ELSEVIER

Journal of Pharmaceutical and Biomedical Analysis
15 (1996) 371–381

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

Voltammetric determination of imipramine hydrochloride and amitriptyline hydrochloride using a polymer-modified carbon paste electrode

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Received for review 3 January 1996; revised manuscript received 1 May 1996

Abstract

In this paper the voltammetric behaviors of imipramine·HCl and amitriptyline·HCl, which are both tricyclic antidepressants, were investigated using a carbon paste electrode, modified by the addition of poly(*N*-vinylimidazole), in various solutions of different pHs. It was shown that the current density for imipramine increased with modification of the carbon paste electrode and amitriptyline, which was electroinactive with the normal carbon paste electrode, became electroactive on the modified electrode. The optimum conditions for the quantitive determination of imipramine·HCl and amitriptyline·HCl were determined and statistical analysis of the linear relationship between current and concentration is given. The method was applied for the determination of these substances in the pharmaceutical dosage forms.

Keywords: Amitriptyline; Imipramine; Polymer-modified carbon paste electrode; Voltammetry

1. Introduction

Imipramine (a dibenzazepine derivative) and amitriptyline (a dibenzocycloheptadiene derivative) are tricyclic antidepressants referred to as monamine re-uptake inhibitors because of their postulated principal mode of action. The pharmacological and structural resemblance to phenothiazines lead to the discovery of the antidepressive effect of imipramine. It was first clinically tested for treatment of schizophrenia and although it was found that this drug had no antischizophrenic effect it did have antidepressive activity [1]. Amitriptyline has the same general properties as imipramine.

There have been voltammetric investigations of some of the tricyclic antidepressants using various solid electrodes, e.g. rotating Au and Pt disc electrodes [2]. Wang et al. [3] developed a method for the measurement of tricyclic antidepressants

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PII S0731-7085(96)01866-3

with glassy carbon and carbon paste electrodes following an interfacial accumulation period [3].

In a paper concerning the voltammetric behavior of tricyclic antidepressants it was reported that a reliable response could not be obtained with a carbon paste electrode [4], but with an antimony-doped tin oxide electrode reproducible results and linear calibration curves could be obtained for imipramine and desipramine.

Turk et al. [5] described the design of a polymer electrode using reticulated glassy carbon as a support with poly(carbazole) or poly(thiophene) electrochemically coated onto it. This electrode was used for the electrochemical study of some tricyclic drugs, including amitriptyline which had been accepted as being electroinactive before. Some ion-selective electrodes were also developed for the analysis of amitriptyline [6–8].

In the last decade the need for high sensitivity and selectivity for the analysis of biomolecules has been increasing. The development of modified electrodes is based on this need. Electrodes can easily be modified either by dispersing the modifier with a paste [9–12] or by physically adsorbing it

