SELECTIVE DETERMINATION OF DOPAMINE USING MODIFIED ELECTRODES BY DIFFERENTIAL PULSE VOLTAMMETRY†

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Abstract. Selective detection of dopamine (DA) shows physiological and pathological importance because DA was widely accepted as one of the most important neurotransmitters involved in physiological processes in the mammalian central nervous system and as a prognostic biomarker for many types of diseases. In this paper a highly sensitive electrochemical method for selective determination of DA in the presence of ascorbic acid (AA), one of the most potentially interferent coexisting in the cerebral systems, is investigated. Chemically modified gold electrodes with thin layers of cobalt (II)-porphyrins (CoP) were used and characterized for DA and AA selective preconcentration and detection. The presence of CoP was favorable for the affinity adsorption of DA. This led to the decrease in the oxidation potential of AA and the enhanced oxidation peak currents of DA at the CoP-modified Au electrode. By differential pulse voltammetry (DPV), the oxidation potentials of DA and AA, at the CoP-modified Au electrode in a binary mixture were found to be well resolved so their simultaneous determination could be achieved. Under the optimized experimental conditions in DPV technique both DA and AA reveal sensitive oxidation peaks for micromolar range of concentrations.

Key words: dopamine, porphyrins, electrochemical sensors.

INTRODUCTION

Dopamine (DA) is a neurotransmitter, one of the most significant catecholamine, which plays a very important role for functioning of mammalian central nervous system (CNS), hormonal, renal and cardiovascular systems [41]. DA helps control the brain's reward and pleasure centers and also it helps regulate movement and emotional responses, and it enables us not only to see rewards, but

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to take action to move toward them. DA deficiency results in Parkinson's and Alzheimer's diseases, restless leg syndrome, attention deficit hyperactivity disorder (ADHD), schizophrenia, or HIV infection [22, 25, 32, 40]. People with low dopamine activity may be more prone to addiction, since DA acts as a neurotransmitter which is vital for message transfer functions: the use of illegal drugs or substance abuse such as heroin, cocaine, nicotine, and alcohol blocks the DA transport that inhibits the re-uptake of DA and eventually increases the DA levels, causing an increased risk of depression and drug addiction [8, 23, 26, 28]. The presence of a certain kind of dopamine receptor is also associated with sensation-seeking people, more commonly known as "risk takers" [15]. Thus, DA has been widely accepted to be one kind of prognostic biomarker for several kinds of diseases [2].

The strategies for monitoring neurotransmitters in the brain can be used both *in vivo* and *in vitro*. *In vitro* methods are generally simple; most only require a snapshot of the chemical environment in the brain or sample from tissue immersed in an artificial environment [12]. Methods for *in vivo* monitoring can be noninvasive or invasive. Positron emission tomography as a noninvasive technique is expensive and not very sensitive, detecting a limited number of neurotransmitters. Invasive methods use probes (such as chemical sensors) inserted into the brain to collect sample for analysis. In the past years, various methods, such as liquid chromatography, spectroscopy, capillary electrophoresis mass spectrometry and chemiluminescence were used for DA detection [37]. Although these methods provide high sensitivity in the detection of DA, they have several drawbacks. They require long time-consumption, high cost, and take a substantial large amount of workspace. Besides these methods, electrochemical analysis has received much attention due to its considerably high sensitivity, rapid response, low cost and ease of operation. Electrochemical determinations of biogenic amines using bare and chemically modified electrodes, mainly carbon electrodes (glassy carbon electrodes, screen-printed electrodes and carbon paste electrodes) together with nanocomposite materials have been reported in the literature [5, 16, 17, 24, 25, 32, 29, 30, 31, 35, 36, 37, 39, 40, 41]. Although electrochemical methods have been proved to be very potent for *in vivo* and real-time measurements of DA in the CNS, such methods have been limited mainly by the lack of the resolution between DA and other electroactive species coexisting in the cerebral systems. Ascorbic acid (AA) remains to be the most potential interferents [38] because it can be electrochemically oxidized at potential closed to that used for DA, and the response from AA overlaps that from dopamine resulting in difficulties in distinguishing the individual peak potentials. Also, the concentration of this interferent is much higher (100–1000 times) than the concentration of DA in CNS [32, 34]. Hence, an effective way to resolve this issue is by surface modification technique of the working electrode to circumvent the overvoltage and slow kinetics of the electrode process. Through this, achieving a suitable modification to obtain high sensitivity and selectivity towards DA sensors is the ultimate goal.

