazine class of major tranquillisers. It has been a subject of many electrochemical studies because there is significant evidence that the drug interacts with dopamine receptors and that the cationic radical formed by oxidation of chlorpromazine may be pharmacologically active [1].

RuO₂ is of considerable interest as an effective electrocatalyst for some reactions [2]. The aim of this work was to examine the electrochemical behaviour of chlorpromazine using an electrolytically RuO₂-coated ruthenium electrode.

Experimental

A Wenking model HP10 potentiostat and a type 250 function generator were employed for fast sweep linear voltammetry. The curves were recorded on an X–Y recorder (Yokogawa Ltd., type 3022,A4). A ruthenium wire and a platinum wire were used as the working and counter electrodes, respectively. The potential was measured with reference to a saturated calomel electrode; however, potentials were read relative to a standard hydrogen electrode.

The measurements with a 10 mV s⁻¹ scan rate were made with a PRG-3 polarograph; an EPL2 recorder (Tacussel electronique) was used for recording the curves.

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All the chemicals and standards were of analytical grade. The solutions were protected from light. Pure nitrogen gas was bubbled through the electrolytic solution to remove dissolved oxygen before each experiment.

Pretreatment of the electrode

To obtain a clean surface the ruthenium wire electrode was electrolytically reduced at -100 mV for 5 min and was then oxidised at 400 mV for 15 min in 0.5 M H_2SO_4 solution before each experiment. As the potential of 400 mV does not correspond to any stable oxide layer, the electrode pretreated in this manner was called the non-oxidised electrode.

Another group of experiments was performed using a ruthenium wire electrode which was first reduced at -100 mV and then oxidised at 1350 mV for 30 min. After repeating this procedure nearly 80 times, the electrode became dark brown and was coated by a permanent and stable oxide layer; the resulting voltammograms were highly reproducible.

Before each experiment this oxide-coated electrode was reduced at -100 mV for 5 min and was then oxidised at 1350 mV for 30 min.

Results and Discussion

In order to see the difference in behaviour of oxidised and non-oxidised ruthenium electrodes, voltammograms were recorded in 0.2 M H_2SO_4 solutions. In Fig. 1a the curves were obtained using the non-oxidised electrode. There are two steps in the oxidation process. The first step is at about 120 mV and is related to hydrogen desorption; the second step at 850 mV corresponds to oxidation of the electrode surface [3].

There are two reduction peaks at 1050 mV and 800 mV, due to oxide reduction. In Fig. 1b voltammograms of oxidised electrode are shown. Three anodic peaks at 100, 750 and 1180 mV are related to hydrogen desorption, oxide rearrangement and oxygen adsorption, respectively.

There are five cathodic peaks at 230 mV (hydrogen adsorption), 430, 730, 930 and 1180 mV (oxide rearrangement region) [4]. The currents increase as the scan rates increase.

In Fig. 2 the curves were recorded in solutions of 0.2 M H_2SO_4 and 4×10^{-4} M chlorpromazine hydrochloride containing 0.2 M H_2SO_4 using a non-oxidised electrode with a scan rate of 300 mVs^{-1} . There is no marked difference between the two curves. The reason may be the coverage of the electrode surface by adsorbed chlorpromazine hydrochloride molecules; when the scan rate is fast, an insufficient number of chlorpromazine hydrochloride molecules is oxidised. This is the case when the chlorpromazine hydrochloride concentration is higher than 2×10^{-5} M and the scan rate is higher than 20 mVs^{-1} .

The effect of H_2SO_4 concentration on the oxidation of chlorpromazine hydrochloride has been shown by voltammograms obtained in 0.2, 2 and 6 M H_2SO_4 solutions containing 2×10^{-5} M chlorpromazine hydrochloride, using various sweep rates (Fig. 3a–c). In 0.2 and 2 M H_2SO_4 there is one oxidation peak at 800 mV; in 6 M H_2SO_4 there are two peaks at 900 and 1250 mV, as reported [5]. As the sweep rate increases, the current increases in each solution. However, there is a considerable decrease in current with the increase in H_2SO_4 concentration in the order 0.2, 2 and 6 M H_2SO_4 .

