Selective voltammetric detection of dopamine using ferrocene modified carbon paste electrode

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Abstract. A selective sensor based on carbon paste electrode with ferrocene (Fc/CPE) has been investigated. The Fc/CPE was prepared for selective dopamine (DA) in presence of interference compounds as ascorbic acid (AA) and uric acid (UA). The Fc/CPE can well resolve the peak oxidation of DA, AA and UA. The modified electrode exhibited better electrocatalytic activity and catalytic efficiency 3.5 times higher than using the unmodified electrode. The electrochemical behaviours of DA at the surface of the modified electrode were studied by cyclic voltammetry (CV). Using differential sweep voltammetry (DPV) at the optimum condition the determination of DA was measured in the concentration range of 0.5 μM – 10 μM with a detection limit of 0.2437 μM and a correlation coefficient of 0.9995. The Fc/CPE has been applied to determination of DA spike into simulated sample and showed good recovery.

1. Introduction
Dopamine (DA) is a neurotransmitter that play critical rule in central nervous, cardiovascular, renal and hormonal system. An abnormal concentration of DA can lead neurological diseases such as schizophrenia, parkinson’s diseases and Huntington chorea [1, 2]. Several studies have reported for the detection of DA in selective and sensitive method. The electrochemical method is one of the effective tool for detection of dopamine, it is considered the rapid detection time, cost effectiveness, high sensitivity and easy operation [3]. Dopamine is a redox-active compound that has specific electrical property as a marker the present of dopamine [4]. However, the detection of DA in human metabolism have signal interference such as ascorbic acid (AA) and uric acid (UA) that coexisted in biological fluid, serum, blood and urine at high concentration level [5]. The signal interference can cause low response resolution in detection of DA, because the similarity of oxidized potential of DA, AA and UA on the bare working electrode [4, 6, 7]. To clarify this problem various modified electrodes based carbon paste have been used for determination of DA [8–11].

Ferrocene is an organometallic compound which had been used as redox-mediator[12–14], organic synthesis, medicinal functions and material engineering[15]. The stability of the ferrocenyl group makes
ferrocene attractive in a biological area, such as the detection of glucose and ascorbic acid [16] could be utilized to form a stable layer onto the surface of the electrode. In the other case, ferrocene has properties that needed to support electroanalytical determination. The properties are low relative molar mass, reproduced low potential reversible, fast reacting, pH–independent, stable in oxidized and reduced forms, unreactive with oxygen and nontoxic [17].

Determination of dopamine using carbon paste electrode have been reported [18,19], which result rather poor selectivity, reproducibility and fouling potential because the presence of ascorbic acid (AA) and uric acid (UA). In this paper, we aim to develop a simple and reliable biosensor ferrocene modified carbon paste for the selective determination of DA. Differential sweep voltammetry (DPV) and CV method was selected to exploit the selective detection of DA and to study the electrocatalytic behaviour on the electrochemical oxidation of DA. The result showed that the modified electrode Fe/CPE enhance electron transfer with a low detection limit and the peak potential separations were enough well-resolved peak shape without any overlapping of oxidation peak current values. The Fe/CPE was successfully applied for the determination of DA in real sample.

2. Experimental
2.1. Apparatus and reagent
All the reagents and solvent were of analytical grade and without further purification. Carbon from Puslitbang Bogor, Indonesia. Dopamine, ascorbic acid, uric acid and ferrocene were purchased from Sigma-Aldrich. Ultra high pure water was used for the preparation of all solutions. All electrochemical measurements were performed with a voltammeter EDAQ e-corder 410. Three electrodes were used such as a platinum wire, an Ag/AgCl and Fc/CPE as auxiliary, reference and working electrode, respectively.

2.2. Preparation of modified electrode (Fc/CPE)
Modified electrode Fe/CPE were prepared by mixing carbon, ferrocene and paraffin with the optimum weight ratio of 6:3:1 [8]. The mixture was blended and heated until a uniformly-wetted paste was obtained. Then, the paste packed into the end of a micropipette tip. A copper ware inserted into the paste to provide the electrical contact. The Fe/CPE was dried at room temperature and when necessary, a new surface was obtained by pushing excess of the paste out and polishing with a weighing paper. For comparison, the unmodified electrode was fabricated with the same procedure.