Porphyrins are among the most important ligands in the biochemistry of organic compounds [18]. The interaction of analytes with porphyrin active layers, which result in changes of various physical parameters and their conversion into an electrical signal, combining the macrocycle film with appropriate transducers has allowed the development of several kinds of chemical sensors: 5,10,15,20-tetrakis(4-carboxylphenyl)porphyrin was used as sensor in the determination of Zn in natural waters and nutritional supplements [20], manganese porphyrins deposited onto chemically modified electrodes, epoxidates the styrene with molecular oxygen [19] and the Langmuir–Blodgett thin film fabrication and gas sensing properties of metal free 2,3,7,8,12,13,17,18-octaethyl-21H,23H-porphine and its derivatives containing iron chloride, cobalt and magnesium were also reported [6]. Less studied are porphyrins used as substrate or mediator in (bio)sensors and their interaction with different analytes. In addition, the electron transfer from porphyrins to detection system is not well-understood due to less information related to properties of the electrode-porphyrins interface.

In this paper a highly sensitive electrochemical method, for selective determination of DA in the presence of AA, is investigated employing chemically modified gold electrodes with thin layers of cobalt (II)-porphyrins (CoP). Porphyrin complex was used both as mediator and as insoluble oxidation polymer catalyst for DA and its interaction with DA and AA was analyzed. The developed sensors were characterized in terms of selectivity, sensitivity, detection limit, linear range, preconcentration time and potential, and the results were discussed.

MATERIALS AND METHODS

MATERIALS

Dopamine hydrochloride, ascorbic acid, 2,3,7,8,12,13,17,18-Octaethyl-21H,23H-porphine cobalt(II), chloroform, nafion 5% (v/v), ethanol were purchased from Sigma Aldrich and used without further purification. The electrolyte used in the electrochemical studies was sodium phosphate buffer, NaPB, (0.1 M Na_2HPO_4 + 0.1 M NaH_2PO_4), pH 7.4. Dajhan LabTech deionized water (resistivity >18 MΩ) was used for the preparation of all solutions. Working solutions of DA and AA were prepared daily. Experiments were carried out at room temperature.

INSTRUMENTATION AND METHODS

Measurements were made in a one-compartment cell which consisted of a modified bulk gold electrode (area 0.00785 cm^2) as working electrode, a platinum wire as counter electrode, and a saturated Ag/AgCl electrode as reference. Voltammetric experiments were carried out using a PC-controlled compact electrochemical interface PalmSens (PalmSens BV, The Netherlands), controlled by PSTrace electrochemistry software. Differential pulse voltammograms were recorded between –0.40 V and +0.40 V at 10 mV s^{-1}, using a pulse amplitude of 50 mV (optimized conditions) with preconcentration at a fixed potential for chosen time in order to increase the signal response.

PREPARATION OF PORPHYRIN COBALT(II) FILM MODIFIED GOLD ELECTRODE

The Au bulk disc electrode was cleaned by cyclic scanning in a 0.1 M sulfuric acid solution in the potential range from –0.5 V to 1.5 V at a scan rate of 100 mV s^{-1}. The clean electrodes were modified with CoP film by their immersion into fresh solutions of 1% and 0.5% concentration of CoP (dissolved in chloroform), without and with Nafion solution, for 20 min, followed by their drying at the room temperature.

RESULTS AND DISCUSSION

An electrochemical sensor is able to produce an electrical output signal into digital signal for further analysis through a series of principal stages. Basically, the response obtained in electrochemical sensors is due to the interaction between a recognition element directly in contact with the transducer which transforms the resulting information into a measurable signal and is based on potentiometric, amperometric, and conductivity measurements [30]. Two main factors are important in the fabrication of electrochemical sensors for DA: the enhancement in electrocatalytic activity towards DA and the selectivity of DA with several potential interfering species. The rate of the electrochemical reactions is significantly influenced by the nature of the electrode surface. Generally, the electron-transfer rate is slow and the electrochemical response signal of the analytes is not obvious at low concentration at the bare electrode surface [16], which leads to the development of several surface modification methods based on chemical, electrochemical as well as electrochemical oxidative treatments. Besides, the fouling effect occurring at the bare electrode limits the sensitivity and selectivity capabilities towards DA detection [5].

