Voltammetric Determination of Paracetamol using Polyvinyl Alcohol (PVA)-Fe₃O₄ Modified Glassy Carbon Electrode

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Abstract. Modifications of glassy carbon electrodes (GCE) as working electrodes have been carried out by polyvinyl alcohol (PVA)-Fe₃O₄ membranes. The PVA-Fe₃O₄ membrane was superimposed on the surface of a glassy carbon electrode. This study influences the percentage of paracetamol in the membrane, the effect of modulation time, the effect of modulation amplitude, the effect of scan rate, the effect of pH and supporting electrolytes. The performance evaluation of the modified electrode was based on a voltammogram of cyclic voltammetry (CV) and the analysis was carried out with a differential pulse voltammetry (DPV) method. The effect of pH was studied in the range of 2-7 by Britton – Robinson buffer. The results showed that the percentage of paracetamol in the membrane affected the diffusion of current. The best performance of GCE modified was produced by a membrane with paracetamol percentage of 3% (w/w). The optimum operational condition of the instrument was at modulation amplitude of 10 mV, the modulation time of 0.1 s and the scan rate of 12.5 mV/s. pH affects the shift of the anodic peak of paracetamol in a more negative direction. The results of the analysis of paracetamol using DPV method showed that more sensitivity was achieved when phosphate buffer as a supporting electrolyte was used. The sensitivity of the GCE modified by the PVA-Fe₃O₄ membrane was 0.2922 µA/µM in the linear concentration range of 0-100 µM and limit of detection (LoD) of 8 µM.

1. Introduction
Paracetamol is one of the headaches and fever medications that is circulating in the community [1-3]. The spectrophotometry method is a fast, simple and inexpensive method of determining paracetamol, but this method has several limitations [4]. The presence of spectral disturbances caused by other components in the drug, the maximal wavelength of paracetamol 244 nm, can be disturbed by propyphenazone,266 nm, and caffeine,273 nm [5]. Therefore, the method of determining paracetamol in drugs requires a more selective method that is more sensitive.

Paracetamol is an electroactive compound that can be detected using electroanalytical methods such as voltammetry. Voltammetry method has high sensitivity, precision, inexpensive cost, low limit of detection and wider linear range [6]. Determination of paracetamol using voltammetry has been widely used in the blood samples, water, medicine and mixed compounds. The results showed a recovery range of 97-102% and highly reproducible response [7-10]. The oxidation reaction of paracetamol is shown in Scheme 1.
Scheme 1. The oxidation reaction of paracetamol to be N-acetyl-p-quinonimine in acidic condition [11].

Modification of carbon electrodes using molecular imprinted polymer (MIP) technique can increase the sensitivity and selectivity of paracetamol determination. The presence of specific molecules in the membrane allowing only specific species of sizes and shapes diffused to the surface of the electrode. In this study, polyvinyl alcohol (PVA) is used as base polymer, paracetamol as template molecule, glutaraldehyde as crosslinker and citric acid as catalyst.

Polyvinyl alcohol (PVA) is one of the basic polymers in the manufacture of selective membrane. PVA is biocompatible and nontoxic material. It also has mechanical and pH resistance and formidable hydrophilicity. It has been widely used in the field of biosensors and sensors, such as determination of 2,4-DNT vapor and paracetamol [12-13].

Magnetite (Fe₃O₄) is a superparamagnetic metal oxide that is biocompatible and low toxicity. It has high surface reaction activity, high catalytic efficiency and high conductivity so it can increase electron transfer [14]. Modification of carbon electrodes with magnetite has been studied for the determination of glucose, dopamine, and ascorbic acid [14-15]. He (2017) modified glassy carbon electrode with magnetite and graphene to increase the sensitivity of sulphanilamide determination.

Herein, an electrochemical sensor for paracetamol in MIP PVA-Fe₃O₄ modified glassy carbon electrode will be studied. Some conditions for this study are the effect of the differential of paracetamol concentration as template in membrane, the effect of pH and supporting electrolyte.