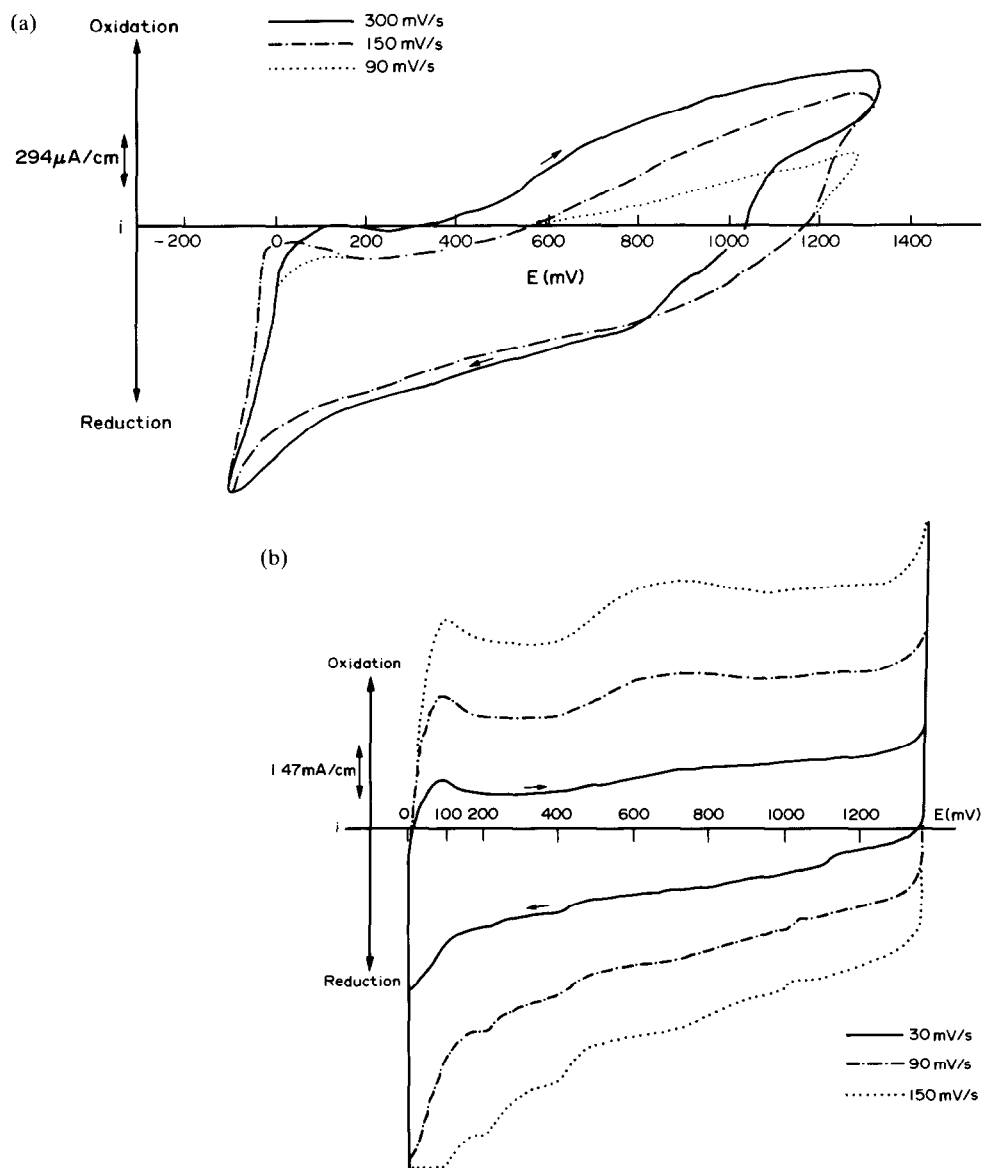


Figure 1
 Voltammograms of chlorpromazine hydrochloride in 0.2 M H_2SO_4 ; (a) with the non-oxidised electrode; (b) with the oxidised electrode.