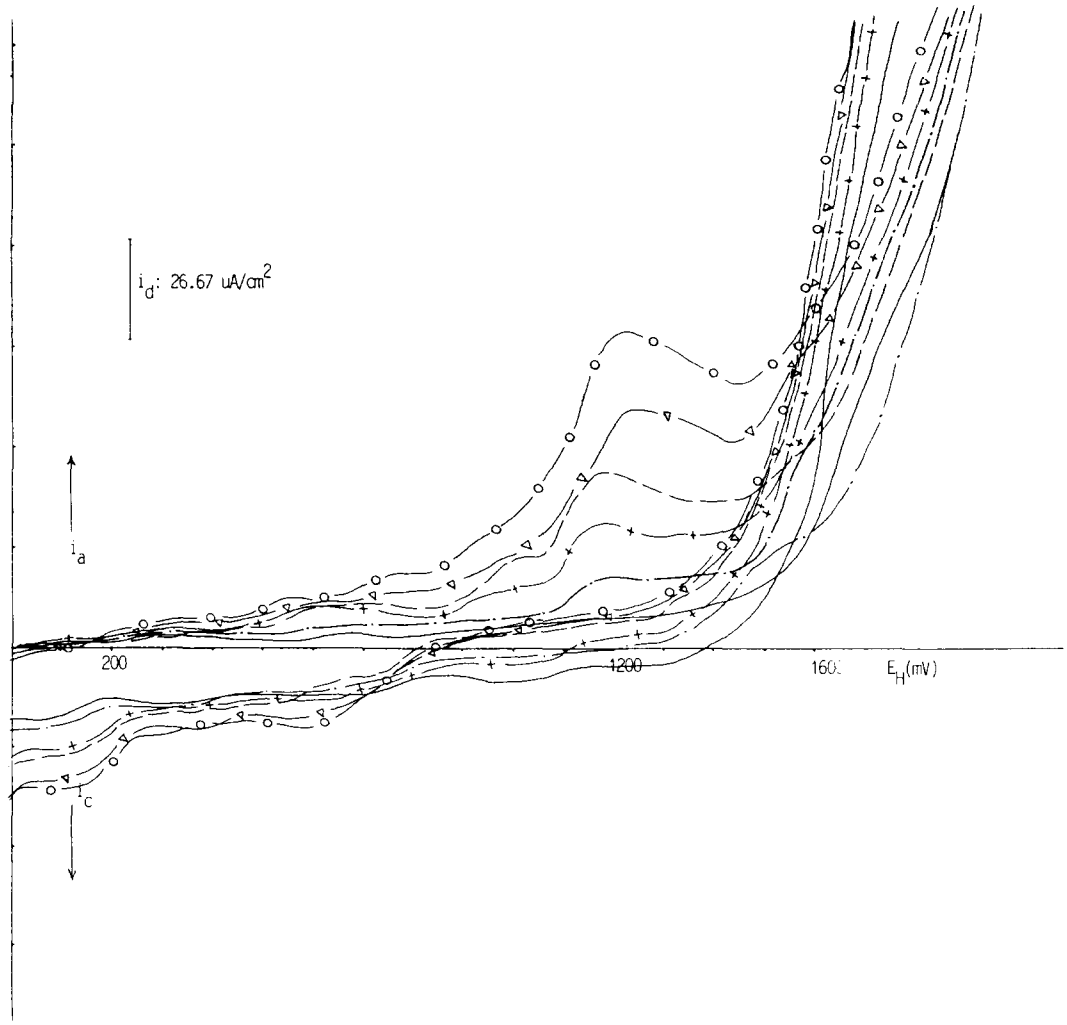

Fig. 1 (a)

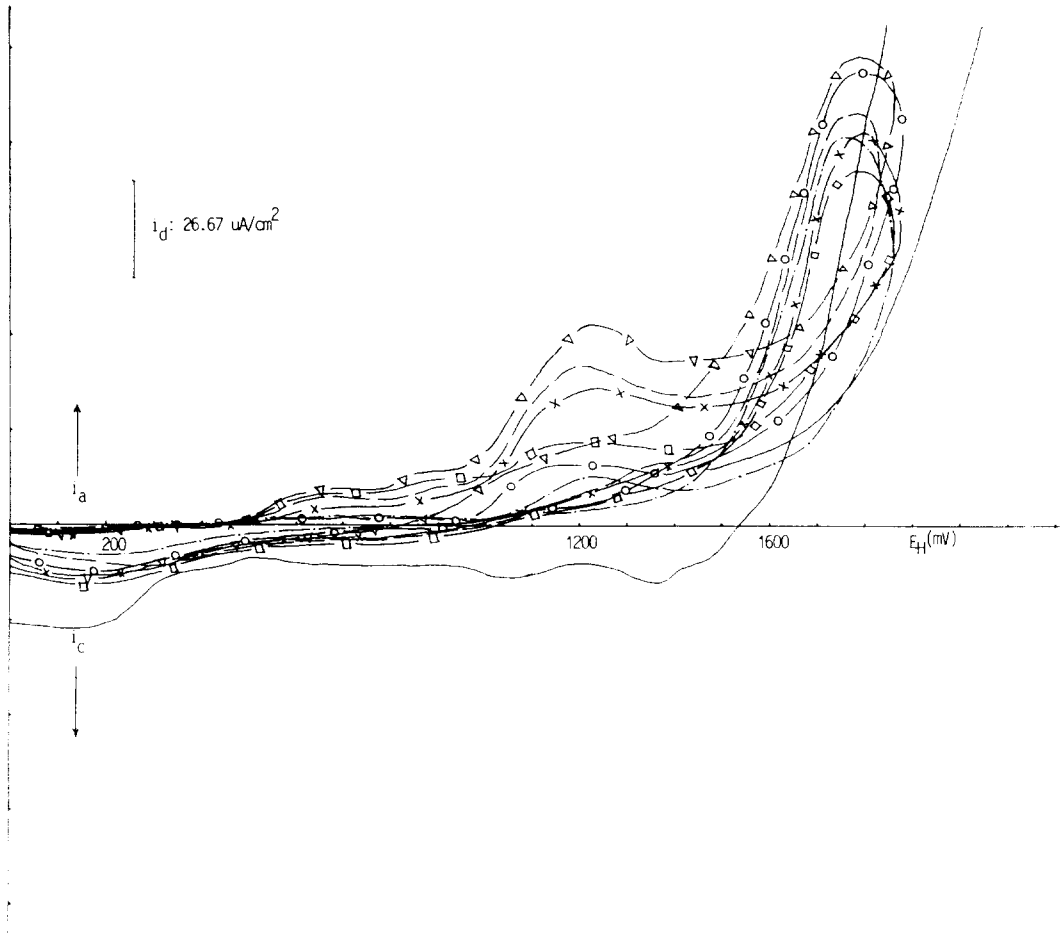

Fig. 1 (b)

