ISSN: 1410-8917
Jurnal Kimia Sains & Aplikasi
e-ISSN: 2597-9914

Jurnal Kimia Sains dan Aplikasi 22 (6) (2019): 227–234

Jurnal Kimia Sains dan Aplikasi
Journal of Scientific and Applied Chemistry

Journal homepage: http://ejournal.undip.ac.id/index.php/ksa

Preparation and Validation of Fe_2O_3 Modified Carbon Paste Electrode for Measurement of Dopamine by Voltammetry Method

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https://doi.org/10.14710/jksa.22.6.227-234

Article Info

Article history:

Received: 10th July 2019
Revised: 17th September 2019
Accepted: 11th October 2019
Online: 30th November 2019

Keywords:
carbon paste electrode, dopamine, Fe_2O_3, voltammetry

Abstract

Preparation and validation of the Fe_2O_3 modified carbon paste electrode have been carried out for the analysis of dopamine by the voltammetry method. Validation parameters of carbon paste electrodes (CPA) tested include linear concentration range, Limit of Detection (LoD), Limit of Quantification (LoQ), accuracy, and selectivity in the presence of ascorbic acid and uric acid. The results obtained in the optimization of the composition and condition of the Fe_2O_3 modifier in graphite are 0.8% mass at pH 6 solution with the Brinton Robinson buffer solution. The peak potential shifted 32 mV in the negative direction from the initial peak potential of 319 mV at the carbon paste electrode without modification to the peak potential of 287 mV at the 0.8% Fe_2O_3 modified carbon paste electrode. The linear concentration range at concentrations of 8 µM–100 µM obtained a linear equation y= 1.1204 + 0.1289x with R^2=0.99943. LoD value obtained is 0.23 µM, and the LoQ is 0.77 µM. In the selectivity test obtained in the dopamine analysis using 0.8% Fe_2O_3 modified carbon paste electrode, the anodic peaks of dopamine (75 mV), ascorbic acid (190 mV), and uric acid (200 mV) can be separated. This method has acceptable repeatability because it produces a Horwitz Ratio value of 0.0417, which is smaller than two. Preparation and validation of 0.8% Fe_2O_3 modified carbon paste electrode can be declared as eligible for the measurement of dopamine.

1. Introduction

Dopamine is a type of neurotransmitter found in a variety of vertebrate and invertebrate animals and is closely related to the function of core organs such as the heart, brain, and suprarenal glands [1, 2]. The primary function of dopamine is as a hormone to inhibit the release of prolactin from the pituitary gland. The hormone dopamine has effects similar to cocaine, which can cause a sense of comfort and pleasure center in the area of the brain that can help fight depression symptoms such as anxiety. Some of the diseases found to be associated with abnormal hormone metabolism from dopamine are Parkinson's disease, schizophrenia, epilepsy, and senile dementia [3]. Various types of drugs used to treat these diseases are generally a modification of dopamine transmission. The use of various types of drugs that contain dopamine is often misused as a hormone. Therefore it is essential to develop sensitive and simple measurement methods in the determination of dopamine [2].

Up until now, several detection methods have been used in dopamine determination such as spectrophotometry [4], ion chromatography [5], capillary electrophoresis [6], chemiluminescence [7], and voltammetry methods [8]. Chromatography and electrophoresis methods, although selective and specific, are costly, and the process is complex and complicated. The fluorometry method requires many samples and a considerable amount of time [3].

In recent years, the voltammetry method is one of the most beneficial techniques for dopamine determination because it has a fast response, high sensitivity, low detection limit, has a wide linear range, and easy sample preparation and processing [8, 9, 10]. The differential pulse voltammetry technique has high sensitivity due to the reduced background current at the time of measurement, making this technique very suitable for quantitative analysis [11].

In determining dopamine, other species can interfere, such as ascorbic acid and uric acid, that accompany dopamine in the biological fluids [12, 13]. The concentration of dopamine in the extracellular fluid in the central nervous system is only in the range of 0.01-1µM, whereas the concentration of ascorbic acid is very high in the range of 100-500 µM [14, 15]. Dopamine, ascorbic acid, and uric acid are oxidized at almost the same potential on unmodified electrodes, causing an overlapping voltammetry response in the oxidation of a mixture of dopamine, ascorbic acid, and uric acid. Potentials that are not significantly different from one another will result in poor selectivity and sensitivity.