2. Materials and Methods

2.1. Materials and Equipment

The material used in this experiment were paracetamol (Sigma Aldrich), polyvinyl alcohol, glutaraldehyde 50% (Sigma Aldrich), citric acid, magnetite (Fe₃O₄), sodium hydroxide (Merck), sodium dihydrogen phosphate, phosphate acid (Merck), acetic acid (Merck), boric acid, ethanol (Merck), hydrobath aqua demineralization, potassium chloride, and chloride acid (Merck).

The equipment in this study were galvanostat potentiostat (Autolab PGSTAT204), glassy carbon electrode as working electrode, platinum (Pt) wire as counter electrode, and silver chloride Ag/AgCl as reference electrode.

2.2. The Preparation of Membrane

The membrane was made in different percentage of paracetamol in membrane. The compositions of MIP PVA were 5% PVA 0.9 mL, 4% glutaraldehyde 0.1 mL, 5% citric acid 0.1 mL and 1% paracetamol 54 µL, 110 µL and 167 µL for percentage of paracetamol 1; 2; 3% (w/w) in membrane, respectively. Meanwhile, the compositions of MIP PVA-Fe₃O₄ were same for other composition except 1% paracetamol 55 µL, 113 µL, 171 µL for percentage of paracetamol 1; 2; 3% (w/w) in membrane, respectively, and addition of 23 µL Fe₃O₄ 0.5%. All compositions were mixed and stirred at 50 °C for 30 minutes. The removal template using cyclic voltammetry technique as shown in 2.3.
2.3. Modification of GCE

The GCE (length = 6.5 cm; d = 2.0 mm). The GCE was rinsed with ethanol and dried at 50°C for 20 min. Next, the GCE was immersed three times in mixture that left in hot condition (50°C). The first and the second immersion were dried at 50°C for 10 min then the last immersion was dried at 50°C for 2 h. The paracetamol was removed to form a template by cyclic voltammetry for 5 cycles.

2.4. Cyclic Voltammetry (CV) and Different Pulse Voltammetry (DPV)

The study of paracetamol percentage in membrane used paracetamol 0.05 mM solution in pH 4 Britton Brinson buffer. The electrochemical behaviors of paracetamol in modified electrode were studied by cyclic voltammetry (CV) and analyzed quantitatively by different pulse voltammetry (DPV). The potential range of CV was -1.200 to -1.200 V and the scan rate was 0.05 V/s. Meanwhile, the potential range of DPV was 0.2 – 1.2 V with amplitude of 0.1 V, modulation time of 0.12 s and scan rate of 0.025 V/s. In the next step, the DPV method was used to measure pH and supporting electrolyte effects. The settings were potential range of 0.2-1.2 V, amplitude of 0.1 V, modulation time of 0.1 s and scan rate of 0.0125 V/s.

3. Results

3.1. The effect of paracetamol concentration in membrane

The percentage difference of paracetamol in the membranes produce different current response. Measurements were carried out by the DPV method and analyzed based on the height of anodic peak currents.

![Voltammogram DPV](image)

**Figure 1.** Voltammogram DPV of the effect of percentage of paracetamol (PR)% (w/w) in membrane with paracetamol 1; 2; and 3% (w/w).

The Figure 1 showed the relationship of percentage of paracetamol in the membrane with the anodic peak current. The high percentage of paracetamol generates higher current. This is due to the increase of the number of templates in the membrane according to the percentage of paracetamol. However, the higher percentage of paracetamol in membrane may decrease the selectivity of the sensor because the greater number of templates resulted in the diffusion of other components or
interferents on the surface electrode if their potential is sufficient. For this case, the optimum of percentage of paracetamol in the membrane was 3% (w/w).

| Membrane | Paracetamol % (w/w) | E_{pa} (V) | I_{pa} (µA) |
|-----------|---------------------|------------|-------------|
| MP1       | 1%                  | 0.62805    | 52          |
| MP2       | 2%                  | 0.63309    | 57          |
| MP3       | 3%                  | 0.63309    | 60          |

*Note: MP1, MP2, MP3 are membrane with percentage of paracetamol 1; 2; and 3% (w/w), respectively.