Fig. 1. Voltammograms of imipramine recorded in 0.1 M sulphuric acid solutions. Scan rate, 100 m V s $^{-1}$. (a) With modified carbon paste electrode. Solutions: (——), 0.1 M H_2SO_4; (—·—·), 1×10^{-4} M imipramine; (×), 2×10^{-4} M imipramine; ( ), 4×10^{-4} M imipramine; (△), 6×10^{-4} M imipramine; (○), 8×10^{-4} M imipramine. (b) With normal carbon paste electrode. Solutions: (- - -), 0.1 M H_2SO_4; (– · – · –), 1×10^{-4} M imipramine; (o), 2×10^{-4} M imipramine; (□), 4×10^{-4} M imipramine; (×), 6×10^{-4} M imipramine; (– – –), 8×10^{-4} M imipramine; (Δ), 1×10^{-3} M imipramine.

to the electrode surface. An alternative way of modifying the electrode is by covalently bonding the modifier to the surface [13,14] or modification by a lipidic substance [15,16].

In this paper, a modified carbon paste electrode was simply prepared by adding the polymer, poly(*N*-vinylimidazole), to the carbon paste instead of by electroplating. In this way the correct amount of polymer could be used. Voltammograms obtained for imipramine and amitriptyline with this electrode were compared with those obtained using a normal carbon paste electrode. The tests were performed in 0.1 M H_2SO_4 solutions and in phosphate and acetate buffers of different pHs.

The method was applied to pharmaceutical

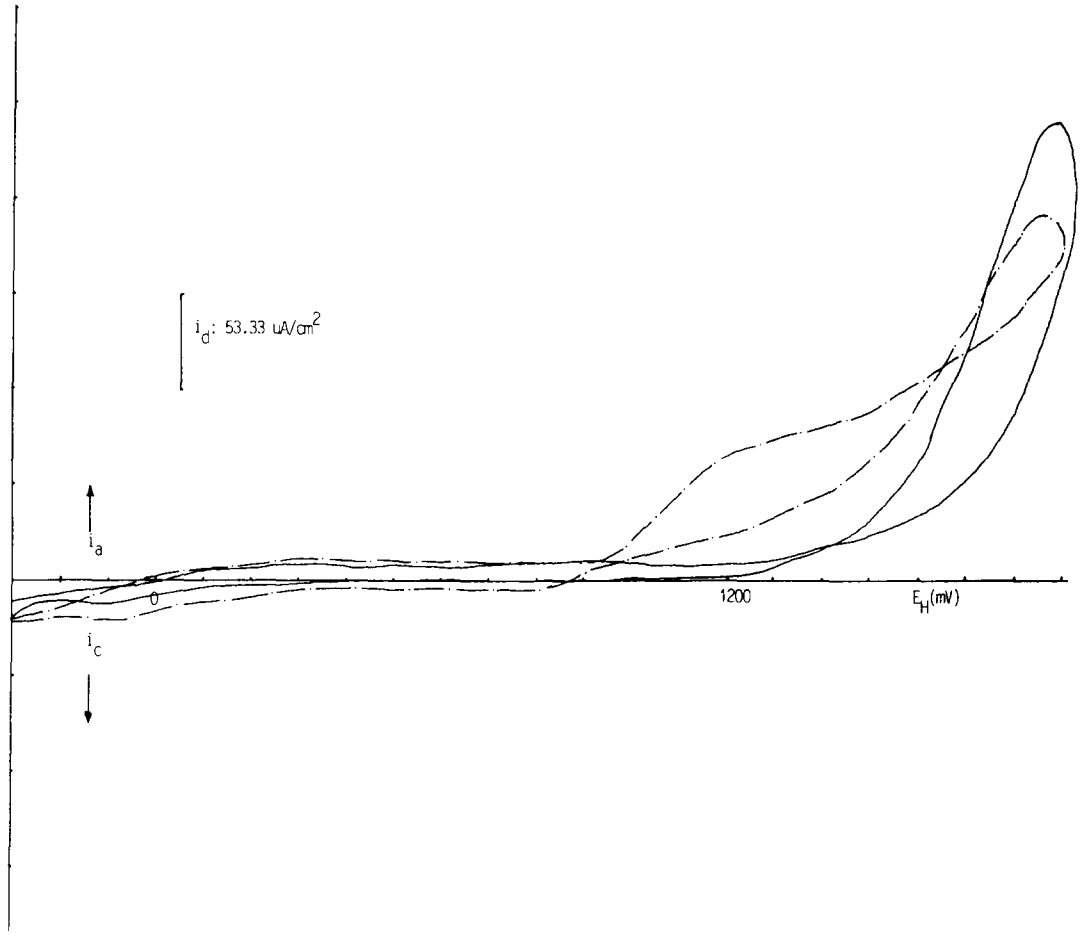

Fig. 2 (a)

preparations of imipramine and amitriptyline available in Turkey.

