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Aminothiophenol Furfural Self-assembled Gold Electrode Sensor for Determination of Dopamine in Pharmaceutical Formulations

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Abstract

A new Schiff base 2-aminothiophenol furfural self assembled monolayer (SAM) has been fabricated on a bare gold electrode as a novel sensor for determination of dopamine. Electrochemical impedance spectroscopy was utilized to investigate the properties of the Au 2-aminothiophenol furfural self assembled monolayer modified electrode (Au ATF SAM-ME) using the $[Fe(CN)_6]^{3-/4-}$ redox couple. The electrochemical behavior of dopamine on the Au ATF SAM-ME was studied by cyclic voltammetry and differential pulse voltammetry, using phosphate buffer solution as supporting electrolyte. The ascorbic acid has no response on the modified self-assembly electrode. A calibration curve was obtained for dopamine in a linear range of 2.0×10^{-6} to 1.0×10^{-4} M. The detection limit for dopamine was found to be 3.0×10^{-7} M. The results indicated that the Au ATF SAM-ME could be employed for the determination of dopamine in pharmaceutical formulations.

Keywords: Dopamine; Ascorbic acid; Self-assembled monolayer; Gold electrode

1. Introduction

One of the important catecholamine neurotransmitter in the mammalian central nervous system is dopamine, which plays important role in concerning the nervous system and exhibits important physiological functions and pharmacological characteristics [1]. Among various methods reported for dopamine determination, electrochemical techniques are preferential because of their advantages, which include high selectivity, rapid detection and low cost. However, a major problem in the electrochemical detection of dopamine is the coexistence of ascorbic acid in relatively high concentration. An overlapping voltammetric response for the oxidation of mixture of dopamine and ascorbic acid is obtained [2, 3]. In order to selectively detect dopamine in the presence of ascorbic acid, or simultaneously separate the oxidation potential peaks of dopamine and ascorbic acid, many studies have focused on the modification of the electrode surface by utilizing various materials such as carbon materials [4, 5], polymers [6], enzymes [7] and self-assembled monolayer [8-10]. Self-assembly procedure as a precise modification of the surface structure in nanometer-scale is recently employed in surface protection [11], fabrication of sensors [12], and biosensors [13]. There are reports for eliminating of ascorbic acid response [10, 14].

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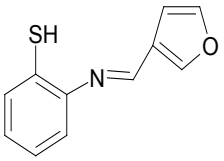
In the early work Li et al. [15] used a graphene-modified electrode for elimination of ascorbic acid response and determination of dopamine. π-π interaction between the modified surface and dopamine was a reason for dopamine response and elimination of ascorbic acid response. In the present work, an Au ATF self assembled monolayer modified electrode (Au ATF SAM-ME) was fabricated and its application for dopamine sensing in the presence of high concentration of ascorbic acid was reported. Electrochemical impedance spectroscopy (EIS) method was used for the characterization of monolayer and cyclic voltammetry (CV) and differential pulse voltammetry (DPV) were used for determination of dopamine.

2. Experimental Reagents

2-Aminothiophenol, furfural aldehyde, dopamine and ascorbic acid were purchased from MERCK (Germany). All the other chemicals were of analytical reagent grade. The polycrystalline gold disk electrode (Au, 99.99%, 0.0314cm^2) was purchased from Azar Electrode Co., Urmia, I. R. Iran.

Synthesis of ATF

The aromatic Schiff base of ATF (Scheme 1) was prepared according to the literature through a well known procedure [16] as follows: 2-Aminothiophenol (1.25 g, 0.01 mol) was mixed with 50 ml distilled ethanol in a 250 ml round bottom flask, which was stirred using a magnetic stirrer. Furfural aldehyde (0.01 mol) dissolved in a 25 ml of distilled ethanol (96.0%) was added dropwise using a dropping funnel to the above solution. The contents were refluxed for 4 h at 80 °C, and then cooled at room temperature. The solid product was filtered, and the product was re-crystallized from ethanol.