Peak currents for chlorpromazine hydrochloride in H_2SO_4 become higher in the order 6, 2 and 0.2 M H_2SO_4 .

The shapes of the curves obtained in base electrolytes are similar to those obtained in chlorpromazine hydrochloride solutions with the exception of 6 M H_2SO_4 solutions. For 6 M H_2SO_4 solutions, the supporting electrolyte curves are completely different from chlorpromazine hydrochloride curves (Fig. 3d). The oxide region begins at very low anodic potentials (about 200 mV) and there is no peak at more positive potentials.

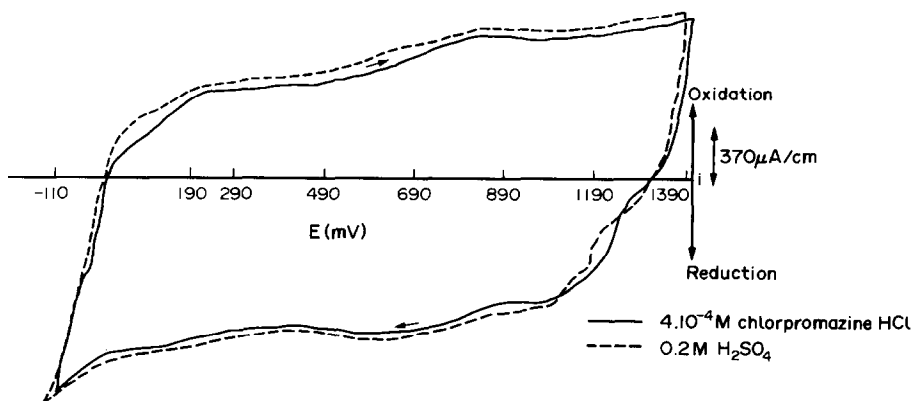


Figure 2
Current-potential curves obtained in 4×10^{-4} M solutions of chlorpromazine hydrochloride in 0.2 M H_2SO_4 (Curve 1) and in 0.2 M H_2SO_4 (Curve 2). Scan rate 300 mVs^{-1} .

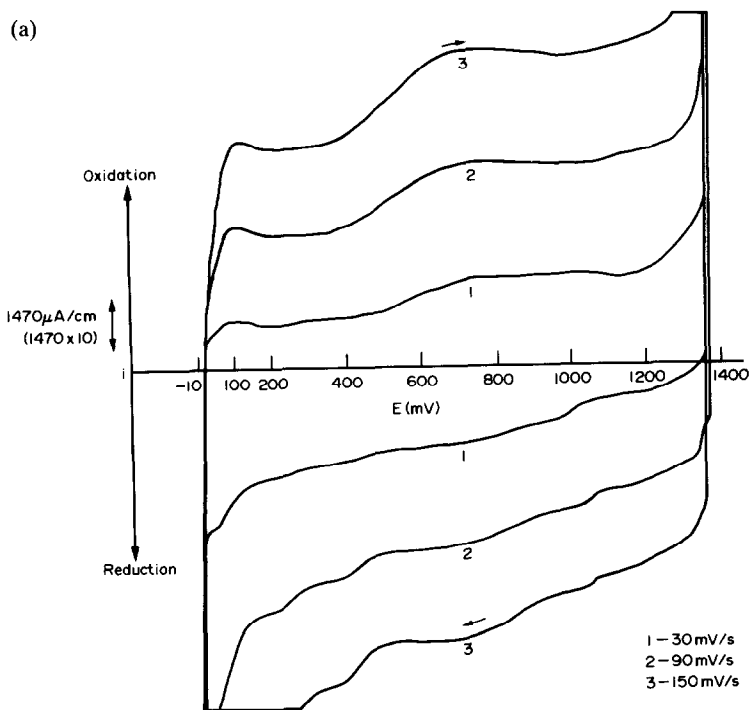


Figure 3
Cyclic voltammograms of 2×10^{-5} M chlorpromazine hydrochloride in (a) 0.2 M H_2SO_4 ; (b) 2 M H_2SO_4 ; (c) 6 M H_2SO_4 with the oxidised ruthenium electrode; (d) voltammograms in 6 M H_2SO_4 without chlorpromazine hydrochloride.