The anodic peak potential of paracetamol in different membranes are shown in Table 2. The $E_{pa}$ shifts slightly to positive and there is no significant difference between MP1, MP2 and MP3. Thus, the percentage difference of paracetamol doesn’t give the specific change for electrochemical oxidation of paracetamol.

### 3.2. Optimization of Different Pulse Voltammetry Parameters

The parameters of DPV have to be optimized for the analytical application. There are three parameters of modulation amplitudes, modulation times and scan rates.

![Volammogram of optimization of DPV](image)

**Figure 2.** Voltammogram of optimization of DPV a) modulation amplitude (0.1 -0.2 V); b) modulation times (0.025 – 0.125 s) and scan rate (0.01 – 0.025 V/s)

The height of anodic current peak from the different modulation amplitude is shown in Figure 2(a). The peak current increases with the increasing modulation amplitude and the height of peak current.
Thus, voltammogram of DPV 0.1 V is chosen as the optimum of modulation amplitude. The modulation time is the duration of the potential pulse. Figure 2(b) indicates that there is no different high peak current between 0.075; 0.1; and 0.125 s. The highest anodic peak current is obtained at 0.025 s. The modulation time at 0.1 s is used for the next application. The scan rate influences the height of anodic peak current because it can increase the rate of controlling time. The observation of electrochemical oxidation of paracetamol can’t be shown at the higher scan rate more than 0.025 V/s. For the next application, 0.0125 V/s is chosen for measurement.

3.3. The effect of pH and supporting electrolytes
The electrochemical oxidation of paracetamol in different pH by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) can be viewed in Figure 3. The anodic peak potential shifts from 0.6 V to 0.3 V with increasing pH value. It indicates that the voltammetric determination of paracetamol is pH dependent. The CV voltammogram showed one anodic peak potential indicating the irreversible reaction [17]. Meanwhile, the DPV voltammogram showed that the highest anodic peak current occurred at pH 2, so it is chosen as optimum pH for measurement.

![Figure 3. CV (a) and DPV (b) voltammogram of pH measurement of paracetamol 1 mM in Britton Robinson buffer 0.04 M pH 2-7.](image)

The electrolyte solutions are used to reduce obstructions from solution and added conductivity. It also used for controlling potential during measurement to reduce the effect of electron migration. Based on the data in Table 2, the highest peak current is carried out with Britton Robinson buffer 0.04 M. However, the supporting electrolyte phosphate buffer has the lowest background current, thus, it is chosen as optimum supporting electrolyte.

| Supporting electrolyte | \( E_{pa} \) | \( I_{pa} \) (\( \mu A \)) |
|------------------------|-------------|------------------|
| BR 0.04 M              | 0.67337     | 174.76           |
| Phosphate buffer 0.04 M| 0.64819     | 172.35           |
| HCl 0.1 M              | 0.653229    | 168.93           |

3.4. The Performance of GCE-PVA-\( \text{Fe}_3\text{O}_4 \)
To understand the relationship between concentration and peak current, DPV technique was used to determine paracetamol in concentration range from 0 – 100 \( \mu \)M. The determination is under the optimized experimental condition using unmodified carbon electrode (GCE), MIP PVA and MIP PVA-\( \text{Fe}_3\text{O}_4 \),modified glassy carbon electrode (as shown in Figure 4).
Figure 4. a) DPV voltammogram and b) standard curve of Paracetamol 0–100 µM in phosphate buffer 0.04 M pH 2 measured by GCE-PVA-Fe₃O₄.

The anodic peak current values versus concentration of paracetamol plots is shown in Figure 4(b). The equation of the linear regression plots is \( I_p (\mu A) = 0.2922x + 1.0827 \) (µM) with the correlation coefficient 0.9958. The analytical parameters of paracetamol obtained using three difference working electrodes produced difference performance (as shown Table 3).