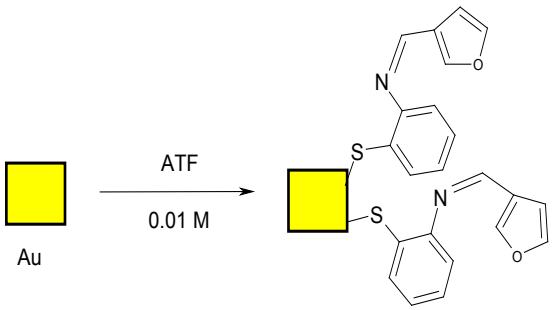


Scheme 1. Chemical scheme of ATF

Preparation of Au ATF SAM-ME

The bare gold electrode was polished to a mirror-like surface with 0.5 and 0.05 μm α-Al_2O_3, then rinsed ultrasonically with water/chloroform/water baths, each for 5 minutes, for the removal of any physically adsorbed species. Then the electrode was kept in Piranha solution (on (Scheme 2) for 10 h at 25 °C, washed thoroughly with dichloromethane and demineral water to remove unadsorbed materials. 1:3, v/v; 30% H_2O_2 and concentrated H_2SO4 [Caution: Piranha solution is extremely corrosive and must be handled carefully]) for 3.0 minutes and rinsed thoroughly with demineral water. This electrode was voltammetrically cycled and characterized in 0.5 M NaOH and then 0.5 M H_2SO_4 with a 100 mVs^{-1} scan rate until a stable cyclic voltammogam was obtained.

The cleaned Au electrode was immersed in 1.0 × 10^{-2} M ATF dichloromethane solution (Scheme 2) for 10 h at 25 °C, washed thoroughly with dichloromethane and demineral water to remove unadsorbed materials.



Scheme 2. Schematic representation of formation of ATF monolayer on Au electrode.

Electrochemical measurements

The CV, DPV and EIS measurements were carried out using an Autolab Potentiostat/Galvanostat PGSTAT30 (Eco Chemie, Utrecht, The Netherlands) which is controlled by General Purpose Electrochemical Systems (GPES) and Frequency Response Analyzer (FRA) 4.9 software. Then a conventional three-electrode system was adopted. The bare Au electrode or Au ATF SAM-ME was used as working electrodes and platinum wire and Ag/AgCl were used as auxiliary and reference electrode, respectively. The electrochemical measurements were conducted in phosphate buffer solution (PBS) and DPV analysis

was used for determination of dopamine in samples. All electrochemical measurements were carried out in an unstirred electrochemical cell at room temperature (approx. 25 °C).

3. Results and discussion

Electrochemical characterization of the SAM

The modification of Au electrodes was controlled by EIS. Figure 1 shows the Nyquist plots of the bare Au electrode and Au ATF SAM-ME in 0.1 M KCl solution containing 5.0 mM $[Fe(CN)_6]^{3-/4-}$. The Nyquist plots of bare Au and Au ATF SAM-modified electrodes show two distinct regions: (1) a semicircle in high frequencies, related to charge-transfer process; (2) a 45° line defining a region of semi-infinite diffusion of species in the electrode. Our attention is focused on the semicircle region, at a high frequency. The Rct (semicircle diameter) for the bare gold electrode is 0.65 kΩ, and the assembly of ATF layer on the electrode surface generates a barrier to the interfacial electron transfer [$(Rct)_{modified}$ = 65 kΩ]. The electrode surface coverage (θ%) can be calculated as [17]:

$$\theta\% = 100\ [1- (Rct)_{bare} / (Rct)_{modifie}] \qquad (1)$$

Using these values and equation (1), the surface coverage value was estimated to be 99%. It can be seen that the semi-circular diameter enlarged dramatically with modification, implying a high electron-transfer resistance, and very slow electron-transfer kinetics of $[Fe(CN)_6]^{3-/4-}$ probe on Au electrode due to insulation nature of the ATF monolayer on the electrode surface.

Electrochemical behavior of dopamine on Au ATF SAM-ME

The cyclic voltammograms of 1.4×10^{-4} M dopamine in 0.1 M PBS (PH 6.0) on the bare Au electrode and Au ATF SAM-ME are shown in Figure 2. It is verified that the presence of the ATF at the electrode surface reduces the overpotential of dopamine oxidation, shifting the potential value by -60. At the bare Au electrode (Figure 2a), the oxidation and reduction peaks of dopamine appear at 340 mV and 160 mV, respectively. At the Au ATF SAM ME (Figure 2b),