The porphyrin is a macrocyclic tetrapyrrolic system, with π conjugated double bond and different substitutes connected to the periphery. The complex can accept or yield two hydrogen ions, the last possibility leading to porphyrin systems with metallic ions, called metalloporphyrins [3]. These systems not only have low energy excitations in the visible spectral region but they also accept or donate electrons easily. The two-dimensional geometry of porphyrins and their electronic structure both promote very rapid a vectorial electron transfer and the thorough interaction of these macrorings with analytes [13]. Moreover, other researchers have already pointed out that two fundamental cooperative effects take place in the sensing phenomenon and mainly determine the performances of chemical sensors based on porphyrins: weak interactions (such as Van der Waals or London forces and hydrogen bonding) and the coordination of analytes [7]. The interaction of the porphyrin thin films with the gas molecules by the conjugated π electron system was explained through appearance of charge transfer between the molecules [4], condensation of molecules on the thin film that changes the optical properties, and physical absorption by dipole-dipole forces or hydrogen bonding between the thin film and the gas molecules [27]. The central metal of the metalloporphyrin also affects sensing in terms of their electron affinity, ionization energy, and metallic character.

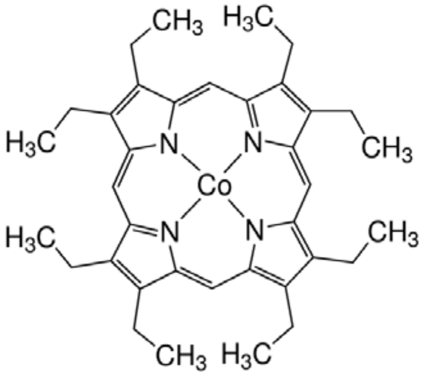

Fig. 1. Structure of 2,3,7,8,12,13,17,18-Octaethyl-21H,23H-porphine cobalt(II) [14].

Among the methods utilized in order to immobilize the active layers based on porphyrins some of the most used are the simple and immediate solvent casting or spin-coating, and the more elaborated self-assembly, electropolymerisation, and

Langmuir–Blodgett or Langmuir–Schäfer techniques. The presence of aggregates or insoluble particles in the metalloporphyrin solutions can appear inside the films. Such aggregates produced different film morphologies, and different amounts of accessible binding sites in the films. [11].

Thus, we consider that CoP modified Au electrode will have good electrocatalytic activity toward dopamine oxidation. The combination of CoP will enhance the electronic conductivity and DA accessibility, which promote the electron transfer rate between the DA and electrode surface, and thereby cause a good synergistic effect in the electrocatalysis. The chosen immobilization method in this work was the simplest one obtained by mere immersion of gold electrode into CoP solution for a period of time followed by solvent evaporation in air atmosphere.

DA contains a protonated amine group at physiological pH in mammalian brain [21]. A schematic representation of the electrocatalytic oxidation of DA at the CoP modified Au electrode is shown in Fig. 2. DA is easily oxidized electrocatalytically and forms dopamine quinone (DAQ) at the electrode surface when a potential is applied to the electrode, after the exchange of 2 electrons and 2 protons. Later, these electrons are donated to the electrode and produce a faradaic current.

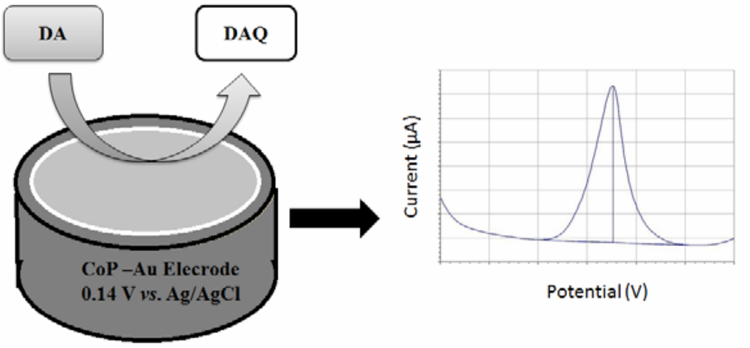

Fig. 2. Mechanism for electrocatalytic oxidation of dopamine at CoP modified Au electrode.