The performance of the voltammetry method is strongly influenced by the working electrode material. Popular work electrodes used in the voltammetry method include mercury electrodes, carbon electrodes, or precious metal electrodes, especially platinum and gold. Mercury electrodes have limitations in the potential anode range, so they cannot be used for the measurement of readily oxidized compounds. Solid electrodes have a wider anode potential range than mercury electrodes. Of the various solid materials that can be used as work electrodes, the most commonly used are carbon (graphite), platinum, and gold [16].

Graphite is a conductive carbon which is often used as an electrode material. Graphite material has special mechanical properties similar to metals, lightweight, and has excellent properties. In terms of economics perspective, a base material for artificial graphite is abundant, and the price is relatively low [17]. The carbon paste electrode is inexpensive, has a low background current, its surface can be renewed and modified, porous, and can be made into small shapes. Modification of carbon paste electrodes is popular as a mercury replacement electrode [16, 18]. The carbon paste electrode can be chemically modified to improve their performance in detecting samples at tiny concentrations by mixing the modifier with the carbon (bulk modification) or by coating the surface of the electrode with a thin film of the modifier (surface modification) [16, 19].

The acidity (pH) of the solution is an essential factor in determining dopamine on the surface of the modified electrode. The effect of pH on the peak current of dopamine was studied in the pH range of 2.0-11.0. Peak currents increase with increasing pH in the range 2.0-9.0. The highest peak current occurs in the pH range of 8.0-9.0 and decreases at pH 9.0-11.0 [13]. Electrodes modified with polymer films have been used for the determination of dopamine and ascorbic acid [14]. This modification has succeeded in increasing the redox peak current so that it can be more sensitive in identifying and separating the peak currents of dopamine and ascorbic acid in a phosphate buffer solution of pH 5.5 with a concentration of 0.1 M.

The metal oxide is one type of compound that can be used as a modifier because it has a high electrical capacity and low resistance. This grounds the premise that the presence of metal oxides can increase the capacity to be 10-100 times higher [20]. Fe_2O_3 is an example of metal oxide, which has the advantage of having the Fe and its oxide forms easy to obtain. Moreover, modifications can be made with a simple method and relatively inexpensive cost. Therefore, in this study, the synthesis and validation of Fe_2O_3 modified carbon paste electrodes were conducted for the analysis of dopamine by the voltammetry method based on the highest peak current generated on the voltammogram.

2. Methodology

The research is divided into several stages, starting from the preparation of tools and materials, optimization of measurement conditions, and validation of the working electrodes. The basis of optimization of measuring conditions is the pH of the solution and the composition of the modifier. The validation parameters tested include linearity, the limit of detection, the limit of quantification, selectivity, and repeatability of the measurement.

2.1. Research equipment and materials

The tools used include potentiostat (Ingsens 1030), pH meter (Cyberscan 1100), G3 membrane glass tube (Pyrex), 0.5 mm diameter platinum and silver wires (Nilaco), 2 mm diameter platinum disc electrode (BAS), microelectrode tube (Pyrex), and copper wire. The ingredients used include dopamine HCl, ascorbic acid, uric acid, graphite, liquid paraffin (Wako), KCl, $K_4Fe(CN)_6.3H_2O$, $K_3Fe(CN)_6$, H_3BO_3, CH_3COOH, H_3PO_4, NaOH (Merck), and Fe_2O_3 (reaction product of $FeCl_3$ and NaOH).

2.2. Procedure

2.2.1. Determination of optimum pH of dopamine analysis

Cu wire with a diameter of 1 mm was cut to a length of 8 cm and then inserted into the electrode tube with a diameter of 1.5 mm. A total of 100 mg of graphite and 45 µL of liquid paraffin were mixed and then stirred until homogeneous to form a carbon paste. A mixture of graphite and paraffin was inserted at the bottom of the electrode tube. The electrode surface was rubbed on a parchment paper until it was smooth and glossy. The current measurement was done by a three-electrode system, namely the working electrode as the anode, auxiliary electrode as the cathode, and the reference electrode. The schematic of the apparatus for voltammetry measurements is displayed in Figure 1. Before and during the experiment, the solution was not flowed with inert gas.