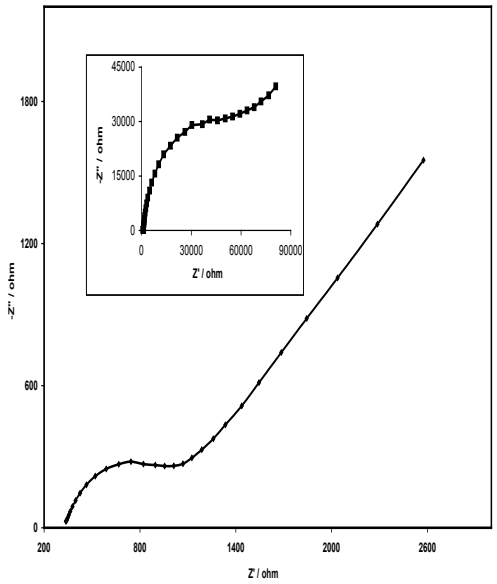


Fig. 1. Nyquist plot of bare Au electrode in the presence of 5.0 mM $Fe(CN)_6^{3-/4-}$ in 0.1 M KCl solution. The frequency range was 1.0×10^4 to 0.1 Hz. Inset shows the Nyquist plot of Au ATF SAM-ME in the same solution

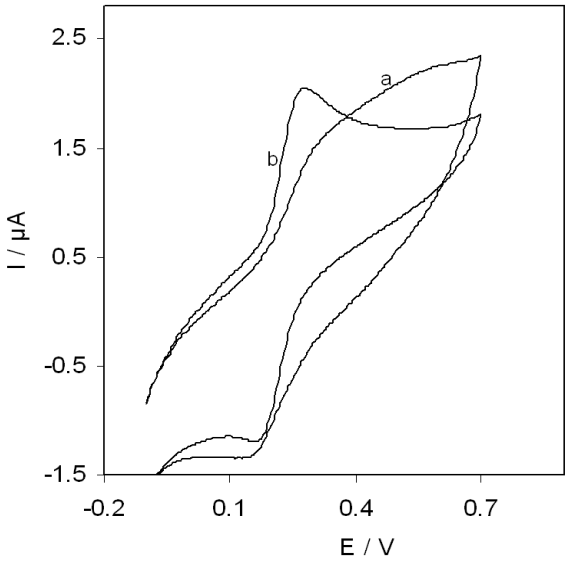


Fig. 2. CVs of 1.4×10^{-4} M dopamine on bare Au (a) and Au ATF SAM-ME (b) in 0.1 M PBS (pH 6.0). Scan rate: 30 mV/s.

the oxidation and reduction peaks of dopamine appear at 272 mV and 152 mV, respectively. The ΔE_p of dopamine was 180 and 120 mV for the bare Au electrode and Au ATF SAM ME, respectively. The ratio of anodic to cathodic peak current of dopamine for Au ATF SAM-ME was about 1.6; therefore, the oxidation peak of dopamine was used for the following experiments. The oxidation peak current of dopamine on the Au ATF SAM-ME were 3 times greater than that

The oxidation peak current of dopamine on the Au ATF SAM-ME were 3 times greater than that on the bare Au electrode. The lower overpotential (-60 mV) and the current enhancement due to an increase in the electron transfer rate could be attributed to a catalytic effect of the Au ATF SAM-ME on the oxidation of dopamine [18]. The π-π interaction between the phenyl group of dopamine and phenyl group of ATF on the surface of Au electrode may accelerate the electron transfer of dopamine in comparison with the bare Au electrode [15].

Oxidation of dopamine at the bare Au and Au ATF SAM-ME in the presence of high concentration of ascorbic acid

The detection of biogenic amines on the bare gold electrode is hindered by the presence of ascorbic acid; therefore, avoiding ascorbic acid interference is an important target for all dopamine detection analytical methods.