2. Experimental

A PRG 3 (Tacussel) polarograph with an EPL 2 recorder (Tacussel) was used to record the voltammograms. Reference and counter electrodes were a saturated calomel (Tacussel XR 100) and a Pt wire respectively. Carbon paste and polymer-modified carbon paste electrodes (9.8 mm in diameter) were used as working electrodes.

Carbon paste was prepared by mixing 0.8 g of graphite powder (Aldrich) and 1 ml of mineral oil (Sigma). 50 mg and 40 mg of poly(*N*-vinylimidazole) were added to this mixture to obtain modified carbon paste electrodes for imipramine and amitriptyline respectively. The amount of poly(*N*-vinylimidazole) used was varied and optimum results were found to be obtained by the addition of the amounts of polymer given above for the two substances.

Poly(*N*-vinylimidazole) was prepared as men-

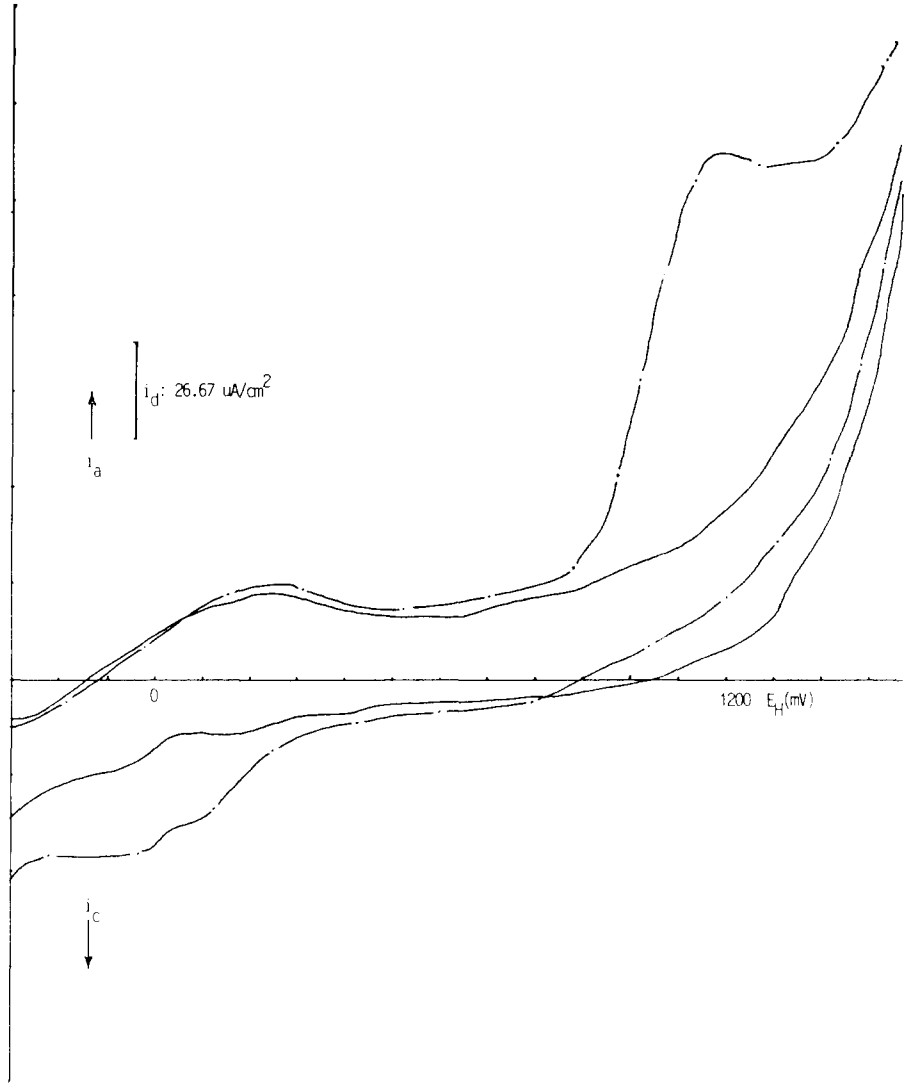

Fig. 2 (b)

Fig. 2. Voltammograms of imipramine recorded in phosphate buffer pH 7.4 Scan rate, 100 m V s $^{-1}$. Solutions: (——), phosphate buffer pH 7.4; (— · —), 4×10^{-4} M imipramine. (a) With modified carbon paste electrode. (b) With normal carbon paste electrode.

tioned elsewhere [17]. Imipramine and amitriptyline were kindly supplied by Ciba Geigy and Roche respectively.

All reagents were of analytical grade. Doubly-distilled water was used to prepare the solutions.

3. Results and discussion

It was suggested that the oxidation of imipramine occurred at the ring nitrogen [2–4]. Bishop and Hussein [2] reported that one electron is removed from the nitrogen and a cation radical is formed which can exist in a number of resonance forms. This monocation dimerises or reacts with an unoxidised molecule. The dimerisation is accompanied by the loss of two protons per dimer. The dimer is more easily oxidised than the monomer and a product dication results with the loss of two electrons per dimer.

