DOI: 10.21776/ub.jpacr.2022.011.03.677 *J. Pure App. Chem. Res.*, **2022**, 11 (3), 182-188
14 November 2022

Mini Electrode Based on Chitosan-Activated Carbon Membrane for Detection Paracetamol in Herbal Medicine

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Received 2 February 2022; Accepted 14 November 2022

ABSTRACT

A tube type mini electrode has been made to detect paracetamol levels in herbal medicine, the electrode is made of a glass tube with a diameter of 0.7 cm, a length of 3 cm. As the membrane is a mixture of chitosan, activated carbon from rice husk, and cetyl trimethyl ammonium (CTA)-paracetamol. The internal solution is a standard solution of 0.01 M paracetamol in a solution of phosphoric acid pH 2. The average sensitivity of the paracetamol sensor is (22.60 ± 0.01) mV/decade in a linear concentration range of 10^{-6} – $5x10^{-3}$ M, with an average recovery of (90.6 ± 0.5) %. Paracetamol sensor electrodes can be applied to samples of herbal medicine on the market, with an average error of (9.4 ± 0.1) %.

Keywords: Paracetamol; herbal; chitosan; activated carbon, mini electrode

INTRODUCTION

Some researchers have reported paracetamol content in traditional herbal medicine on the market [1, 2, 3]. Herbal medicine comes from plants that contain natural medicines, not chemical drugs. Paracetamol is a chemical drug, so if it is in herbal medicine, it is illegal. Therefore, it is very important to determine paracetamol in herbal medicines on the market. Electrochemically, paracetamol determination methods have been developed [4, 5, 6, 7, 8], but these methods are generally disposable devices, which are less efficient and generating waste. In an effort to provide a cheap and simple tool in this research, a tube type mini electrode has been made for the determination of paracetamol in herbal medicine samples. The electrode is commonly referred as a potentiometric sensor, where its measurement only requires a simple potentiometer. Potentiometric sensors with detection limits in the range of 10^{-6} to 10^{-11} M, are easy to apply to solve real-world analytical problems [9]. The manufacture of ion-selective electrodes as a potentiometric sensor has been developed, both conventionally (large size) and contemporary (miniaturized) [10, 11].

Chemically, paracetamol is a phenol derivative compound which is weak acidic, pK_a = 9.38. As a weak acid, paracetamol will ionize in water at pH > pK_a [12]. Potentiometry is a potential measurement method based on ionic activity in aqueous solution, so that paracetamol can be determined potentiometrically as an ion at pH > pK_a. Determination of paracetamol by acid-base titration shows that paracetamol is a weak acid [13]. The manufacture of paracetamol potentiometric sensors can refer to the potentiometric sensors for phenol [14]. In this study, the

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p-ISSN : 2302 – 4690 | e-ISSN : 2541 – 0733

electrode design refers to the membrane electrode, where the electrode potential is based on the membrane potential [15]. However, this study did not use an internal reference electrode. With the development of new conductive membranes, it is possible to develop new designs of ion-selective electrodes [16]. Chitosan membrane is a conductive membrane, activated carbon is a super capacitor which can increase the conductivity of chitosan membrane. In this study, the two membranes were compared.

Chitosan is a biopolymer that can be applied in various aspects of life, because of its special chemical properties. Chitosan is easily soluble in acidic solutions at pH < 6.0, where the $-NH_2$ group will be protonated to $-NH_3^+$ (pKa = 6.3) [17]. The amine group in chitosan is an advantage because it is easily modified through a crosslinking reaction, glutaraldehyde as an efficient crosslinking reagent [18, 19, 20]. By cross-linking, chitosan becomes a hydrogel that can be used as a potentiometric sensor support membrane [21]. Activated carbon from rice husks can be developed into porous carbon which is a supercapacitor and is a raw material for electrodes [22, 23, 24, 25]. However, activated carbon from rice husk has not been widely developed as a membrane in electrochemical sensors. To facilitate the assessment of herbal medicines, it is necessary to develop paracetamol sensors based on natural ingredients that are cheap and easy to apply to herbal samples. In this study, a paracetamol sensor based on chitosan-activated carbon from rice husk has been developed.

EXPERIMENT

Chemicals and instrumentation

The materials used are standard paracetamol / acetaminophen (Sigma Aldrich), Phosphate Buffer (PB) solution (pH 2; 0.01M), glutaraldehyde (Sigma Aldrich), acetic acid (merck), chitosan and charcoal from acid-activated rice husks (local product), herbal samples, cetyltrimethyl ammonium bromide (CTAB) (Merck), chloroform (Merck)

The apparatus used in this study, are mini tubes (5 mm OD, 50 µL), mini-Ag/AgCl reference electrode IPPG junction, 4.5 mm OD, 52µL (Achema, RE-1S), 0.2 mm carbon electrode (local product), digital multimeter phorex MY-60 (local product), Glassy Carbon electrode of 0.5 mm (Metrohm RDE.GC50) with electrode shaft, potentiostat galvanostat (Autolab PGSTAT204), pH meter Senz TI-13MO597, Yenaco YNC-OV oven 30L, shaker and glassware.

Procedure reaction

CTA-Paracetamol preparation

CTAB (cetyltrimethyl ammonium bromide) 0.292 g added with 0.302 g standard paracetamol and 1 mL 0.1 M HCl. The mixture was then dissolved with distillated water to 1 L in a beaker. Every 100 mL of this solution was extracted with 10 mL of chloroform for 60 minutes at 220 rpm. The chloroform phase is separated and collected, then evaporated in a vacuum evaporator. The residue was removed and dried at 30 °C until constant weight.