Table 3. Analytical performance of difference working electrode

| Parameters               | GCE       | GCE-PVA   | GCE-PVA-Fe₃O₄ |
|--------------------------|-----------|-----------|---------------|
| Sensitivity/ (µA/µM)     | 0.4871    | 0.2695    | 0.2922        |
| Correlation coefficient  | 0.9799    | 0.9906    | 0.9958        |
| LoD/ (µM)                | 17        | 12        | 8             |
| Linear range/ (µM)       | 0–100 µM  | 0–100 µM  | 0–100 µM      |

The modified glassy carbon electrode with PVA and PVA-Fe₃O₄ can increase the performance of determination compared to unmodified glassy carbon electrode. The highest correlation coefficient is MIP PVA-Fe₃O₄ with the limit of detection of 8 µM.

4. Conclusion

The simple carbon electrode which increase the performance of paracetamol determination using voltammetry technique was established. The best concentration of paracetamol in membrane was 3% (w/w). The best DPV parameters were obtained at modulation amplitude 0.1 V, modulation time 0.1 s and scan rate 0.0125 V/s. The pH value can influence the peak current and potential of paracetamol. The highest peak current occurred at pH 2. The supporting electrolyte of phosphate buffer was chosen for the next measurement. The modified glassy carbon electrode with PVA-Fe₃O₄ has the highest correlation coefficient with LoD 8 µM.

References

[1] A. Mao, H. Li, D. Jin, L. Yu, and X. Hu 2015 Talanta. 144 252–7
[2] C. M. Kuskur, K. Swamy BE, and Jayadevappa H 2015 J. Anal. Bioanal. Tech. 6 1-6
[3] G. Yang, L. Wang, J. Jia, and D. Zhou 2012 J. Solid state Electrochem 16 2967-77
[4] H. Montaseri, and P. B.C. Forbes 2018 Trends in Analytical Chemistry 108 122-134
[5] K. Delvadiya, R. Kimbahune, P. Kabra, Sunil K, P. Patel 2011 Int J Pharm Pharm Sci 3 170-174
[6] A. Ejaz and S. Jeon 2017 Electrochimica Acta 245 742–751
[7] S. Berto 2018 *Electrochimica Acta* **284** 279–286
[8] Tanuja SB, Kumara SBE and Vasantakumar PK 2018 Ind. Chem. **4**(124) 1-10
[9] M. Akbari, H. Shayani-Jam, M. R. Yaftian, and M. Parinejad 2018 *J. Electroanal. Chem.* **827** 160–6
[10] L. Ozcan and Y. Sahin 2007 Sensors Actuators B Chem. **127**(2) 362–369
[11] P. Alagarsamy, R. Settu, S.M. Chen, T.W. Chen, I.S. Hong, and M. M. Rao 2018 *Int. J. Electrochem. Sci.* **13** 7930-8
[12] M. F. Koudehi, and S. M. Pourmortazavi 2018 *electroanalysis* **30** 1-10
[13] Nandhita A., Manokaran J., and Balasubramanian N 2014 *Res. J. Chem. Environ.* **18** 54-61
[14] A. L. Kavitha, H. G. Prabu, S. A. Babu, and S.K. Suja 2013 *Journal of Nanoscience and Nanotechnology* **13** 98-104
[15] C. Fernandez, Z. Heger, R. Kizek, T. Ramakrishnappa, A. Borun, and N. H. Faisal 2015 *Int. J. Electrochem. Sci.* **10** 7440-52
[16] B. He, and S. Yan 2017 *Int.J. Electrochem. Sci.* **12**, 3001-11
[17] C. Engin, S. Yilmaz, G. Saglikoglu, S. Yagmur, and M. Sadikoglu 2015 *Int. J. Electrochem. Sci.* **10** 1916–25