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Determination of paracetamol using screen-printed carbon electrode

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***Abstract*---**A sensitive and selective electrochemical sensor based on screen-printed carbon electrode (SPCE) for detecting paracetamol has been studied. The SPCE performance was observed using cyclic voltammetry (CV) in 0.1 M phosphate buffer solution at various pH. The measurement was done at a potential range from -0.75 V to +1 V at room temperature. The response of SPCE shows that paracetamol can be detected clearly from its oxidation (0.63 V) and reduction (-0.36 V) peaks in 0.1 M phosphate buffer solution at pH 9. The obtained calibration curve followed a linear equation ipa = 3.159 + 0.134x, with R2 = 0.975 for anodic current peak and ipc = -3.373 – 0.102x, with R2 = 0.990 for cathodic current peak. The limit of detection (LOD) of the SPCE to detect paracetamol was 0.70 µM and 0.51 µM for oxidation and reduction peaks, respectively. The sensitivity of SPCE was 2.628 µA.mm-2.µM-1 for oxidation peak and 1.996 µA.mm-2.µM-1 for

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reduction peak. The reaction between the SPCE and paracetamol demonstrated diffusion-controlled behavior. The selectivity study indicates no interference signal from ascorbic acid, urea, uric acid, and glucose during paracetamol measurement.

***Keywords*---**paracetamol, SPCE, cyclic voltammetry, electrochemical sensor.

Introduction

Paracetamol (N-Acetyl-P-Aminophenol) is an acylated aromatic amide [1] and falls under weak acid material with pKa 9.7 [2]. It is also an analgesic and antipyretic drug widely used in the world for several diseases [3]. Paracetamol is used to relieve muscular aches, migraine headaches, and chronic pain [4]. In addition, paracetamol is also used to reduce fever and is the primary ingredient of flu and fever medicine [5]. The mechanism of action of paracetamol is interconnected with the obstruction of prostaglandin production in the Central Nervous System (CNS), which will automatically reduce the pain. Moreover, paracetamol also freezes the hypothalamus which is responsible for the heat-controlling system. It will reduce the fever in a short time [2]. At the therapeutic dose (50-100 μM), paracetamol is safe to be consumed and does not have serious side effects [5]. However, a paracetamol overdose can produce a toxic substance that leads to hepatotoxicity and nephrotoxicity [6].

Several methods have been applied to determine paracetamol, such as spectrophotometry [7], chromatography [8], and electrophoresis [9]. Unfortunately, these methods are expensive, relatively consume-time, and complicated. Therefore, a rapid, simple, and cheap analysis is needed. The potential method that can be developed for paracetamol detection is an electrochemical sensor [10]–[13]. The electrochemical sensor uses the principle of reduction and oxidation reaction of target analysis [11], [12]. Furthermore, paracetamol is an easily oxidized material, so the electrochemical sensor is suitable [3]. One of the electrochemical sensors is a screen-printed carbon electrode (SPCE). In contrast to conventional electrodes, SPCE has all three electrodes' systems, including reference, counter, and working electrodes, on a single platform. SPCE has attracted more attention than conventional electrodes systems due to its low cost, the possibility for miniaturization, and disposable [14]–[16]. In addition, the good LOD and repeatability of SPCE make it an ideal analytical platform for sensing applications. We used the electrochemical sensor based on SPCE for paracetamol detection in this work. The performance of SPCE for paracetamol detection was evaluated using cyclic voltammetry (CV) in 0.1 M phosphate buffer solution at various pH at room temperature. The interference study was conducted in the presence of ascorbic acid, uric acid, glucose, and urea. The performance of the SPCE was compared with other work.

Experimental

Chemical

SPCE was purchased from POTEN. Paracetamol [$C_8H_9NO_2$] was obtained from a

local market. Uric acid [$C_5H_4N_4O_3$, 99%] was purchased from Sigma Aldrich. L(+)-Ascorbic acid [$C_6H_8O_6$], D(+)-Glucose [$C_6H_{12}O_6$], and urea [$CO(NH_2)_2$ 99.5%] were purchased from Merck. All chemicals were used without any purification. A 0.1 M phosphate buffer with various pH (pH 5, pH 7, and pH 9) was prepared in the Laboratory of Instrumentation and Analytical Sciences, Chemistry Department, Faculty of Science and Data Analytics, Institut Teknologi Sepuluh Nopember. Demineralized water was bought from a local market and used for cleaning and chemical preparation.