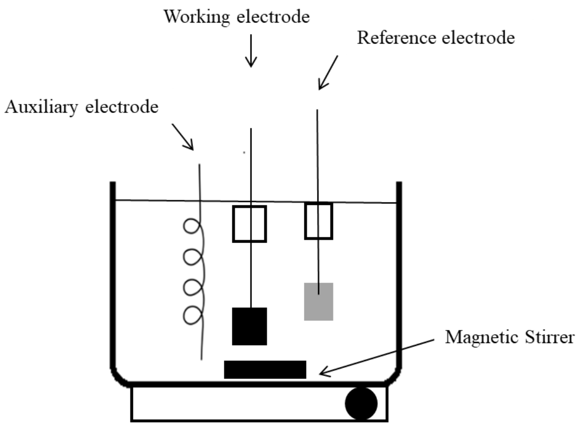


Figure 1. Voltammetry current measurement scheme

In determining the optimum pH of dopamine analysis, the cyclic voltammetry method was used. The test solution used was 1 mM dopamine HCl in Brinton Robinson buffer solution with a pH variation of 3.0; 3.5; 4.0; 4,5; 5.0; 5.5; 6.0; 6.5; 7.0; 7.5; 8.0. The Brinton Robinson buffer consisted of 0.1 M H_3BO_3 solution, 0.1 M H_3PO_4 solution, 0.1 M CH_3COOH solution, and 0.2 M NaOH solution. The pH adjustment was conducted by adding 0.2 M NaOH solution into the mixture until the solution obtained the desired pH. Each blank and sample solution was put into a voltammetric cell. The electrodes used were Ag/AgCl electrode as the reference electrode, unmodified carbon paste electrode as the working electrodes, and platinum wire as the auxiliary electrode. The three electrodes were then connected to a potentiostat. Measurements were made in the potential range of -100 to 600 mV with the cyclic voltammetry method. The peak currents obtained from the measurement of each voltammogram was corrected with the appropriate blank voltammogram. Optimal conditions for measurements were obtained from the highest peak current.

2.2.2. Preparation of carbon paste electrodes

Synthesis of Fe_2O_3 modified carbon paste electrode was carried out in the same manner as making carbon paste electrodes without modification. In the making of modified carbon paste, the addition of Fe_2O_3 modifier was done with percent variation of the modifier composition (w/w) of 0.1%, 0.2%, 0.4%, 0.6%, 0.8%, 1%, 1, 2% and 1.4% mass of graphite.

The determination of the optimum Fe_2O_3 modifier composition for dopamine analysis was carried out under the optimum pH condition. A 0.1 mM dopamine test solution was put into a voltammetry cell container, and 3 electrodes were installed, namely the Ag/AgCl electrode as a reference electrode, Fe_2O_3 modified carbon paste electrode with a specific composition as a working electrode and platinum wire as an auxiliary electrode. Measurements were made with a potential range of -100 to 600 mV using the differential pulse voltammetry method.

The steps above were carried out in the same way in different modifier compositions. The percent composition of the Fe_2O_3 modifier that produced the highest peak current was then selected for further analysis.

2.2.3. Validation of Fe_2O_3 modified carbon paste electrode by differential pulse voltammetry

Validation parameters determined are linear concentration range, the limit of detection, the limit of quantification, selectivity, and repeatability analysis. In determining the linear concentration range, the dopamine solution used was set into concentrations of 8 µM to 100 µM. Determination of limit of detection and linear concentration range was obtained from the peak voltammogram generated, while selectivity is determined based on the peak potential of each multi-component compound containing dopamine, ascorbic acid, and uric acid. The addition of the Fe_2O_3 modifier to carbon paste electrodes was done to reduce the detection limit in determining dopamine levels. Each solution was tested in voltammetry cells and measured for its peak currents at each concentration by the differential pulse voltammetry method.

From the peak current data obtained, the linear regression equation is calculated. The linear regression equation is in the form of y = a + bx, where a is the intercept and b is the slope. To determine the limits of detection and quantification, the dopamine analysis is performed on the composition of the optimum Fe_2O_3 modifier on a linear curve. The standard deviation (SD), relative standard deviation (RSD), and coefficient of variation (CV) values are then determined. The limit of detection is determined by equation 3 $S_{y/x}/b$, and the limit of quantification is calculated by equation 10 $S_{y/x}/b$. The value of $S_{y/x}$ is the deviation of the value of y (peak current) with respect to x (concentration) on the linear line of the calibration curve [21].