Table 1
Results of linear regression analysis of imipramine and amitriptyline concentration–peak currents relationships for the modified carbon paste electrode in sulphuric acid

Substance	Medium	Concentration range (M)	Slope (μA l mol^{-1})	Intercept (μA)	Corrl. coeff.	SE of slope (μA l mol^{-1})	SE of intercept (μA)
Imipramine·HCl	0.1 M H_2SO_4	6×10^{-5}–8×10^{-4} ($n = 8$)	5.64×10^4	6.11	0.9992	9.11×10^2	0.37
Amitriptyline·HCl	0.1 M H_2SO_4	1×10^{-5}–1×10^{-4} ($n = 6$)	4.90×10^4	−0.25	0.9988	11.83×10^2	0.07

Amitriptyline, which has no ring N atom, was previously reported to be electrochemically inactive. Turk et al. [5] investigated this substance using a reticulated glassy carbon electrode, electrochemically plated by poly(carbazole) or poly(thiophene). The electroactivity found by Turk et al. [5] is possibly due to the presence of electron-rich sulfur or nitrogen atoms on the polymer surface which facilitate the formation of a cation radical.

In the present study a carbon paste electrode was modified simply be the addition of poly(*N*-vinylimidazole). The electrode was tested by mixing different amounts of polymer with different carbon paste compositions. The most suitable scan rate was found to be 100 m V s^{-1}. The stability of the electrode and the reproducibility were checked in 0.1 M H_2SO_4 solution by the multiscan technique for about 100 cycles and it was observed that they were satisfactory. When the same test was performed in imipramine solution a gradual decrease in current due to adsorption was observed. Therefore, the first curve was always used to make the calibration graph and a fresh carbon paste surface was obtained by smoothing with filter paper.

Figs. 1a and 1b show voltammograms of imipramine recorded in 0.1 M H_2SO_4 solution with modified and normal carbon paste electrodes. Only one oxidation peak could be obtained in each case. Although the peak potentials are nearly the same in Figs. 1a and 1b, there is an increase in peak current and the peak becomes sharper in the curve obtained with the modified carbon paste electrode. It was observed that the peak current–concentration relationship was linear.

In phosphate solutions of higher pH the difference between the peak currents of the normal carbon paste electode and the polymer-modified carbon paste electrode disappeared. In the solution of pH 7.4 the current density relating to imipramine obtained with the modified carbon paste electrode became even less than that obtained with the carbon paste electrode (Fig. 2). A limiting current region is seen instead of the peak in Fig. 1a. In phosphate buffers of different pHs the limiting current–concentration correlation was unsuitable for analytical evalution.

The results of the linear regression analysis for the peak current–concentration dependence in 0.1 M H_2SO_4 are given in Table 1.

During the investigation of amitriptyline the peak current reached its highest value with the polymer-modified carbon paste electrode when 40 mg of poly(*N*-vinylimidazole) was added. With higher amounts of polymer, the peak current decreased. With 60 mg of poly(*N*-vinylimidazole) the shapes of the curves and the current densities in the voltammograms of the supporting electrolyte(0.1 M H_2SO_4) and 4×10^{-4} M amitriptyline became nearly the same, indicating that there was no significant electroactivity of the substance. The optimum scan rate was found to be 100 m V s^{-1}.

The voltammograms of amitriptyline were recorded in 0.1 M H_2SO_4 and 0.3 M H_3PO_4 with phosphate buffers ph 2, 4.8, 5.6, 6.6, 7.0, 8.5, and 9.0 and acetate buffers pH 3.5 and 4.7. In 0.1 M H_2SO_4 solutions (Fig. 3) an oxidation peak is seen