Figure 3 shows the CVs recorded for a single ascorbic acid and dopamine and a mixture of ascorbic acid and dopamine at the bare Au electrode and Au ATF SAM-ME in 0.1 M PBS (pH 6.0). At the bare Au electrode (Figure 3A), the oxidation peaks of dopamine and ascorbic acid appear at 340 mV and 355 mV, respectively. The mixture of dopamine and ascorbic acid give a broad peak at about 370 mV, so, the determination of dopamine in the presence of ascorbic acid is a difficult task to do. However at the Au ATF SAM-ME (Figure 3B), the oxidation peak of dopamine appears at 272 mV but no peak was found for ascorbic acid. At this electrode the current response for 1.4×10^{-4} M dopamine is 1.21 μA and after addition of high concentration of ascorbic acid (7.0×10^{-4} M), the current response changes only 3.5%, which indicates that the determination error of dopamine concentration was in the permission region (± 5%) [19], so, this electrode can be used for determination of dopamine in the presence of high concentration of ascorbic acid. Molecular structures of dopamine and ascorbic acid are distinct from each other. The strong π-π interaction between dopamine and ATF, unlike the weak interaction between ascorbic acid and ATF, may accelerate the electron transfer on this Au ATF SAM-ME [15].

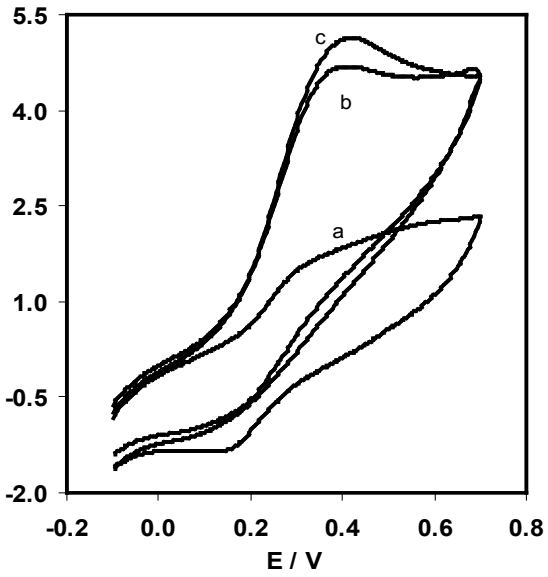


Fig. 3A

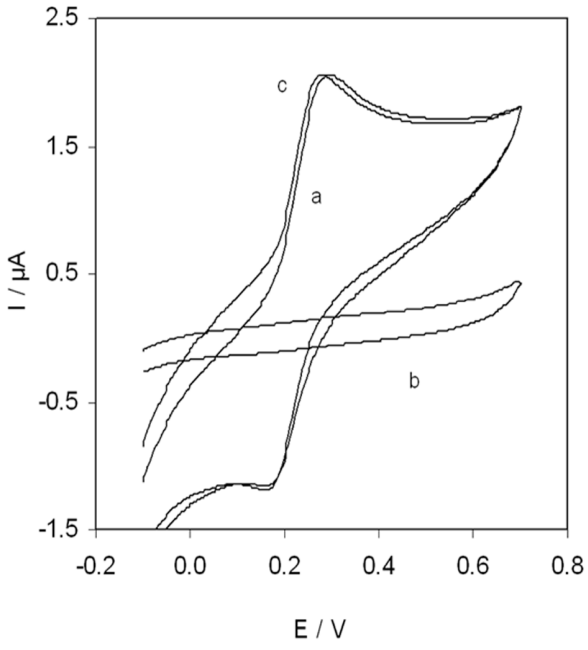


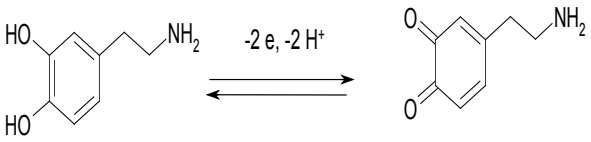
Fig. 3B

Fig. 3. CVs of dopamine and ascorbic acid on bare Au electrode (A) and Au ATF SAM-ME (B) in 0.1 M PBS (PH 6.0), a: 1.4×10^{-4} M dopamine; b: 7.0×10^{-4} M ascorbic acid; c: 1.4×10^{-4} M dopamine + 7.0×10^{-4} M ascorbic acid, scan rate: 30 mV/s.

