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# ELECTROCHEMICAL STUDY OF EPINEPHRINE AT PLATINUM ELECTRODE

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The scope of the present paper was to study the epinephrine electrochemical behaviour at bare Pt electrode by using cyclic voltammetry at an unmodified Pt electrode in 0.2 M – 0.2 M PBS (phosphate buffer solution) of pH 7. The effect of the scan rate and of the initial direction of the sweep (starting from 0.0 V versus SCE) on the electrochemical behaviour of the epinephrine were investigated.

## INTRODUCTION

Epinephrine (see Fig. 1) is one of the most important neurotransmitters in mammalian central nervous system which predominant form of existence depends upon the pH.

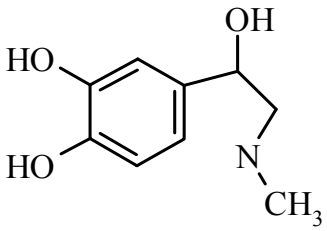


Fig. 1 – Structure of (2,3) L-epinephrine.

In solution of small pH it can exist as a relatively large cation due to the protonation of the basic N atom of the secondary amine. In neutral pH solution it exists predominantly as a neutral relatively large molecule. From a physiological point of view, the epinephrine acts at the central nervous system controlling a series of biological reactions and nervous chemical processes. A part of these are essentially of electrochemical nature. [1,2] As a consequence the electrochemical investigation of epinephrine was intensively done by using either bare electrodes as Pt, GC, pretreated GC, CPE and Au or various chemically modified electrodes supported on GC or Au. [3-8]

This paper deals with the CV studies of epinephrine behaviour at Pt bare electrode in 0.2 M – 0.2 M PBS of pH 7. The effect of scan rate, of the starting potential, in close connection with the initial direction of the sweep of working electrode potential, on the electrochemical behaviour of the epinephrine was investigated at pH 7. As far as we know, on Pt electrode the epinephrine was investigated in sulphuric acid solution at pH 3.0 in a thin layer electrochemical cell. [3] The electrochemical behaviour during CV experiments at pH 7 supposes an oxidation of catechol/o-benzenequinone type giving rise to epinephrinequinone (an open-chain quinone), the last being able to lose fast a hydrogen cation followed by a fast isomerization to leucoadreno-chrom. Then another enough fast disproportionation reaction between leucoadrenochrome and epinephrinequinone gives rise to adrenochrome and protonated epinephrine which are in agreement with reported behaviour of epinephrine.[5,6,9] Adrenochrome can participate to a quasireversible to reversible electrode reaction at the Pt electrode.

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## EXPERIMENTAL

**Apparatus**: Electrochemical experiments were carried out using the potentiostat-galvanostat system AutoLab PGStat 12, controlled by General Purpose Electrochemical System (GPES) electrochemical interface for Windows (version 4.9.007). Three electrodes in one-compartment cell (10 ml) were used in all experiments. Platinum disc electrode served as a working substrate electrode. All potentials were measured and given referred to SCE electrode used as reference electrode. The counter electrode was a glassy carbon electrode rod-like.

**Measurements:** All measurements were carried out at room temperature. All solutions were deaerated by dry argon stream for 5 min before every experiment and an argon atmosphere was maintained above the solution during the experiment.

**Chemicals**: All chemicals were reagent grade (epinephrine from Fluka and the components of the phosphate buffer solution (PBS) from Carlo Erba) and used without further purification; the aqueous solutions have been prepared using doubly-distilled water. Before modification, the platinum surface was polished with alumina slurry on a polishing pad, washed with distilled water and sonicated for 3 minutes in doubly distilled water.