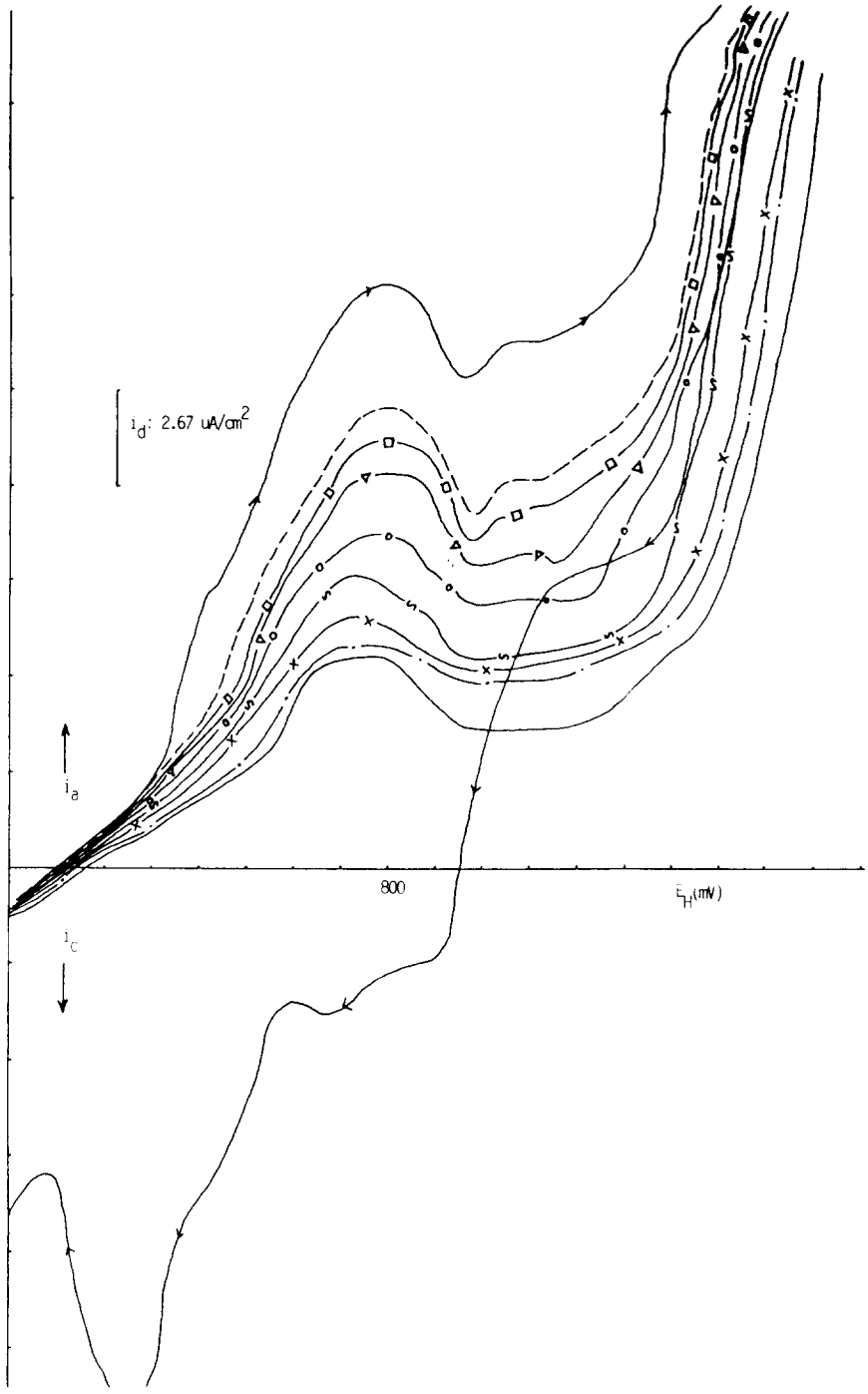

Fig. 3. Voltammograms of amitriptyline recorded in 0.1 M sulphuric acid solutions with modified carbon paste electrode. Scan rate, 100 m V s^{-1}. Solutions: (——), 0.1 M H_2SO_4; (—·—·), 1×10^{-5} M amitriptyline; (×), 2×10^{-5} M amitriptyline; (~), 4×10^{-5} M amitriptyline; (o), 6×10^{-5} M amitriptyline; (Δ), 8×10^{-5} M amitriptyline; (□), 1×10^{-4} M amitriptyline; (- - -), 2×10^{-4} M amitriptyline; (→), 4×10^{-4} M amitriptyline.