Effect of PH and scan rates

To investigate the oxidation mechanism of dopamine, the effects of PH and scan rate on its peak currents were studied. With the PH increasing, the peak currents of dopamine reached the maximum at PH 6.0, after that, the

peak currents decreased. Therefore, the pH 6.0 was selected for the further studies. Also the relationship between dopamine potential peak and pH was studied. It can be found that the peak potential shifted negatively with the pH increase. The linear regression equation was obtained as: E_{pa} (mV) = -56.0 pH + 608 (R= 0.9992), which showed that the overall process was proton dependent and the electron transfer was accompanied by the transfer of an equal number of protons. The linear dependence of peak current on square root of scan rate reflected the diffusion-controlled nature of electrode reaction. The probable catalytic processes of dopamine may be expressed as follows [20]:



Calibration plot and interference study

The differential pulse voltammograms showed good linear relationship from 2.0 ×10^{-6} to 1.0 ×10^{-4} M dopamine (R= 0.9971) with the detection limit of 3.0 × 10^{-7} M (Figure 4). To characterize the reproducibility of the Au ATF SAM-ME, repetitive measurements were carried out in a solution containing of 4.0 × 10^{-5} M dopamine. It was found that the relative standard deviation (RSD) of voltammetric responses for 10 successive determinations on the Au ATF SAM-ME was 1.2%. The results indicated excellent reproducibility of the sensor prepared and showed that the modified electrode was not subjected to surfaces fouled by the oxidation products.

Real sample analysis

Determination of dopamine in medical samples

The accuracy of the method was evaluated through analysis of two samples of dopamine injectable formulations (Tamin Pharmaceutical Co. Rasht-Iran) by the proposed DPV method with Au ATF SAM-ME. A 0.2 mL sample from dopamine hydrochloride injection was taken and added into 10 ml PBS (0.1 M). A 0.5 mL of this sample was added to a 10 ml buffer cell and a standard addition method was applied to measuring accuracy. The values of experimentally determined dopamine were compared to the reported dopamine amounts in injections and the results are summarized in Table 1.

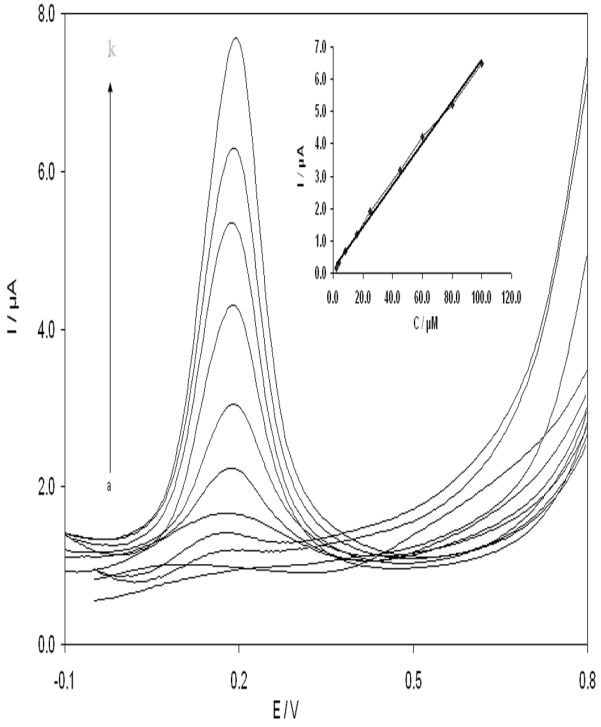


Fig. 4. DP voltammograms of blank (a), 7.0× 10^{-4} M ascorbic acid (b) and (2.0, 4.0, 8.0, 16.0, 25.0, 45.0, 60.0, 80.0 and 100.0) × 10^{-6} M dopamine (from c to k) on Au ATF SAM-ME in the 0.1 M PBS (PH 6.0). Interval time: 300 ms; modulation time: 50 ms; modulation amplitude: 100 mV and step potential: 4 mV. Insert shows a linear relationship between the oxidation peak current and the concentration of dopamine

Table 1: Determination of dopamine in two pharmaceutical formulations using the Au ATF SAM-ME.

Sample	Stated content (M)	Detected content (M)	RSD (٪)
DOPADIC(Batch No: 035)	0.21	0.205	2.5
DOPADIC (Batch No: 040)	0.210	0.219	2.1

4. Conclusion

The Au 2-aminothiophenol furfural SAM-modified electrode was characterized by using the EIS and voltammetric methods. The results demonstrate that the prepared SAM-modified electrode exhibits high catalytic activities

toward the oxidation of dopamine, and shows almost no response for the oxidation of acid. The proposed method is simple, rapid, dispense with the use of organic solvents and presents lower costs in comparison to chromatographic methods. The results offer a good possibility for extending the proposed method to clinical analysis of dopamine in real samples.

Acknowledgment

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