ELECTROCHEMICAL BEHAVIOUR

Cyclic voltammetry

Selectivity is an important factor of sensor performance. The performances of unmodified and modified Au electrodes were investigated by cyclic voltammetry (CV) in 0.1 M NaPB at pH 7.4 at a scan rate of 50 mV s^{-1}.

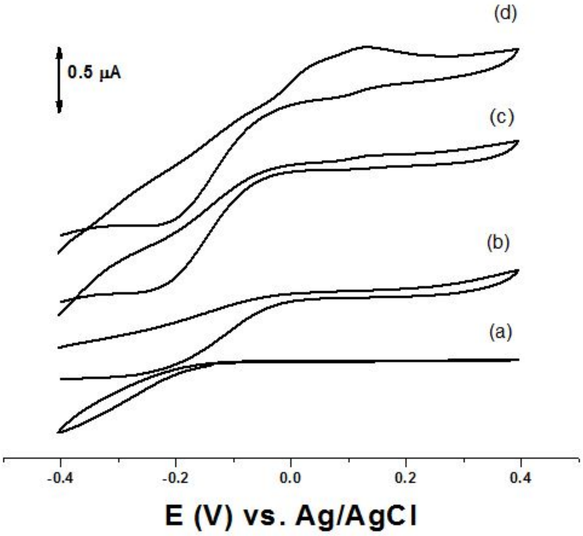

Fig. 3. Cyclic voltammograms for (a) unmodified Au electrode, (b) CoP-modified Au electrode, (c) CoP modified Au electrode in 30 μM DA, (d) CoP modified Au electrode in 30 μM DA + 200 μM AA (in 0.1 M NaPB at pH 7.4). Scan rate 50 mV s^{-1}.

Figure 3b shows (by comparison with Fig. 3a) that an improvement in electrode response was observed when CoP film was added to the Au electrode. It is obvious that the CV response of modified Au electrode is larger than that of bare Au electrode, indicating that the electron transfer rate is improved due to CoP film deposited on the electrode surface. In Fig. 3c a small peak at 0.14 V suggested the oxidation of 30 μM DA at CoP-modified Au electrode. When 0.2 μM AA is added (Fig. 3d), a second oxidation peak at 0.04 V appears which is partially overlapping with DA oxidation peak.

Differential Pulse Voltammetry

In order to achieve a more rapid, selective and sensitive detection for dopamine in the presence of AA, DPV was used due to its increased current sensitivity (using the experimental parameters described in Instrumentation and Methods section), with preconcentration (deposition of DA) at a fixed potential for a chosen time in order to increase the signal response. The effect of CoP modifying of electrode surface can be noticed by appearing of both DA and AA oxidation peaks at lower potentials compared with those obtained with bare electrode at 0.09 V for DA and –0.03 V for AA (compared with 0.15 V for DA and respectively 0.35 V for DA with bare electrodes, results not shown).

Preconcentration has been previously used to improve sensitivity at nafion-coated clinoptilolite-modified carbon paste electrode [12] where epinephrine (other catecholamine neurotransmitter) was determined by differential pulse anodic stripping voltammetry at carbon film electrode modified with multiwalled carbon nanotubes in a chitosan matrix.