## RESULTS AND DISCUSSION

Fig. 2 shows the cyclic voltammetry behaviour of epinephrine at Pt bare electrode in PBS (0.2 M-0.2 M) of pH 7, in the electrode potential range 0.7 V - -0.5 V with a start electrode potential of 0.0 V. One can see that for an initial cathodic-going scan from 0.0 V to -0.5 V there is no redox response of epinephrine but on the anodic-going scan there is a very well defined anodic peak (a1) (at $E_{pa,1}$ = 0.282 V (for 25 mV/s) to 0.352 V (for 250 mV/s)), but on the cathodic-going scan there is no counterpeak of this anodic peak. On the second cycle, on the negative-going segment (0 V - -0.5 V) a cathodic peak (c2) appears (at $E_{pc,2}$ = -0.222 V (for 25 mV/s) to -0.262 V (for 250 mV/s)) and a corresponding anodic counterpeak (a2) (at $E_{pa,2}$ = -0.161 V (for 25 mV/s) to -0.121 V (for 250 mV/s) V) on the positive-going segment is developed. The initial anodic peak (a1) appears again on the second cycle but its height decreases in comparison with the first cycle. Starting the initial scan from 0.0 V but towards positive electrode potentials, it appears the anodic peak (a1) which has no counterpeak, and, in the cathodic region, there is the couple of peaks (c2/a2) at a half-wave potential $E_{1/2}$ = -0.192 V (irrespective of the scan rate in the range 25 mV/s to 250 mV/s). Of course, the second peak reveals the same redox behaviour. The initial anodic peak (a1) appears again on the second cycle but its height decreases in comparison with the first cycle. This combination of two different initial directions for sweeping the potential shows that the occurrence of the cathodic peak (c2) is genetically linked to the product of the oxidation electrode reaction of epinephrine at (a1).

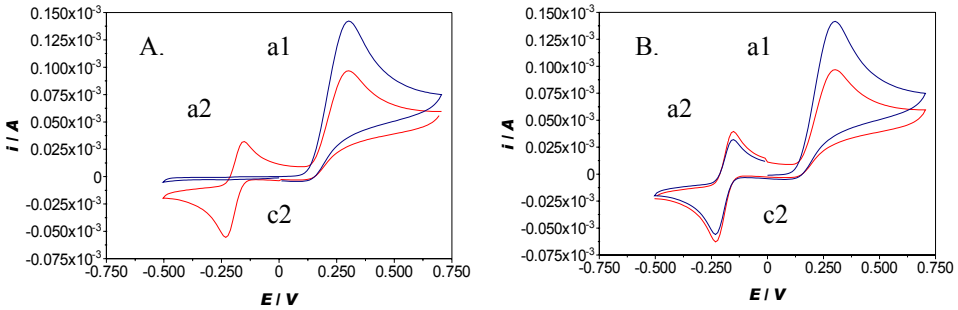



Fig. 2 – Cyclic voltammograms of 0.5 mM epinephrine at Pt bare electrode in PBS (0.2 M – 0.2 M) of pH 7. A. in the range 0.0 V to 0.7 V to -0.5 V, initial scan in anodic direction; B. in the range 0.0 V to -0.5 V to 0.7 V, initial scan in cathodic direction (scan rate 50 mV/s).

The superposition of the second cycle (see Fig. 3) for the two different cyclic voltammetry experiments, differing only by the direction of the initial scan, shows that in the anodic region there is a perfect superposition of two traces but in the cathodic region the trace of the initial cathodic-going electrode potential scan is a little bit smaller than the trace of the initial anodic-going electrode potential scan. In the former case there is only one anodic process producing open-chained epinephrinequinone able to lead, by a suite of chemical reactions, to adrenochrome. In comparison, in the latter case there are two identical anodic processes (one for each cycle) producing open-chained epinephrinequinone able to lead, by a suite of chemical reactions, to adrenochrome.

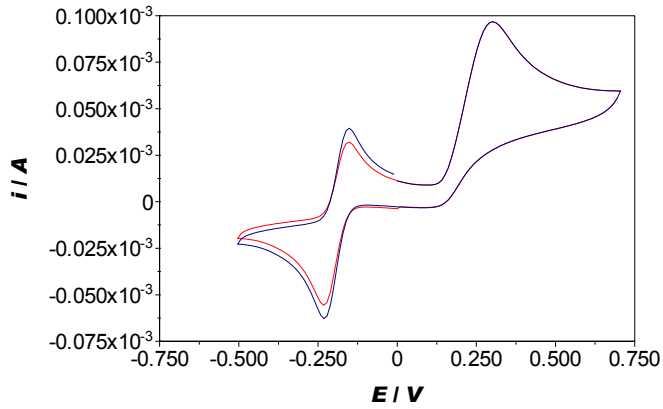
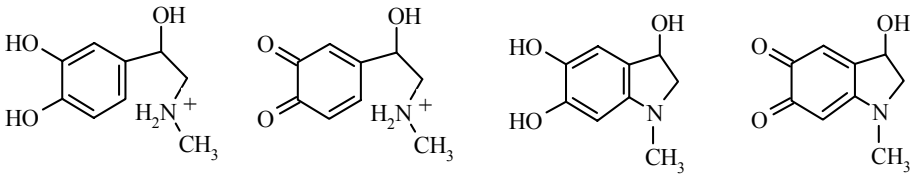