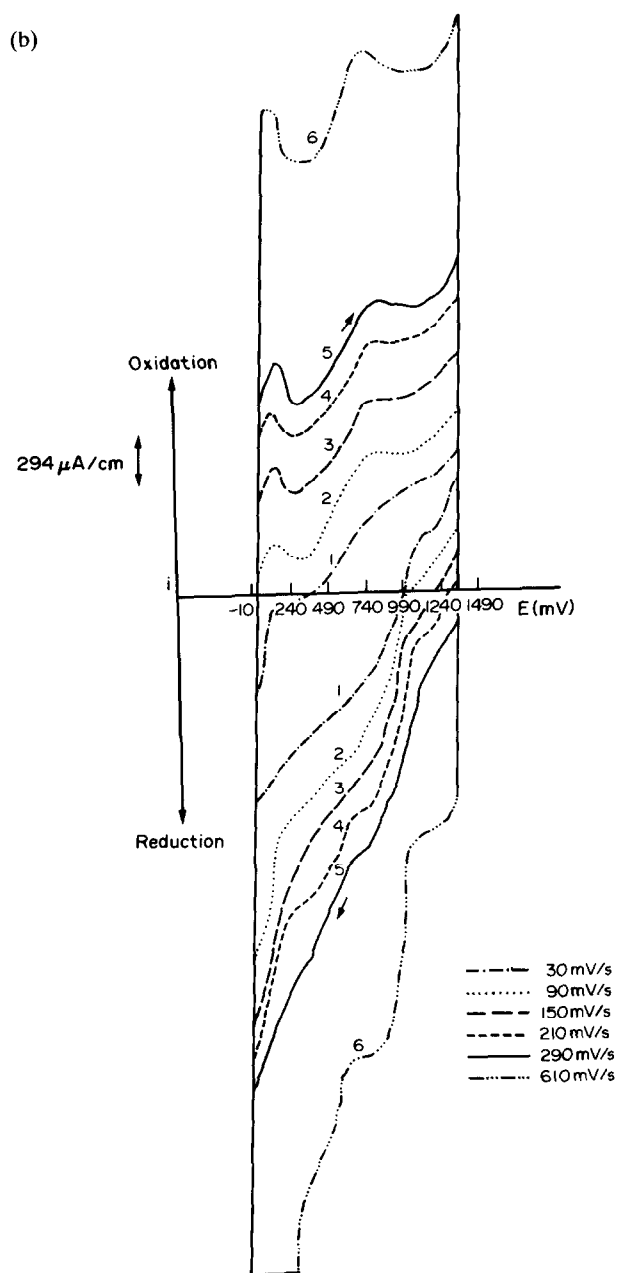


Figure 3 (continued)