Instrumentation

Electrochemical measurement was carried out using a potential from an electrochemical analyzer (model700B, equipped with ALS/CHI700B software) and eDAQ (potentiostat E161 and e-corder 401, equipped with e-chem software version 2.1.13).

Electrochemical Measurement

Electrochemical experiments were performed by cyclic voltammetry (CV). The potential was swept from -0.75 to +1 V. The effect of pH was analyzed by measuring 10 mM paracetamol at scan rate of 100 mV/s. The effect of scan rate was analyzed by measuring 50 µM paracetamol in 0.1 M phosphate buffer solution at the best result pH condition. The various scan rates were applied for 25, 50, 100, and 125 mV/s. The paracetamol stock solutions were made in 0.1 M phosphate buffer solutions. The various paracetamol concentrations used to obtain the calibration curve were 0 µM, 5 µM, 10 µM, 15 µM, 20 µM, and 25 µM. The LOD of paracetamol was determined using a linear calibration curve equation. The calibration curve was plotted from the maximum potential of anodic and cathodic peak current. The selectivity of SPCE was analyzed by measuring 10 mM of paracetamol, ascorbic acid, glucose, uric acid, and urea solutions. All experiments were performed at room temperature.

Result and Discussions
The Effect of pH

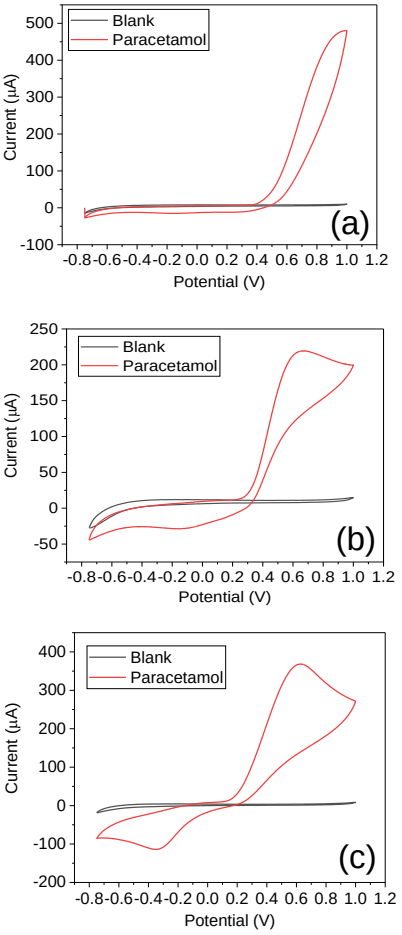

Fig. 1. Cyclic voltammograms of 10 mM paracetamol in 0.1 M phosphate buffer solution at pH 5 (a), pH 7 (b), and pH 9 (c)

The study of the pH effect aims to know the best condition of SPCE for paracetamol detection. Cyclic voltammograms of SPCE in paracetamol solutions at various pH are shown in Fig. 1. In blank conditions without paracetamol, there was no peak during measurement. In contrast, there was an oxidation peak of paracetamol in all pH conditions (Fig. 1a, 1b, and 1c). Moreover, we observe a reduction peak of paracetamol only at pH 9 (Fig. 1c). It indicates that paracetamol can be detected clearly by SPCE from its oxidation and reduction peak in pH 9. The oxidation-reduction reaction of paracetamol is shown in Fig. 2.

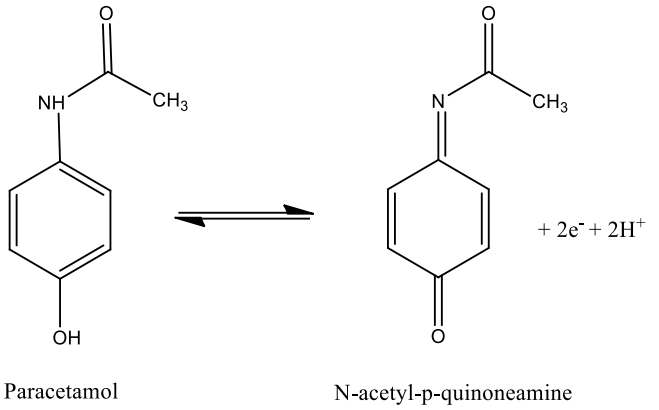

Fig. 2. Oxidation-reduction mechanism of paracetamol.