Fig. 3 – Comparison between the second scan of two cyclic voltammograms recorded at 50 mV/s on the same range of potential and at the same starting potential (0.0 V) but having different initial direction of potential sweeping. A. initial scan in anodic direction; B. initial scan in cathodic direction.

As a consequence, in the positive-going scan of the electrode potential a large quantity of adrenochrome is involved in the reduction occurring at cathodic peak (c2) and, of course, a large quantity of the conjugate redox form, leucoadrenochrome, is involved in the oxidation at anodic peak (a2).

So the anodic peak (a1) remains unchanged while the cathodic peak (c2) and its anodic counterpeak (a2) are smaller for an initial cathodic-going scan than for an initial anodic-going scan, although the difference is not so important.

At pH 7, the anodic peak (a1) is due to the oxidation of epinephrine to its corresponding open-chain quinone (E mechanism), epinephrinequinone (see Fig.4 for invoked structures and names and Fig. 5 for invoked electrode or chemical reactions), but the cathodic peak (c1) for the reduction of the latter does not appear because the red form of the couple gives rise to an irreversible chemical reaction of deprotonation (C mechanism) (the backward reaction is not possible at pH 7 due to the low proton concentration). Then it follows another chemical reaction of cyclization of unprotonated epinephrinequinone to leucoadrenochrome (see Figs. 4 and 5) (C mechanism) which, together with protonated epinephrinequinone, gives rise to a thermodynamically very favourable disproportionation reaction (C mechanism) leading to adrenochrome (see Figs. 4 and 5) and protonated epinephrine.




A B C D

Fig. 4 – Structure of protonated epinephrine (A), protonated epinephrinequinone (B), leucoadrenochrome (C) and adrenochrome (D).

Considering the $pK_a$ of protonated epinephrine ($pK_a$ =8.9), it results that even at pH 7 there is enough open-chained quinone form available to participate to the cyclization reaction. The resulted adrenochrome, as an ox form of the redox couple adrenochrome/5,6-dihydroxyl-N-methylindole, is reduced at the electrode developing the cathodic peak (c2) (E mechanism) at $E_{pc,2}$, followed for positive-going sweep by the anodic peak (a2) (E mechanism) at $E_{pa,2}$, developed by the conjugate form (5,6-dihydroxyl-N-methylindole) which is stable at this pH. All these three peaks (a1), (a2) and (c2) increase at pH 7 with the increase of the scan rate.