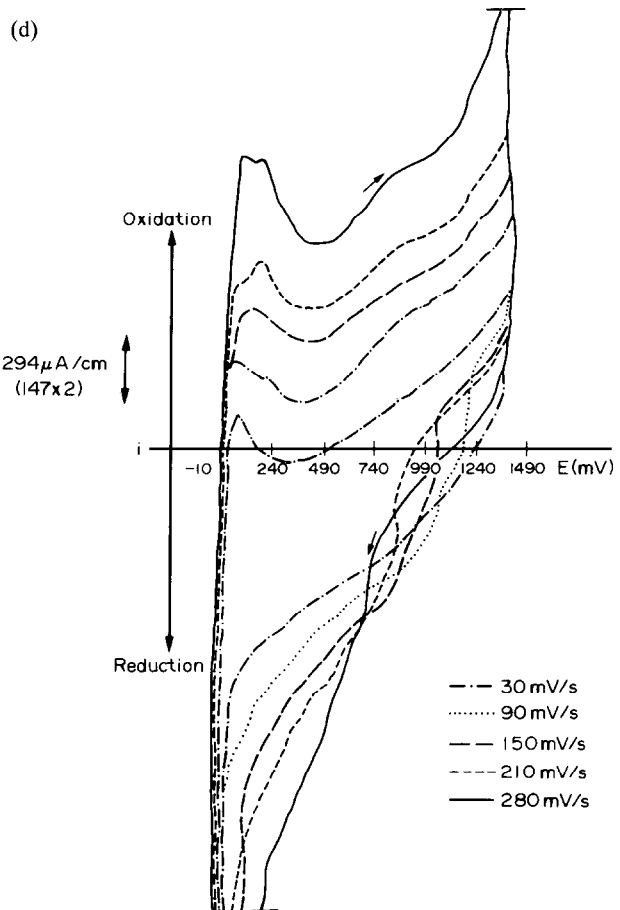
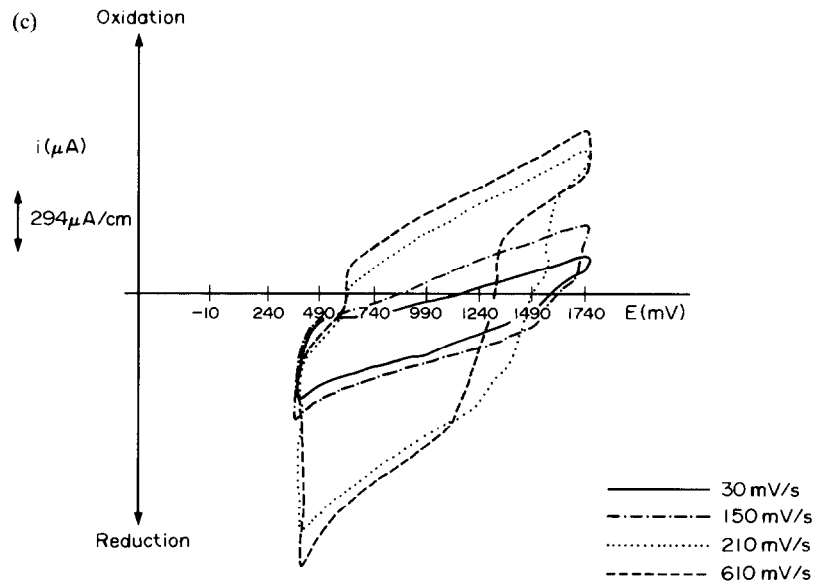


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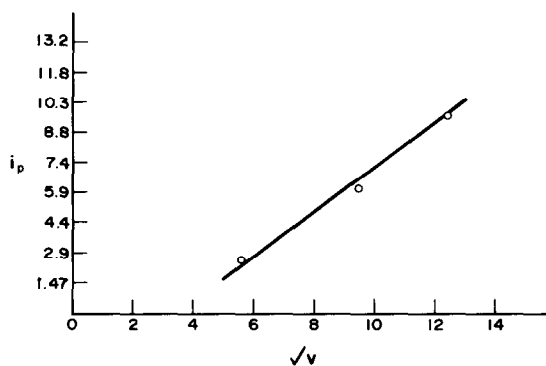


Figure 4
Peak current of the wave at 700 mV against square root of scan rate for 2×10^{-5} M chlorpromazine hydrochloride in 0.2 M H_2SO_4 .