Selectivity was determined from the sequential analysis of 50 µM dopamine, 50 µM ascorbic acid, and 50 µM uric acid to determine the peak potential of each analyte. Furthermore, a multicomponent analysis was performed on solutions containing ascorbic acid, dopamine, and uric acid by differential pulse voltammetry.

The repeated analysis was carried out ten times on a 50 µM dopamine solution at the optimum pH. Measurements were made using the differential pulse voltammetry method. Results and discussion

3. Results and Discussion

3.1. Optimization of Measurement Condition

3.1.1. Optimization of solution pH

Determination of optimum pH in the dopamine analysis with the unmodified carbon paste electrode used a Brinton Robinson buffer solution at pH 3-8. The pH variations made is aimed to determine the effect of pH on the highest peak current generated in the measurement. The plot between the pH and the peak current obtained can be seen in Figure 2.

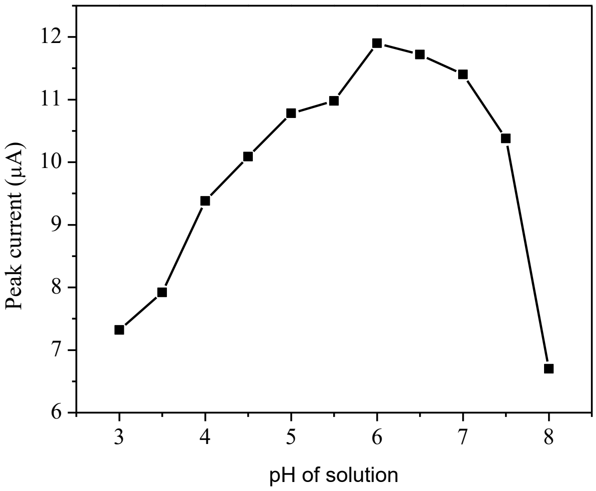
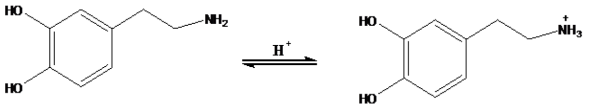


Figure 2. The plot between the pH of the solution and the resulting peak current

From Figure 2, it can be seen that the highest peak current is generated at pH 6. Thus, further measurement and observations in the study were carried out at pH 6. At pH 3 to 6, the peak current experienced an increase due to the incomplete ionization of dopamine. Dopamine under acid conditions is protonated through the oxidation process of amine groups (-NH_2 to -NH_3^+) until the optimum condition is reached. The protonation reaction of the amine group in dopamine is shown in Figure 3.



Dopamine Dopamine ion

Figure 3. The protonation reaction of dopamine to dopamine ions [22]

At pH higher than pH 6, the peak current decreases due to the hydroxyl group reacting with the -NH_3^+ group in dopamine, causing the dopamine ion to reform into the dopamine molecule.

3.1.2. Optimization of modifier composition

Based on the voltammogram of dopamine analysis using a Fe_2O_3 modified carbon paste electrode with variations in the modifier composition, it is found that the optimum peak current appears at a 0.8% Fe_2O_3 composition. The plot between the percent composition of the Fe_2O_3 modifier and the peak current generated can be seen in Figure 4.