The Effect of Scan Rates

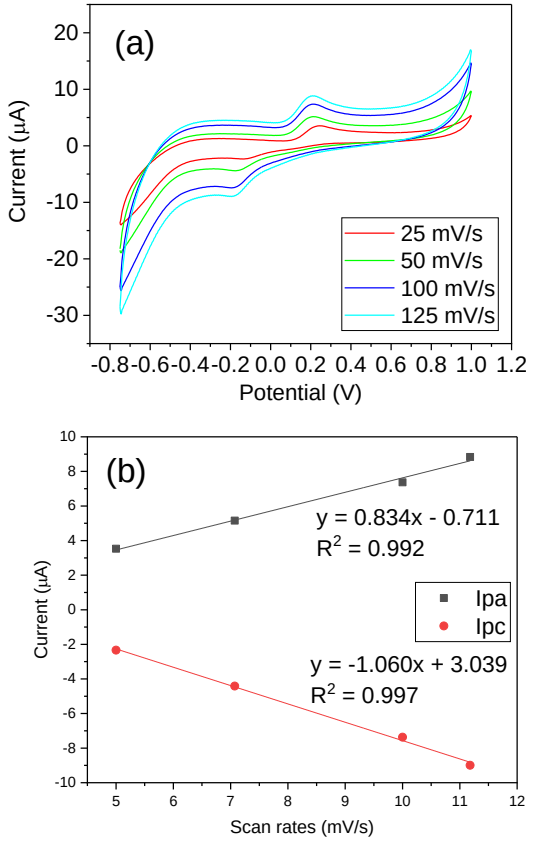

Fig. 3. Cyclic voltammograms for 50 µM paracetamol in 0.1 M phosphate buffer solution at pH 9.0 using SPCE with different scan rates (a). Variation of current against the square root of scan rate (b)

The cyclic voltammogram of SPCE in the presence of 50 μM paracetamol at pH 9 is shown in Fig. 3a. The study of the scan rate effect is to know whether the process on SPCE is diffusion or adsorption controlled [17]. Fig. 3b shows the oxidation current peak proportional to the scan rate's square root, which corresponds with the Randles-Sevcik equation (equation 1) [18].

$$i_p = (2.69 \times 10^5)\, n^{3/2}\, AC\, D^{1/2} v^{1/2}, \quad (1)$$

where i_p is the peak current, n is the number of electrons, A is the electrode area, C is the concentrations, and D is the diffusion coefficient. The linear regression equation obtained for this relation is i_{pa} (μA) = -0.711 + 0.834 v $^{1/2}$ ($mV^{1/2}$ $s^{-1/2}$) with R^2 = 0.992 and i_{pc} (μA) = 3.039 - 1.060 v $^{1/2}$ ($mV^{1/2}$ $s^{-1/2}$) with R^2 = 0.997. The result shows that the interaction between SPCE and paracetamol solution is controlled by diffusion.

Calibration Curve of Paracetamol Detection using Screen-Printed Carbon Electrode

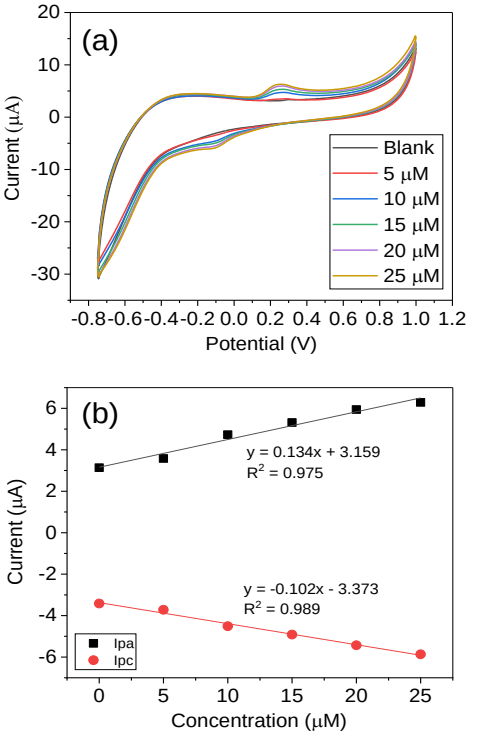

Fig. 4. Cyclic voltammograms obtained for SPCE in various paracetamol concentrations in 0.1 phosphate buffer solution at pH 9.0 with a scan rate of 100 mV/s (a). Calibration curve of paracetamol (b)