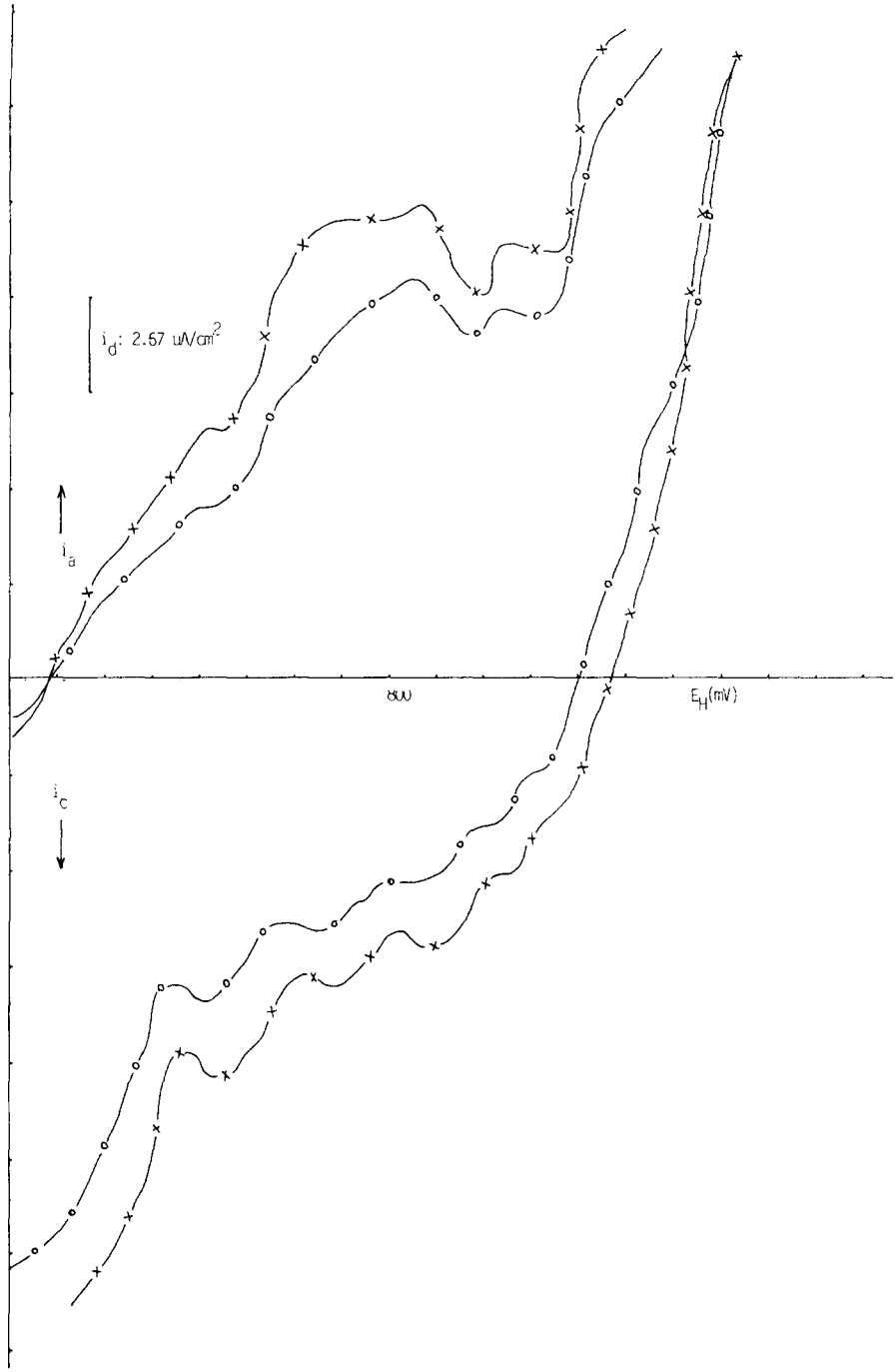

Fig. 4. Voltammograms of amitriptyline recorded in phosphate buffer pH 2.0 with modified carbon paste electrode. Scan rate, 100 m V s^{-1}. Solutions: (o), phosphate buffer pH 2.0; (×), 2×10^{-4} M amitriptyline.