3. Result and Discussion
3.1. Electrochemical behavior of DA at the Fc/CPE
The voltammetric behavior of Fe/CPE was investigated using cyclic voltammetry (CV) at different electrodes. Figure 1 shows cyclic voltammograms of 1 mM of DA in a phosphate buffered solution (PBS) pH 5 at a potential range of -0.5 V to +1.0 V and a scan rate of 250 mVs⁻¹ at a bare CPE (solid line) and Fe/CPE (dashed line). At the CPE showed a pair of weak redox peaks with the anodic (0.187 V) and cathodic (0.036 V) peak potential and their currents (2.979 μA and 5.619 μA), respectively. The DA anodic at the Fe/CPE was slightly shifted more positive (0.334 V) and the current was highly increased 3.5 times to that at the unmodified electrode CPE, indicating the electrocatalytic ability, which meant that ferrocene are good electron mediator and accelerate the electron transfer and it will be used for sensitive detection of DA [20].
Figure 1. Cyclic voltammogram of 1 mM of DA in a buffered solution pH 5 at a) bare CPE (solid line) and b) Fc/CPE (dashed line).

Figure 2(a) shows the cyclic voltammograms of the oxidation of DA at different pH ranges 3 to 8 with a purpose to evaluating the number of protons involved in voltammetric oxidation of DA and the optimum pH value to obtain the best condition in electroanalysis of DA. As shown in Figure 3(b), the peak current slowly increased from pH solution 3 to 5 and then decreased until pH solution 8. The maximum electrocatalytic current was obtained at pH 5.0 for DA oxidation at the surface of Fc/CPE.

Figure 2. (a) Cyclic voltammograms of 1 mM DA at different pH 3 to 8 on Fc/CPE with the scan rate 100 mVs$^{-1}$. (b) The relationship of the oxidation peak current and pH.

The effect of the scan rate on the electrocatalytic oxidation of DA at Fc/CPE was investigated by CV. Figure 3(a) showed the CV’s of 1 mM DA in pH 5 PBS with a potential range of -0.5 V to +1.0 V. The oxidation peak potential shifted to more positive with increasing scan rate in the range of 10 – 250 mVs$^{-1}$, confirming the kinetic limitation of the electrochemical reaction [21]. The anodic peak current ($I_p$) was linearly dependent on the scan rate ($\nu$) with regression equation $I_{pa} (\mu A) = 0.0347 \nu + 1.9116$ with a
correlation coefficient of 0.9732 (Figure. 3(b)). The mechanism that occurs on the surface of the modified electrode can be seen from the slope value of the plot between log \( I_{pa} \) and log \( \nu \). The criteria for the adsorption reaction slope value is 1 and the mixing reaction adsorption and diffusion, if the slope value between 0.5 to 1 [22]. It is clear from Figure. 3(c) the slope value was 0.579, suggesting that the process is diffusion rather than surface control.

At a potential scan rate of 250 mVs\(^{-1}\), the ratio of anodic to cathodic peak current (\( I_{pa}/I_{pc} \)) approximately 0.7 (slightly lower than the unit value for an ideal voltammetric reversibility) and the separation peak (\( \Delta E_p \)) of 0.328 V. Scan rate 250 mVs\(^{-1}\) was chosen as an optimum basis for the \( \Delta E_p \) value that in the range of quasi-reversible and higher Ip value.

### Figure 3.
(a) Cyclic voltammograms of the Fc/CPE in PBS pH 5 containing 1 mM DA at various scan rates; 10, 20, 40, 50, 80, 100, 200, and 250 mVs\(^{-1}\).
(b) plot of \( I_{pa} \) Vs scan rate.
(c) plot of log \( I_{pa} \) Vs log \( \nu \).