Fig. 4a shows the cyclic voltammogram of various concentrations of paracetamol. The anodic current peak increases with the increasing concentration of paracetamol. The cathodic current peak is also more negative with an increasing paracetamol concentration. Fig. 4b shows the calibration curve obtained from i_{pa}

value of 0.256 V for the anodic peak and i_{pc} value of -0.104 V for the cathodic peak. The linear regression equations are i_{pa} = 3.159 + 0.134x (R^2 = 0.975) for anodic current peak and i_{pc} = -3.373 – 0.102x (R^2 = 0.990). The limit of detection (LOD) was calculated by equation 2.

$$LOD = \frac{3S_b}{m} \quad (2)$$

where Sb is the standard deviation of the blank signal and m is the slope of the calibration curve. The detection limit obtained of 0.70 µM for anodic current peak and 0.51 for cathodic current peak. The sensitivity of SPCE for detecting paracetamol is 2.628 $\mu A.mm^{-2}.\mu M^{-1}$ and 1.996 $\mu A.mm^{-2}.\mu M^{-1}$ for anodic and cathodic current peak, respectively. The comparison of the LOD with the other electrodes is shown in Table 1.

Table 1
Comparison of SPCE performance with several electrodes

Electrodes	Linear range (µM)	LOD (µM)	Ref.
MWCNTs/CPE	2-400	0.8	[18]
Gr/CPE	2.5-143	0.6	[19]
Fe2O3/CPE	2-150	1.16	[20]
Ni-41/HCF-LDH/GCE	3-1500	0.8	[21]
GCE/MOF-199	20-300	1.3	[22]
MWCNTs-COOH/GCE	3-300	50	[23]
SPCE	5-25	0.7 (Ox) 0.51 (Red)	This Work

Selectivity Study

The SPCE response was studied against ascorbic acid, urea, uric acid, and glucose in 0.1 M phosphate buffer solution at pH 9. The cyclic voltammograms for phosphate buffer solution (blank), ascorbic acid, urea, uric acid, glucose, and paracetamol are shown in Fig. 5. Paracetamol can be detected specifically by looking at the reduction peak signal. Only paracetamol has a reduction peak, while the other does not have a reduction peak. The result indicates SPCE has good selectivity for detecting paracetamol in 0.1 M phosphate buffer solution at pH 9.

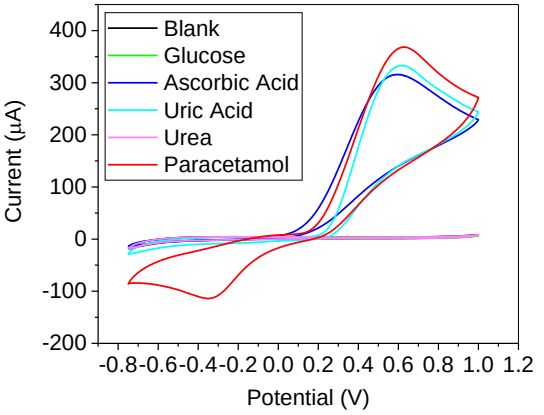

Fig. 5. Cyclic voltammograms of 10 mM glucose, 10 mM ascorbic acid, 10 mM uric acid, 10 mM urea, and 10 mM paracetamol in 0.1 M phosphate buffer solution at pH 9

Conclusion

SPCE shows good performance for detecting paracetamol in 0.1 M phosphate buffer solution at pH 9. It can be seen from the paracetamol reduction peak at -0.36 V. The detection limit of SPCE for paracetamol detection is better than other electrodes. The SPCE also shows good selectivity to detect paracetamol without interference signal of ascorbic acid, urea, uric acid, and glucose.

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