Effect of preconcentration potential and time

The optimization of the deposition (preconcentration) potential and time on the oxidation peak current of 30 µM DA and 200 µM AA at the CoP modified Au electrode were tested, keeping one of these parameters constant and varying the other. The influence of preconcentration potential for Au electrode modified with 1% CoP film was studied between –1.7 and 0.0 V *vs.* Ag/AgCl, with 60 s preconcentration time. The peak of DA increases as the preconcentration potential becomes more positive from –1.7 V up to –0.7 V (at which the highest response for DA was obtained, but no response for AA was observed), with a plateau between –1.2 V and –1.0 V, and above this decreases. In similar conditions the peak of AA decreases, with a plateau between –1.4 V and –1.0 V, and disappearing at –0.6 V (Fig. 4). Hence, –1.2 V was chosen as preconcentration potential. Two distinct peaks appeared, corresponding to both DA and AA oxidation, with a separation around 122 mV, which is enough for avoiding undesired interferences. As for the preconcentration time, this was varied between 20 and 500 s, applying a preconcentration potential of –1.2 V. The oxidation peak current of 30 µM DA and 200 µM AA increases within the first 60 s and then remains stable (until 500 s), indicating a saturated adsorption state has been obtained, this suggesting that nearly all surface sites where adsorption can occur are already occupied after 60 s.

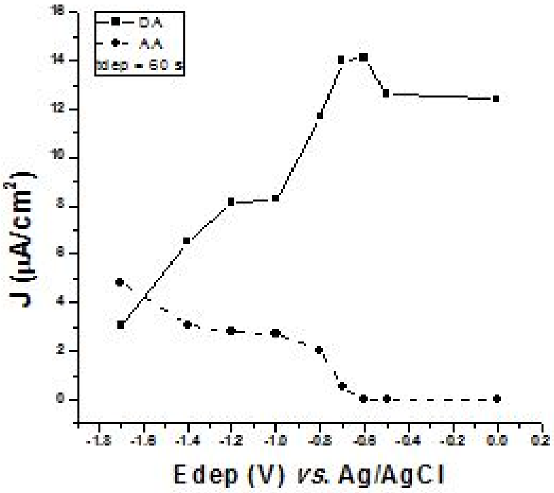

Fig. 4. Response of CoP 1 % modified Au electrode towards (30 µM DA + 200 µM AA) in NaPB, 0.1 M, pH = 7.4 for different preconcentration potentials.

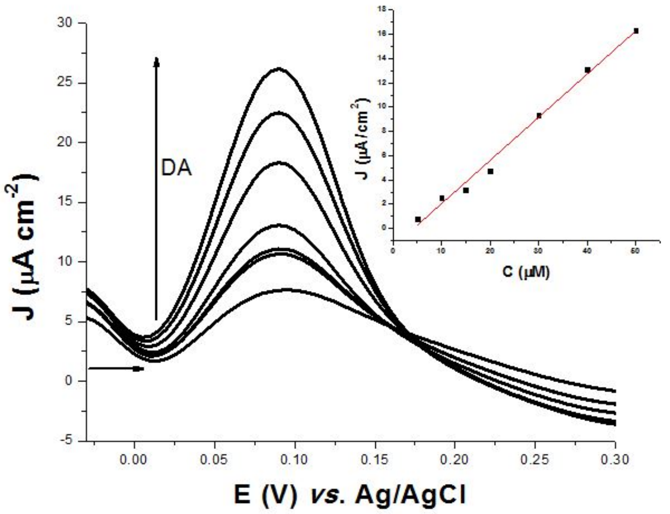

Fig. 5. Differential pulse voltammograms (baseline subtracted) at 1% CoP in 0.1 M NaPB pH 7.4 for 5 to 50 μM DA concentrations. Scan rate 10 mV s^{-1}.

The determination of DA performed under these optimized conditions (Fig. 5) exhibited a linear response up to 50 μM, a sensitivity of 0.36 μA cm^{-2} μM^{-1} and a detection limit of 0.13 μM. Unfortunately, the repeatability of this sensor is low, its performances being limited for the day of production: its sensitivity decreases very much, especially for AA (with 97%) while for the DA decreases with 50% (Fig. 6). This happens especially if the sensor was kept in the air atmosphere, which can be explained since it is known from the literature that CoP was also used in gas sensing.