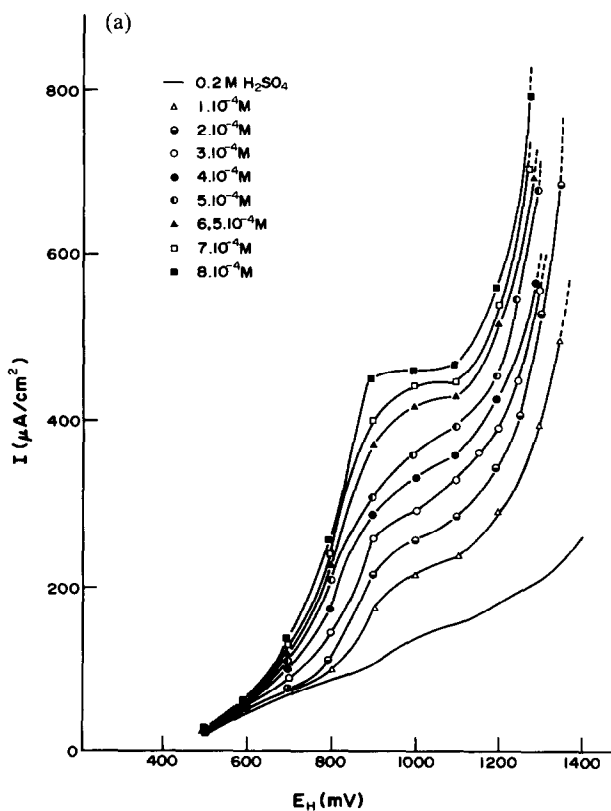


Figure 5
Oxidation curves for solutions in 0.2 M H_2SO_4 of various concentration of chlorpromazine hydrochloride. Scan rate 10 mVs^{-1} (a) with the non-oxidised ruthenium electrode; (b) with the oxidised ruthenium electrode.

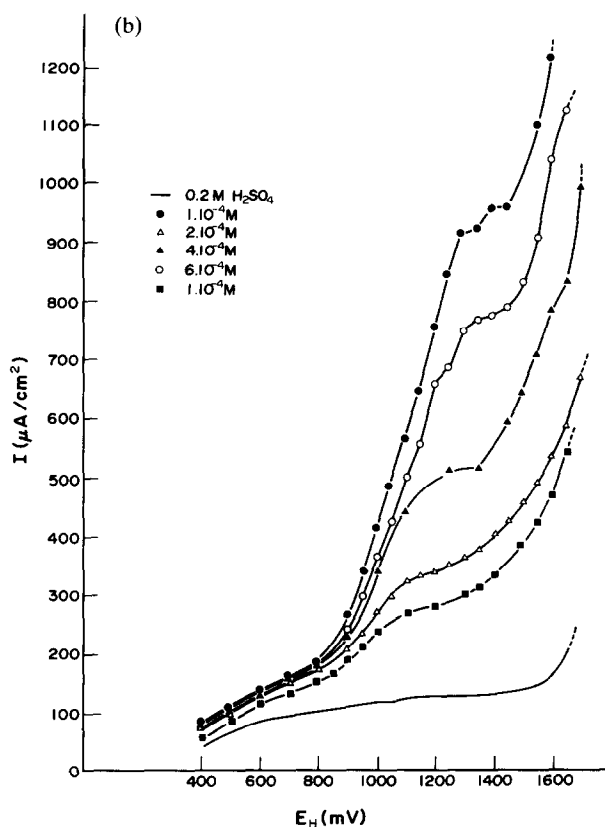


Figure 5 (continued)

The plot of i_p of the peak at 700 mV against the square root of the scan rate, Vs^{-1} , with the data obtained for a 0.2 M H_2SO_4 supporting solution (Fig. 3a) is illustrated in Fig. 4. A straight line is obtained. It does not pass through the origin indicating that the electrode reaction in this solution is not simply diffusion controlled.

There is no regular increase in the peak currents of the corresponding peaks in Fig. 3b, c with an increase in scan rate.

The curves obtained by a 10 mVs^{-1} scan rate for solutions in 0.2 M H_2SO_4 containing various concentrations of chlorpromazine hydrochloride, using oxidised and non-oxidised electrodes in stirred solutions, are shown in Fig. 5a, b.

With this scan rate, oxidation of chlorpromazine hydrochloride takes place even in concentrated solutions and the current densities in the limiting current region are linearly related to the concentration in the range of 1×10^{-4} – 8×10^{-4} M chlorpromazine hydrochloride.