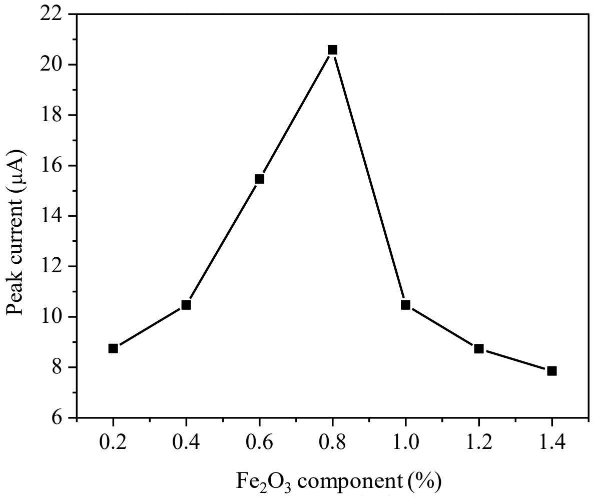


Figure 4. Optimization of Fe_2O_3 modifier composition

From Figure 4, it can be seen that the higher the composition of Fe_2O_3, the peak current generated is also higher. In compositions greater than 0.8%, the peak current generated begins to decrease. Fe_2O_3 is a semiconductor, meaning that it can accelerate the rate of electron transfer. The decrease in peak current is probably due to the reduced composition of graphite on the electrode surface as the Fe_2O_3 modifier was added. The presence of Fe_2O_3 causes the gap between the graphite layer on the surface of the electrode, where electron transfer occurs in the diffusion layer. Adekunle et al. reported that the existence of electron transfer distances could affect the electrocatalytic effectiveness of an electrode. The decrease in the rate of electron transfer occurs due to the increased distance of the electron transfer to the diffusion layer on the surface of the electrode.

Figure 5 is a comparative voltammogram between the analysis of dopamine using a carbon paste electrode without modification and a carbon paste electrode modified with Fe_2O_3. Analysis of dopamine using carbon paste electrodes without modification has a lower peak current and a higher peak potential. An increase in the peak current of dopamine measurements from 11.91 µA on the carbon paste electrode without modification to 20.46 µA on the 0.8% Fe_2O_3 modified carbon paste electrode amounting to an increase of 72.63%. A negative shift at the voltammogram peak potential of 11.15% from the peak potential of 319 mV on the carbon paste electrode without modification to peak potential of 287 mV at the 0.8% Fe_2O_3 modified carbon paste electrode indicates that modification with Fe_2O_3 can accelerate the transfer of electrons on the surface of the electrode.

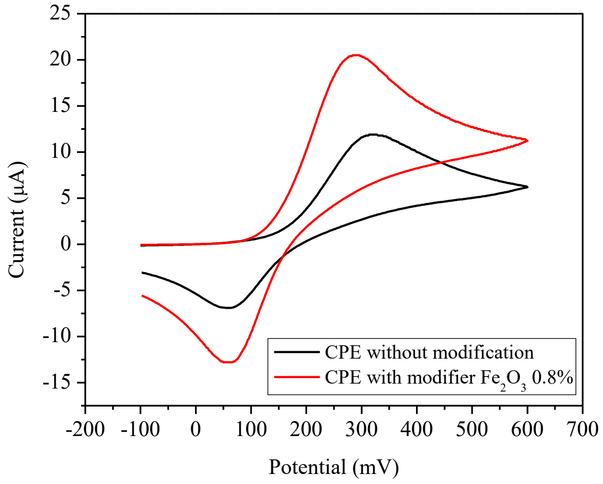


Figure 5. Voltammogram of dopamine analysis using carbon paste electrodes without modification and with 0.8 % Fe_2O_3 modification

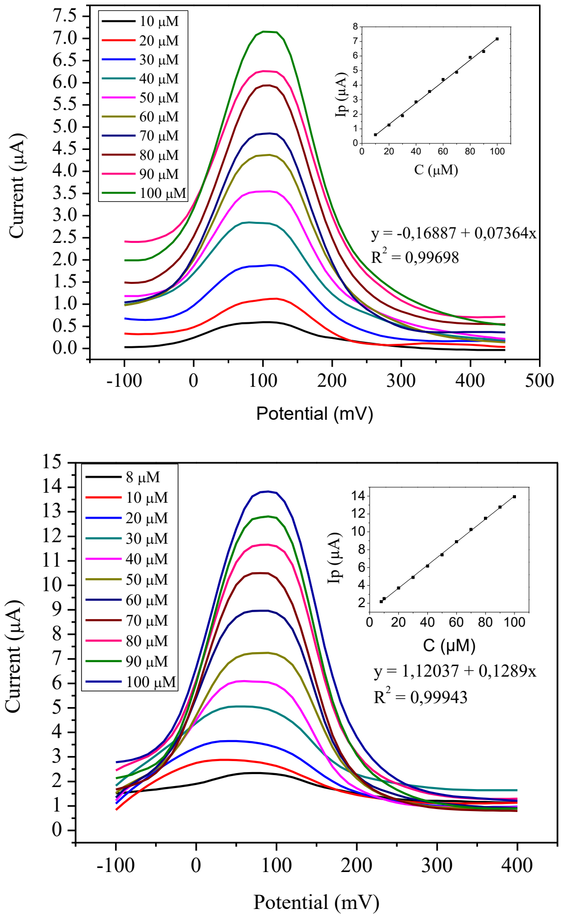
3.2. Validation of Fe_2O_3 modified carbon paste electrode in dopamine measurements

Validation of carbon paste electrodes in dopamine measurements aims to determine the feasibility of the electrodes that have been made. The parameters tested include linearity, the limit of detection, the limit of quantification, selectivity, and repeatability of electrodes.