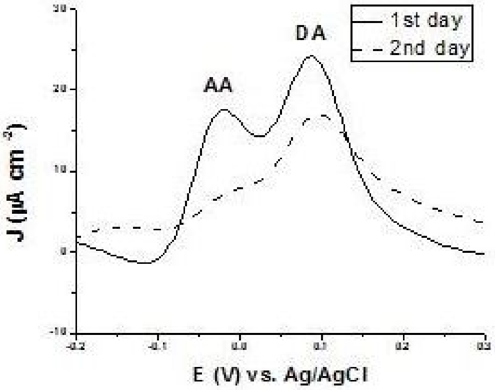

Fig. 6. Differential pulse voltammograms (baseline subtracted) in two different days at 1% CoP sensor for detection of (40 μM DA+200 μM) AA in 0.1 M NaPB pH 7.4. Scan rate 10 mV s^{-1}.

Effect of cobalt (II)-porphyrins film composition

In order to overcome the problem mentioned above, and to study the influence of metalloporphyrin concentration, 0.5% CoP was used for Au electrode surface modification. First, an alternative strategy for producing a more robust sensor was the inclusion of Nafion (a cation exchange polymer) to CoP solution which also should improve the discrimination against possible interferents. Thus, an anionic membrane in order to protect the surface from the interference will be created. Nafion generally exhibits good chemical stability due to its perfluorinated structure, and it rejects anions from electrode surfaces due to its negatively charged sites [1, 9, 10]. The partition coefficients for cations into the membrane have been shown to have large values, and their preconcentration inside the membrane facilitates electrochemical detection [21]. However, the use of Nafion membrane alone cannot solve the selectivity and sensitivity problems. In this situation the optimal experimental conditions included, before the preconcentration step, a conditioning step of the modified electrode, at a negative potential. In this way the sensor was able to discriminate between DA and AA. Thus, conditioning and preconcentration potential was varied between –1.7 and 0.0 V *vs.* Ag/AgCl, with 60 s conditioning time and other 60 s for preconcentration time. The peak of DA increases as the preconcentration potential becomes more positive from –1.7 V up to –0.5 V (at which the highest response was obtained). In similar conditions the peak of AA decreases, as the conditioning potential becomes more positive. Hence, a value of –1.2 V for conditioning potential and one of –0.5 V for preconcentration potential were chosen for selective oxidation of DA and AA.

The effect of both conditioning and preconcentration times was also studied. The appearing of distinct peaks had been monitored together with the corresponding intensity of both peaks. Taking into account that a shorter measuring time is desired, and for 1% CoP modified sensor 60 s were used and it seems this time to be enough for DA adsorption at nearly all surface sites, we have studied the behavior of 0.5% CoP+Nafion modified Au electrode for a total time of 60 s of premeasuring steps (conditioning and preconcentration). Thus, we have noticed that in this situation the peaks for both DA and AA were higher.

Table 1

Response of 0.5% CoP+ Nafion modified sensor at 50 μM DA and 400 μM AA for different conditioning (t_c) and preconcentration (t_d) times

t_c/t_d (s/s)	J (μA cm^{-2})	
	DA	AA
60/60	12.61	9.55
30/30	16.56	16.31
20/40	18.22	12.48
40/20	13.25	22.17

We have also used other three combinations of the conditioning and preconcentration times. We have observed that for the same mixture of DA and AA similar peak intensity was obtained if 30 s were employed for both times, but the DA peak was higher for using of a conditioning time of 20 s together with a preconcentration time of 40 s. (Table 1). By comparison with 1% CoP modified sensor, where the peaks were well separated, we have noticed that for CoP+Nafion modified sensor the separation between the two peaks, around 114 mV, is slightly smaller. From point of view of the stability in time of the sensor, its selectivity decreases for the fifth day after its preparation and it cannot discriminate between DA and AA peaks, even if the current of the two peaks increases corresponding to DA and AA concentrations. These two peaks were very close, with a separation of 69 mV (Fig. 7).

Because Nafion improves sensors stability and sensitivity, but it does not help to increase selectivity of the sensor, we have used 0.5% CoP alone to modify the surface of Au electrode and change the modality of sensor storage when not used: instead to keep it in the air atmosphere we kept it in NaPB 0.1 M. The effect of this condition was studied using DPV with optimized experimental conditions for sensors modified with CoP+Nafion. Response of the modified Au sensors in this case towards the same DA and AA mixture concentration for different conditioning (t_c) and preconcentration (t_d) times was similar with those described in Table 1. The electro-oxidation processes of DA and AA in the mixture were also investigated when the concentration of one species changed, whereas the other was kept constant and the results are shown in Fig. 8.