Preparation of calibration curve

A 10^{-3} M chlorpromazine hydrochloride stock solution was prepared in 0.2 M H_2SO_4 . A series of standard solutions of 1×10^{-4} – 8×10^{-4} M were subsequently prepared by pipetting appropriate aliquots of these solutions into glass-stoppered 100-ml volumetric flasks and diluting to 100 ml with 0.2 M H_2SO_4 ; after transferring to the cell each

Table 1
Concentration-limiting current density relationship* for results in Fig. 5a

Concentration (M)	1×10^{-4}	2×10^{-4}	3×10^{-4}	4×10^{-4}	5×10^{-4}	6.5×10^{-4}	7×10^{-4}	8×10^{-4}
Limiting current density at 1000 mV ($\mu\text{A cm}^{-2}$)	70	115	150	184	215	275	295	315

* Regression line: $y = 3.54 \times 10^5 x + 40.95$; $r = 0.998$ ($n = 8$).

solution was deoxygenated with nitrogen for 15 min. The voltammograms were recorded with a 10 mVs^{-1} scan rate using a non-oxidised electrode pretreated as described in the experimental part. The solutions were stirred magnetically during the experiments. The current densities at 1000 mV were plotted against concentrations. Regression analysis of the data (Table 1) shows that the quantitative determination of chlorpromazine using a non-oxidised electrode can be achieved with acceptable accuracy and sensitivity.

The linear relationship between limiting current density and concentration is rather poor in the case of the oxidised electrode (Fig. 5b). This means that the oxidised electrode is unsuitable for quantitative determination of this drug.

Figure 6a,b show the Tafel plots for 10^{-3}M chlorpromazine hydrochloride (from results in Fig. 5a, b). The exchange current density obtained for the non-oxidised and oxidised electrodes are 240 and $330 \mu\text{A}$, respectively, indicating the catalytic effect of the oxidised ruthenium electrode.

Conclusions

When the electrode was exposed to oxidation at 1350 mV the electrode is coated by RuO_2 [6, 7].

If the electrode is oxidised in $0.5 \text{ M H}_2\text{SO}_4$ at potentials more positive than 1430 mV, the formation of O_2 and RuO_4 takes place simultaneously [3]. RuO_4 is soluble in H_2SO_4 forming unstable Ruthenat complexes; as a result of the decomposition of this anion, hydrous RuO_2 is precipitated on the electrode [8]. The present experiments showed that this layer prevents the oxidation of chlorpromazine hydrochloride.

The curves in Fig. 1b are similar to the voltammetric characteristics of the 110 surface of the RuO_2 single-crystal electrode in $0.5 \text{ M H}_2\text{SO}_4$ [4]. This surface is composed of ruthenium and oxygen atoms.

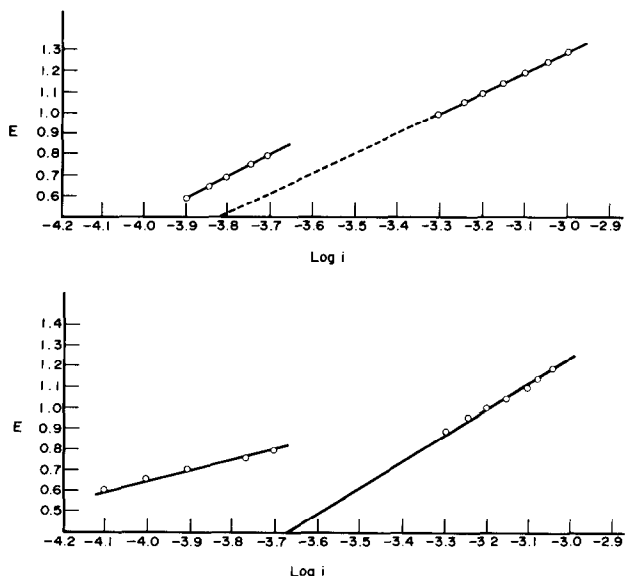


Figure 6

Tafel plot of 10^{-3}M chlorpromazine hydrochloride in $0.2 \text{ M H}_2\text{SO}_4$ with (a) the non-oxidised electrode; (b) the oxidised electrode. Scan rate 10 mVs^{-1} .

Oxygen evolution occurs at about 1400–1430 mV on the non-oxidised ruthenium surface whereas it occurs at about 1700 mV on the oxidised electrode (Fig. 5a, b).

The examination of the oxidation of chlorpromazine hydrochloride for a wide concentration range is only possible by use of a scan rate of 10 mVs^{-1} . This means that oxidation of this drug is rather slow in acidic media.

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