3.2.1. Linearity

The results of dopamine analysis using a carbon paste electrode without modification with variations in concentration to determine the range of linear concentrations are shown in Figure 6.a. Figure 6.b. shows the result for the electrodes with Fe_2O_3 modification.

Figure 6 shows the linear concentration range of the unmodified carbon paste electrode at dopamine concentrations of 10-100 µM. The intercept value obtained is 0.1689, with a slope of 0.0736 and R^2=0.9995. Meanwhile, the modified carbon paste electrode gas linear range is wider, ranging from 8 µM-100 µM, with an intercept value of 1.1204, a slope of 0.1289, R^2= 0.9994. An increase in the value of the slope indicates that the electrode sensitivity also increases because the value of the current response (Y-axis) increases with an increase in the concentration of ions in the solution. The slope value of the modified electrode is higher than without modification, affirming that the sensitivity of the modified electrode is better than without modification. Regression coefficients close to 1 indicate a linear correlation between concentration and peak current.



6.a

6.b

Figure 6. Voltammogram of dopamine analysis with variations in concentration and plot between concentration and peak current, using carbon paste electrodes without modification (a), and with modification using Fe_2O_3 (b)

3.2.2. Limit of Detection and Quantification

The LoD and LoQ values obtained are 4.99 µM and 16.63 µM for the unmodified electrode, while for the modified electrode, the LoD and LoQ values are 0.23 µM and LoQ 0.77 µM. The LoD and LoQ values of the modified carbon paste electrode are lower than the one with no modification, indicating increased sensitivity in the presence of modifiers that functioned as electron transfer media.

3.2.3. Selectivity

The selectivity test was done by measuring the peak currents of the standard solutions of dopamine, ascorbic acid, uric acid, and a mixture of the three standard solutions. Oxidation mixtures of dopamine, ascorbic acid, and uric acid tend to possess an overlapping voltammetric response because oxidation reactions occur at almost the same potential. The resulting voltammogram can be seen in Figure 7.

In Figure 7.a, it can be seen that the peak currents of dopamine and ascorbic acid are at almost the same potential, i.e., 87 mV and 79 mV, while the peak current of uric acid is at a potential greater than the potential of dopamine and ascorbic acid at 214 mV. The presence of hydroxyl groups in the molecular structure of dopamine and ascorbic acid causes both of these compounds to be oxidized at almost the same potential, making it difficult to separate. Measurement of the current flow of dopamine, ascorbic acid, and uric acid produces only one peak at a potential of 90 mV.

Figure 7.b shows that the peak currents of dopamine, ascorbic acid, and uric acid in the analysis with 0.8% Fe_2O_3 modified carbon paste electrode are at separate potentials, which are 75 mV, 190 mV, and 200 mV. Unlike the case with the analysis using a carbon paste electrode without modification, the peak potential of dopamine and ascorbic acid produce adjacent potential making it difficult to separate. The peak potential of the mixture of dopamine, ascorbic acid, and uric acid obtained is at a potential of 94 mV. The addition of 0.8% Fe_2O_3 modifier to the carbon paste electrode is well used in the separation of dopamine from ascorbic acid and uric acid but cannot be used to separate ascorbic acid and uric acid.