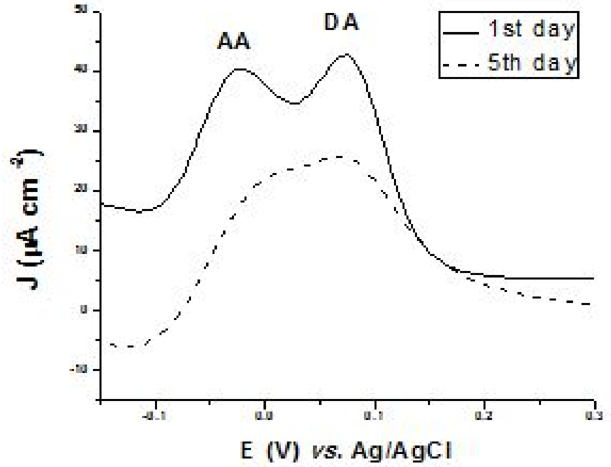

Fig. 7. Differential pulse voltammograms (baseline subtracted) at (0.5% CoP+5% Naf) sensor for detection of (40 μM DA+400 μM AA) in two different days in 0.1 M NaPB pH 7.4. Scan rate 10 mV s^{-1}.

Examination of Fig. 8 shows that the peak current of DA increased with an increase in its concentration while the concentration of AA was kept constant (200 μM). It should be noted that the change of concentration of AA did not have significant influence on the peak current and peak potential of the DA. Indeed, the changes are at the relative standard deviations (RSD) level of individual voltammetric measurement (here about 2.3%). If the concentrations of AA and DA increased synchronously, the peak currents at 0.5% CoP modified Au electrode increase accordingly as shown in Fig. 9. It can be seen that the peak currents for the two analytes increased linearly with their concentrations (data not shown). The peaks were well separated; we have noticed that for 0.5% CoP modified sensor the separation between the two peaks is around 118 mV, which is enough for avoiding undesired interferences. From the point of view of the sensor stability in time, its selectivity remains good for the second day after its preparation with a good discrimination between DA and AA peaks, and separation of 101 mV (Fig. 10). The determination of DA performed under these optimized conditions, (Fig. 8), exhibited a linear response up to 50 μM, a sensitivity of 0.21 μA cm^{-2} μM^{-1} and a detection limit of 0.75 μM. We can notice that even its sensitivity and LOD are slightly smaller than those obtained for 1% CoP modified sensor, its selectivity is better, and this fact recommends it to be used in DA detection.

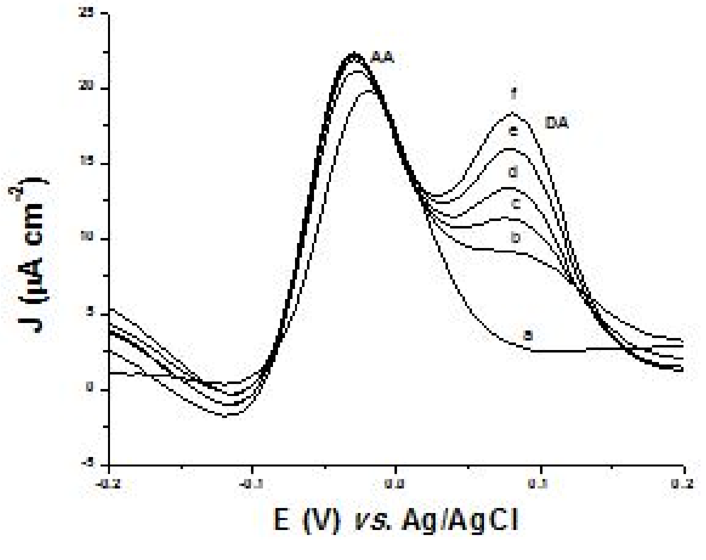

Fig. 8. Differential pulse voltammograms (baseline subtracted) at (0.5% CoP) modified Au electrode in the presence of 200 μM AA in 0.1 M NaPB pH 7.4. DA concentrations (from a to b): 0, 10, 20, 30, 40, 50 μM. Scan rate 10 mV s^{-1}. t_c/t_d = 20 s/40 s.