3.2. Calibration plot and limit of detection
Differential pulse voltammetry method was chosen to determine the concentration of DA (Figure. 4(a)) at potential -0.2 to +0.6 V in PBS (pH 5) with a scan rate of 250 mVs\(^{-1}\). As shown in Figure. 4(b), the oxidation peak current of DA increased when the concentration of DA increased from 0.2 to 10 \( \mu \)M and consisted of a linear segment with a slope of 5.2773 \( \mu \)M. The detection limit of DA was found to be 0.2437 \( \mu \)M. This value is comparable with the value reported by other studies for electrocatalytic oxidation of DA at another modified electrode (see table 1).
Figure 4. (a) Differential pulse voltammetry of Fc/CPE in PBS (pH 5) containing different concentrations of DA. Number 1-15 correspond to 0.2; 0.6; 0.7; 0.8; 0.9; 1; 2; 3; 4; 5; 6; 7; 8; 9 and 10 μM of DA. (b) The plots of the slope of the linearly lines against DA concentration.

Table 1. Comparison of some modified electrodes in the electrooxidation of DA

| Electrode         | Modifier                               | Method | LOD (μM) | Ref   |
|-------------------|----------------------------------------|--------|----------|-------|
| Carbon paste      | -                                      | DPV    | 0.78     | [19]  |
| Glassy carbon     | Tryptophan-graphene                    | DPV    | 0.29     | [23]  |
| Graphite screen   | Graphene nanosheets and NiO nanoparticles | DPV    | 0.31     | [3]   |
| Carbon nanotubes  | Poly (m-ferrocenylaniline)             | DPV    | 0.21     | [5]   |
| Carbon paste      | Sulfated β-cyclodextrin                | DPV    | 0.13     | [24]  |
| Glassy carbon     | Reduced graphene oxide - poly(3,4-ethylenedioxythiophene) | DPV | 1.92 | [25] |
| Carbon paste      | Ferrocene                              | DPV    | 0.24     | This work |

3.3. Interference study and real sample analysis

Under the optimum condition, the interferences test was performed in the presence of uric acid and ascorbic acid. The interfering substance was chosen from the group of substances commonly found with DA in biological fluids. According to the current response (Figure 5), the DPV showed three oxidation peak at 0.17 V, 0.32 V, 0.48 V, which correspond to the oxidation of AA, DA and UA [26]. The result indicated that these substances had no influence on the signal of DA.

In order to confirm the performance of Fc/CPE, the concentration of DA was determined in human urine. The prepared human urine sample was diluted two times in PBS pH 5, then placed into the electrochemical cell. A spiking method was used to evaluate the analytical performance. The DA solution was added to the urine samples according to the amounts shown in Table 2. Satisfactory
recovery was found for DA in the range of 92.56 – 100.23%. This indicated that this modified electrode had good accuracy and can be used effectively for the determination of DA in real samples.

![Graph showing differential pulse voltammograms of Fc/CPE in PBS (pH 5) containing DA in the presence of AA and UA.]

**Table 2.** Determination of DA in real samples

| Sample         | Added (µM) | Found (µM) | Recovery (%) |
|----------------|------------|------------|--------------|
| Human urine    | -          | -          | -            |
| 1              | 0.9256     | 92.56      |              |
| 2              | 1.9687     | 98.44      |              |
| 3              | 3.0069     | 100.23     |              |

**4. Conclusions**

A selective electrochemical sensor was developed for the determination of DA based on Fc/CPE. The modified electrode exhibits good electrocatalytic activity to DA oxidation. Under the optimum condition, excellent linearity was observed by DPV peak current and concentration of DA in the range of 0.2 to 10 µM in PBS (pH 5). The Fc/CPE was utilized successfully for selective determination of DA in the presence of AA and UA with a well-defined peak separation. The detection limit was found to be 0.2437 µM. The practical application of Fc/CPE was demonstrated by measuring the concentration of DA in human urine samples with satisfactory recovery (92.56 – 100.23%).

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