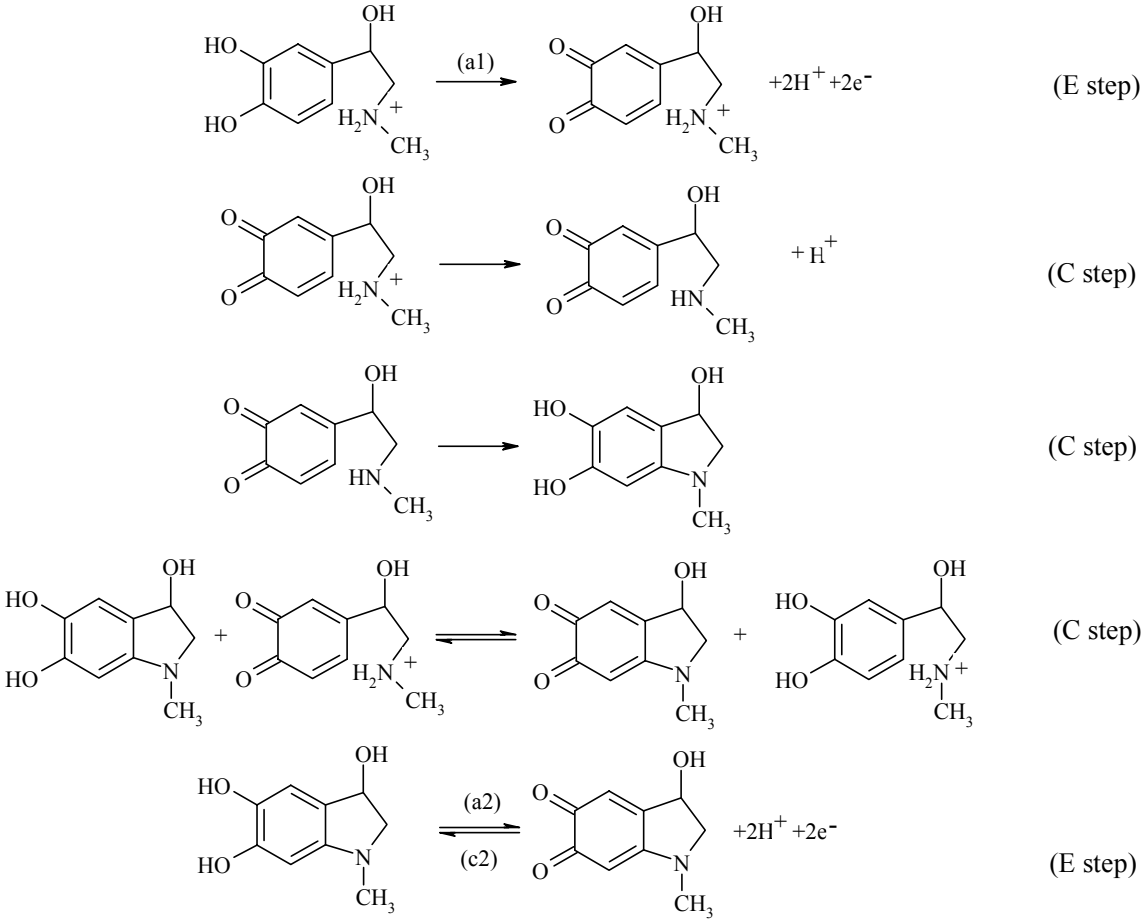



Fig. 5 – Reaction mechanism for epinephrine cyclic voltammetry behaviour at pH 7.

Of course, the counterpeak (c1) of the oxidation peak of epinephrine does not appear due to the fact that the following chemical reactions involving the formed epinephrinequinone (deprotonation and cyclization) are very fast, occurring as one-step reaction. In addition, possible reversible chemical reaction, as for example, the deprotonation of protonated epinephrinequinone, does not work at pH 7 and the disproportionation reaction [10-12], having a very large redox equilibrium constant, works as an irreversible chemical reaction. Let us remark that the backward reaction responsible for the appearance of the cathodic peak (c2) is helped to occur by increasing proton concentration. So at pH 7, and at not so high scan rates, the cathodic reduction of epinephrinequinone is not possible because there is no epinephrinequinone in the OHP.

The scan rate dependence of the cyclic voltammograms is shown in Fig.6. The peak currents increase with increasing scan rates for all three peak currents in a linear way (see Table 1). From the cyclic voltammograms, it is also noticeable that a cathodic counterpeak (c1) of the first anodic peak (a1), looking rather like a shoulder or as a limiting current, could be noticed with increasing scan rate. For high scan rates it may appear due to the fact that in the time-scale of the CV experiment the reduction of the protonated open-chained epinephrinequinone (which is the product of the anodic oxidation at (a1)), may compete with the following chemical reaction.

However, it is hardly visible at this small scan rates used in the present study. As a result, at pH 7 the anodic peak (a1) could be associated with an irreversible oxidation of epinephrine. The anodic peak potential $E_{pa,1}$ and $E_{pa,2}$ shift positively, the cathodic peak potential $E_{pc,2}$ shifts negatively with increasing scan rate. As concern the second couple of peaks (a2/c2), for increasing scan rates the peak separation increases from 0.061 V (for a scan rate of 25 mV/s) to 0.141 V (for a scan rate of 250 mV/s) but the half-peak potential remains constant at -0.1915 V.