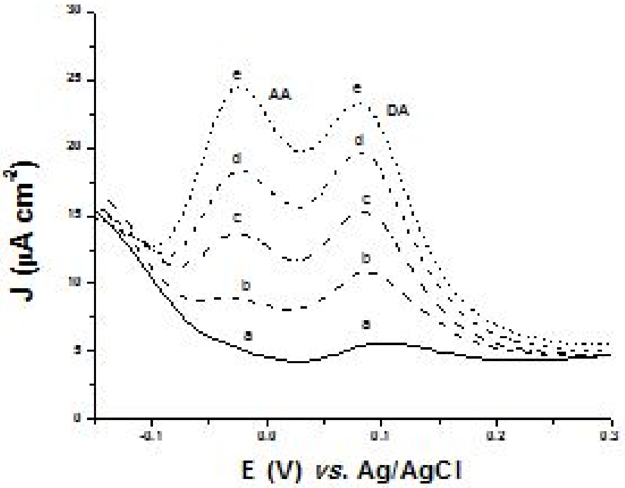

Fig. 9. Differential pulse voltammograms (baseline subtracted) of the mixture containing AA and DA at (0.5% CoP) modified Au electrode in PBS (pH 7.4). Concentrations of the two compounds (from a to e): 10, 20, 30, 40, 50 μM for DA; and 50, 100, 150, 200, 250 μM for AA. Scan rate 10 mV s^{-1}. $t_c/t_d = 20$ s/40 s.

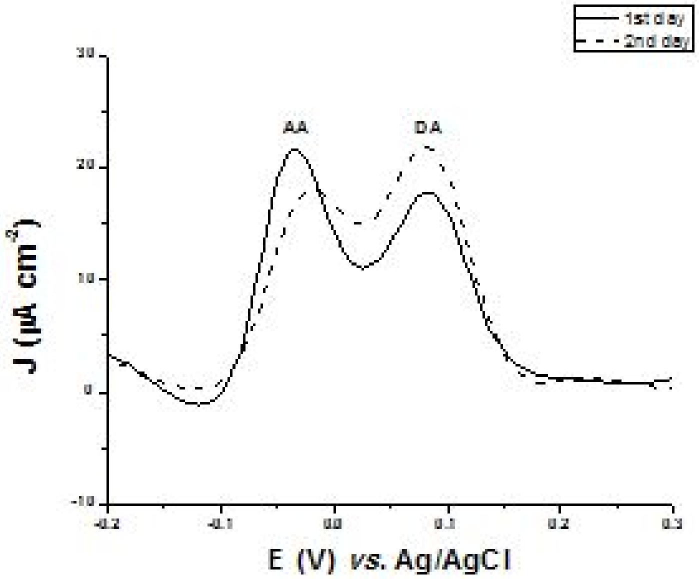

Fig. 10. Differential pulse voltammograms (baseline subtracted) at (0.5% CoP) sensor for detection of (50 uM DA+200 uM AA) in two different days in 0.1 M NaPB pH 7.4. Scan rate 10 mV s^{-1}.

CONCLUSIONS

Chemically modified gold electrodes with thin layers of CoP were used and characterized for DA and AA selective preconcentration and detection. The presence of CoP was favorable for the affinity adsorption of DA. This led to the decrease in the oxidation potential of AA and the enhanced oxidation peak currents of DA at the CoP-modified Au electrode. By differential pulse voltammetry, the oxidation potentials of DA and AA, at the 0.5 % CoP-modified Au electrode in a binary mixture were found to be well resolved so that their simultaneous determination could be achieved. Under the optimized experimental conditions in DPV technique both DA and AA reveal sensitive oxidation peaks for micromolar range of concentrations: a linear response up to 50 μM, a sensitivity of 0.21 μA cm^{-2} μM^{-1} and a detection limit of 0.75 μM. Future works will involve structural and morphological studies of CoP film deposited on Au electrode and dopamine detection for real biological samples.

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