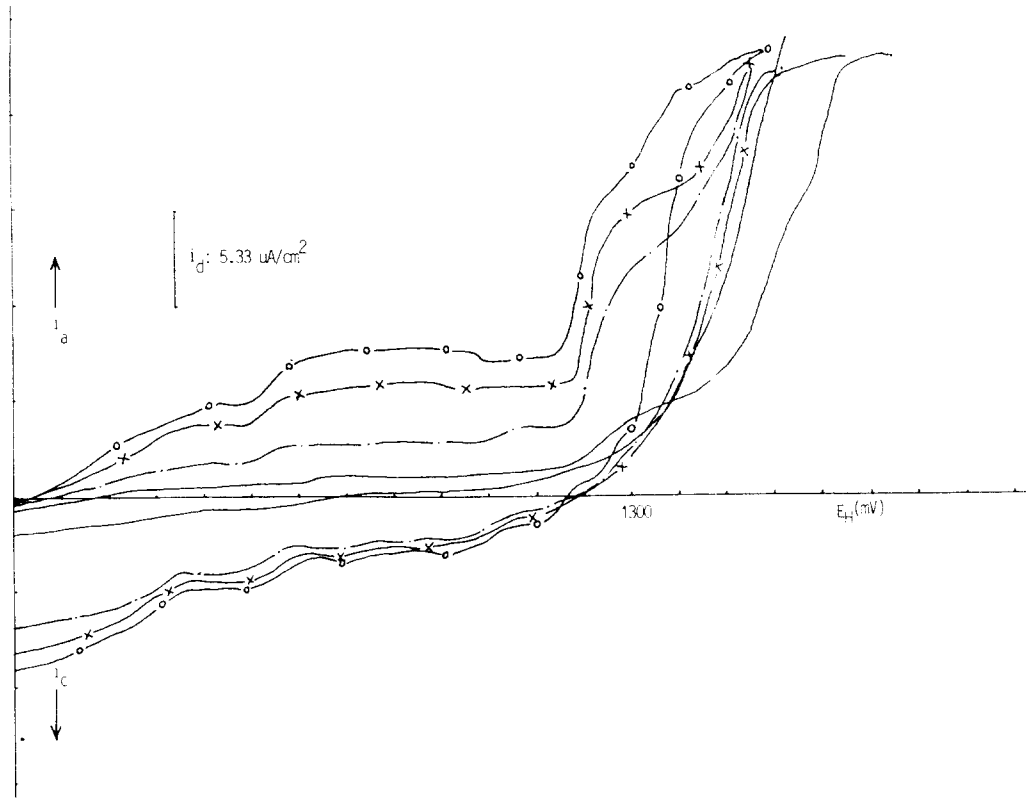

Fig. 5. Voltammograms of amitriptyline recorded in phosphate buffer pH 6.6 with modified carbon paste electrode. Scan rate, 100 m V s $^{-1}$. Solutions: (——), phosphate buffer pH 6.6; (— · — · —), 8×10^{-5} M amitriptyline; (×), 1×10^{-4} M amitriptyline; (o), 4×10^{-4} M amitriptyline.

at about 800 mV and a second, ill-defined small step beginning at about 1000 mV is also observed. The reduction peak relating to the peak at 800 mV on the oxidation branch is seen at about 300 mV. There is linear relationship between the peak current at 800 mV and the concentration. Table 1 shows the statistical analysis of this relationship.

In 0.2 M phosphoric acid solution two anodic steps are seen: the first is a broad peak shape, the potential of which is about 900 mV; the second is a small step which manifests itself with an increase in current at 1200 mV (Fig. 4). When the pH increases the second step becomes pronounced and the first peak disappears. The limiting current

Table 2
Results of analysis of Tofranil[a] sugar-coated tablets for imipramine·HCl[a]

Labelled claim (mg)	Amount found (mg)[b]	SD	Official method (mg)[c]
25.00	25.18	4.92×10^{-1}	24.76

[a] t (95%) = 2.306; t (calc) = 1.152 (not significant).
[b] Each value is the mean of five experiments.
[c] British Pharmacopeia (1980).

Table 3
Results of the analysis of Laroxyl® sugar-coated tablets for amitriptyline·HCl

Labelled claim (mg)	Amount found (mg)[a]	SD	Recovery (%)[b]
25.00	25.31	5.31×10^{-1}	101.4

[a] Each value is the mean of five experiments.
[b] Experiments performed separately by adding a known amount of amitriptyline·HCl.

pH increases the second step becomes pronounced and the first peak disappears. The limiting current at this step increases with the increase in the amitriptyline concentration. Fig. 5 shows the voltammograms obtained in phosphate buffer pH 6.6 as an example. From the analytical point of view the best results were obtained in 0.1 M H_2SO_4 solution. When a multiscan potential sweep was applied to the polymer-modified carbon paste electrode in amitriptyline solution it was observed that as the scan number increased the current also increased gradually. Therefore, for obtaining the calibration plot the first curve was always used.

3.1. Analytical application

3.1.1. Determination of imipramine in Tofranil® sugar-coated tablets

The optimum conditions determined using the standard substance were applied to the commerical formulation of imipramine.

Ten drages of imipramine were accurately weighed and finely powdered. The correct amount of powder was dissolved in the supporting electrolyte and by stirring this solution for about 30 min a stock solution of 10^{-3} M was prepared. All the test solutions were obtained by diluting this stock solution. The results were compared with those obtained by the spectrophotometric method given in the British Pharmacopeia [18].

The statistical analysis of the data is shown in Table 2. As can be seen from this Table there is no significant difference between the voltammetric and spectrophotometric methods. However, the voltammetric method can be applied directly to the sugar-coated tablets and so it is simple and rapid.

3.1.2. Determination of amitriptyline in Laroxyl® sugar-coated tablets

Ten sugar-coated tablets of Laroxyl were accurately weighed and finely powdered. A stock solution of 10^{-3} M was prepared by dissolving the correct amount of this powder in 0.1 M H_2SO_4 solution. All the test solutions were prepared by dilution of this stock solution. The statistical analysis of this test is given in Table 3. The results were checked by a recovery test. From Table 3, it is clear that this method can be used for the analysis of amitriptyline in pharmaceutical dosage forms.

4. Conclusion

The described voltammetric method for the determination of amitriptyline hydrochloride and imipramine hydrochloride in their pharmaceutical preparations is rapid, directly applicable and has sufficient accuracy and precision. Amitriptyline can be determined voltammetrically and potentiometrically only with the modified electrodes, as also reported in the literature [5–8].

In this paper a modified carbon paste electrode was developed which can be prepared simply and is stable for about 100 experiments and for nearly 1 month. The determination limit is lower than that of potentiometric method [8].

Acknowledgements

The authors thank The Ankara University Research Foundation (Grant No: 93030001), and The Turkish Scientific and Technical Research Council Project (Grant No: TBAG 1275) for sup-

port of this research and also Ciba Geigy and Roche Drug Industries (İstanbul, Turkey) which kindly provided pure imipramine·HCl and amitriptyline·HCl.

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