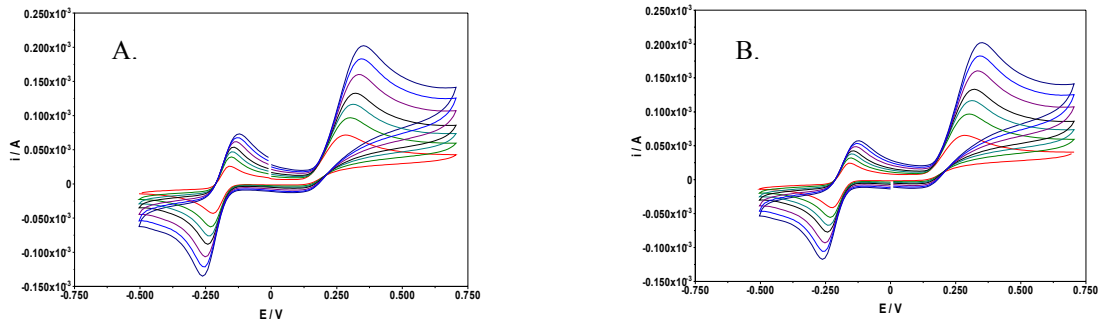



Fig. 6 – Scan rate dependences of the second cyclic voltammograms (of a two-scan CV experiment) recorded on the same range of potential and at the same starting potential but having different initial direction of potential sweeping. Scan rates: 25, 50, 75, 100, 150, 200, 250 mV/s. A. initial scan in anodic direction; B. initial scan in cathodic direction.

*Table 1*

The peak currents versus square root of the sweep rate conclusions

| | **Potential scan 0.0 --- -0.5 --- +0.7 V** | | | **Potential scan 0.0 --- +0.7 --- -0.5 V** | | |
|---|---|---|---|---|---|---|
| **v (V/s)** | **$I_{pa1}$ (A)** | **$I_{pc2}$ (A)** | **$I_{pa2}$ (A)** | **$I_{pa1}$ (A)** | **$I_{pc2}$ (A)** | **$I_{pa2}$ (A)** |
| $I_p$ versus $v^{1/2}$ | linear R=0.9989 | linear R=-0.9998 | linear R=0.9957 | linear R=0.9999 | linear R=-0.9994 | linear R=0.9903 |
| $I_p$=A+B$v^{1/2}$ | A=6.78E-6 B=3.95E-4 | A=-6.29E-6 B=-2.23E-4 | A=1.05E-5 B=9.66E-5 | A=1.10E-5 B=3.84E-4 | A=-2.77E-6 B=-2.66E-4 | A=7.94E-6 B=1.36E-4 |

The plot $\ln I_p$ versus $\ln v$ for each peak current ((a1), (c2) and (a2)) is linear with a slope very close to 0.5. This slope shows that the adsorption of epinephrine is very weak at Pt bare electrode at pH 7 so that the electrode reaction uses only the diffusional epinephrine. Also the plot $I_p$ against $v^{1/2}$ is linear (see Table 1) with very good regression coefficients, being consistent with the diffusional nature of the peaks at Pt bare electrode in PBS of pH 7.

## CONCLUSIONS

The redox behaviour of epinephrine at the Pt bare electrode, at pH 7 (PBS 0.2 M-0.2 M), in the range -0.5 V --- +0.7 V by cyclic voltammetry experiments at different scan rates exhibits an anodic peaks (a1) in the anodic region and an anodic peak (a2) and a cathodic peak (c2) in the cathodic region, looking as a pair of quasi-reversible to reversible couple of peaks. The mechanism seems to be ECCCEE, where the first E is assigned to (a1), followed by deprotonation, first C, cyclization, second C, and disproportionation, third C, and then again E, for (c2), and finally E, for (a2). The initial direction of the first potential sweeping, starting from 0.0 V (*versus* SCE), was used to decide the mechanism of the redox behaviour of epinephrine. The epinephrine seems to participate to the charge transfer reaction as a diffusional species (its adsorption on Pt bare electrode surface at pH 7 (PBS 0.2 M-0.2 M) is practically absent.

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