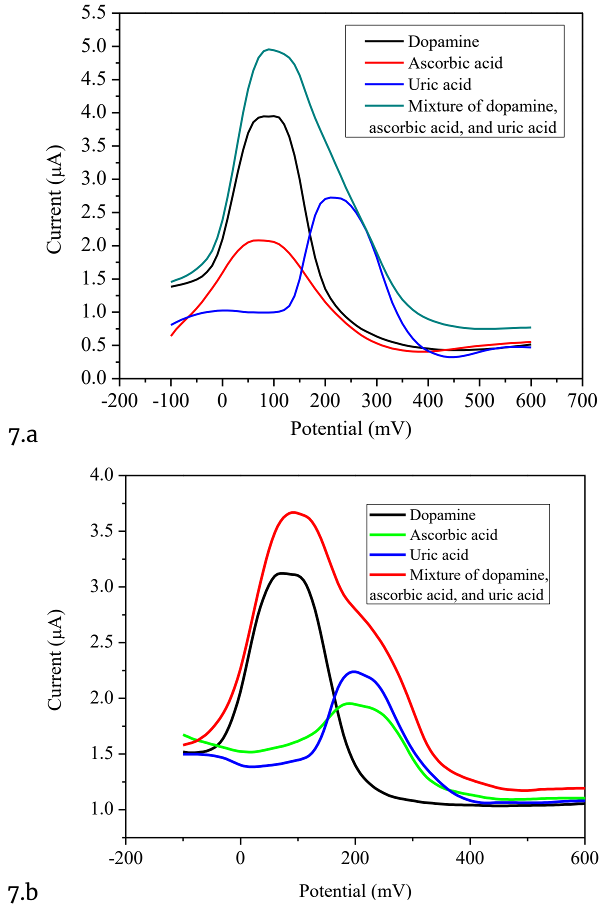


Figure 7. Voltamogram selectivity test for standard solutions of dopamine, ascorbic acid and uric acid with (a) unmodified and (b) modified carbon paste electrodes

3.2.4. Repeatability

Analysis of repeated measurements of 50 μM dopamine by the differential pulse voltammetry method was carried out 10 times and produced a graph shown in Figure 8.

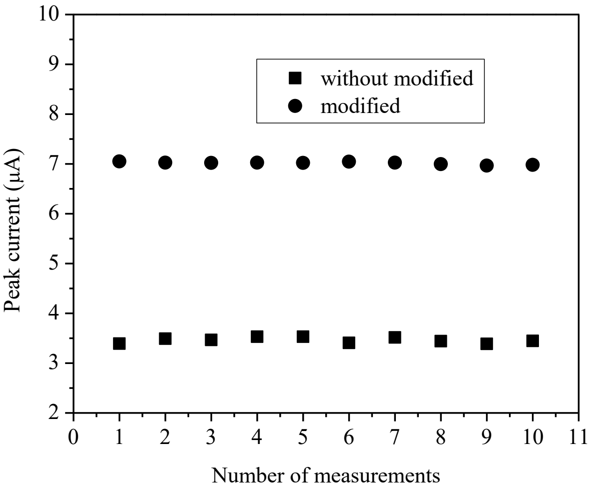


Figure 8. Repeated measurements of 50 μM dopamine on carbon paste electrodes without modification and modification

Based on the repeatability of the dopamine analysis graph, the standard deviation, relative standard deviation, and coefficient of variance of the peak currents produced can be determined. When carbon paste electrode without modification is used the standard deviation value, the coefficient of variation (% CV_{calc} and CV Horwitz), and Horwitz Ratio (comparison of calculated CV and CV Horwitz) are 0.0557; 1.61% and 8.88%; and 0.1813, respectively, while the values obtained for the 0.8% Fe_2O_3 modified carbon paste electrode are 0.0263; 0.37% and 8.88%; and 0.0417. The repeatability value can be accepted if the value of Horwitz Ratio (HorRat) is between zero to two for the measurement of dopamine using carbon paste electrodes to have a good accuracy [23]. The HorRat value using a modified carbon paste electrode is smaller than that of the unmodified electrode, implying that the Fe2O3 modified carbon paste electrode has better equality.

4. Conclusion

The concentration of dopamine can be determined using a carbon paste electrode. To reduce the detection limit and limit of quantification, and increase selectivity, carbon paste electrodes can be modified by adding Fe_2O_3. Validation results show that the values of the detection limit, limit of quantification, selectivity to ascorbic acid and uric acid, and the repeatability of the modified carbon paste electrode are better than the one with no modification.

Acknowledgments

The authors would like to thank the Directorate of Research and Community Service of the Ministry of Research, Technology, and Higher Education for the 2018 Higher Education Fundamental Research Grant (PDUPT) Year 201, contract No. 171.59 / UN14.4.A / LT / 2018.

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