Membrane Preparation

Made a mixture of 0.4 g of chitosan added 3 mL of glacial acetic acid and 9 mL of aquadest, stirred overnight. 2 mL of the chitosan solution was added with 0.1 g of rice husk charcoal, 0.1 g of CTA-paracetamol, and 0.1 mL of glutaraldehyde, then stirred for 6 hours at room temperature. The mixture was spread on the surface of the petri dish and dried for a while until half-dry, then attached to the end of the mini tube.

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Manufacture of paracetamol sensor

The paracetamol sensor is made according to the design in Figure 1. The electrode body is made of mini glass tubes, the bottom of the tube is filled with membrane material then dried at 60 °C for 2 hours. The tube was filled with 200 µL of 0.01 M paracetamol in buffer solution, as an internal solution. The carbon electrode is connected to a banana jack and the single cable is inserted into a tube filled with internal solution, then closed and glued to make it airtight.

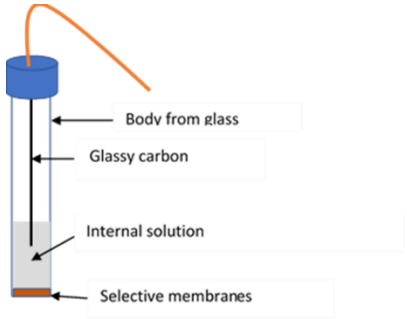

Figure 1. Paracetamol sensor design

Sample preparation

The sample consisted of 5 samples of herbal medicine on the market then dissolved in a phosphate buffer pH 2, this was adjusted to the pH of the DPV paracetamol determination [8, 31]. The solid sample preparation is 0.2 g of the herbal sample, brewed with 25 mL of boiling buffer solution, stirred and cooled. After that it is filtered into a 25 mL volumetric flask and the volume is adjusted by a pH 2 phosphoric acid buffer solution.

RESULT AND DISCUSSION

Paracetamol sensor manufacture

Membrane properties are important in potentiometric sensors. In this study, the presence of activated carbon from rice husks was studied. In the membrane there is CTA-paracetamol as an identification agent and chitosan as a support. If activated carbon is not added to chitosan, the paracetamol sensor is less sensitive and the membrane is easy to leak. Meanwhile, if activated carbon is added, in addition to increasing sensitivity, the sensor membrane is also more durable. The internal solution is 0.01 M paracetamol in water. While the test solutions are 10^{-9}-10^{-2} M paracetamol solutions in water, without adjusting the pH. Figure 2 is the curve of the relationship between -log[paracetamol] to electromotive force (EMF) in mVolts. Figure 2 it can be seen that, in the concentration range of 10^{-7} - 10^{-3} M, the sensitivity of the paracetamol sensor with chitosan membrane is 0.71 mV/decade and 9.3 mV/decade for chitosan-activated carbon membrane.

Activated carbon in the chitosan membrane, can increase the sensitivity of the sensor significantly. The activated carbon from rice husk is a supercapacitor that can store charge in the layer [22-25], so that the membrane conductivity increases. However, this membrane still leaks so that the sample solution slowly enters the internal solution and causes the sensor performance to decrease. This may be due to insufficient glutaraldehyde for cross-linking. To prevent leakage, the glutaraldehyde concentration was increased to 4% (w/v, in water).

In the manufacture of this paracetamol sensor, CTA-paracetamol was used as a recognition agent. CTA-paracetamol is the result of the reaction between CTAB

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(cetyltrimethylammonium bromide) and paracetamol in an acidic solution. CTAB is a cationic surfactant that can form ion-pair complexes with simple anions or anions of anionic surfactants [27, 28]. CTAB has been used in the modification of working electrodes in voltammetry [29], and as a phenol ion pair in the manufacture of potentiometric phenol sensors [30]. As a CTA-paracetamol recognition agent, it acts depending on the pH, as well as the ionization of paracetamol. Therefore, in this study, measurements of the paracetamol solution were carried out at pH 2 and 11, as well as the pH of the internal solution. The results show that at pH 2, the sensor performance is better than pH 11, this is different from the initial prediction, where at pH 11 the ionization of paracetamol is better than pH 2 (Figure 3). Maybe this is caused by OH^- interference and also affects the equilibrium CTA-paracetamol in the membrane. The sensitivity of the sensor at pH 2 is 23.4 mV/decade in the concentration range of 10^{-6} – 5 x10^{-3} M, and at pH 11 is 4.6 mV/decade at 10^{-9} - 5 x 10^{-3} M.

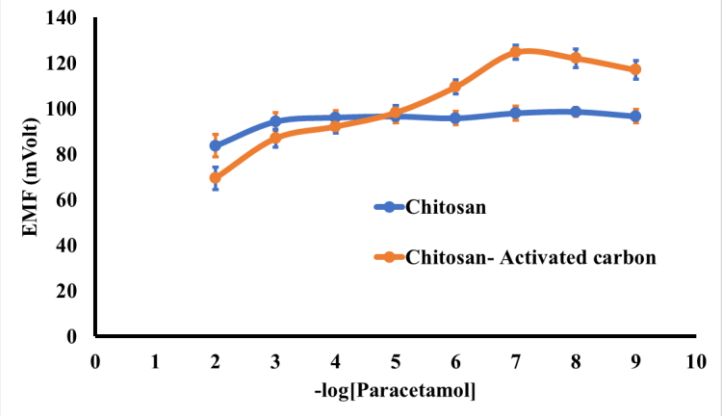

Figure 2. Relationship curve between -log[paracetamol] to EMF, for paracetamol sensor with chitosan and chitosan-activated carbon membrane

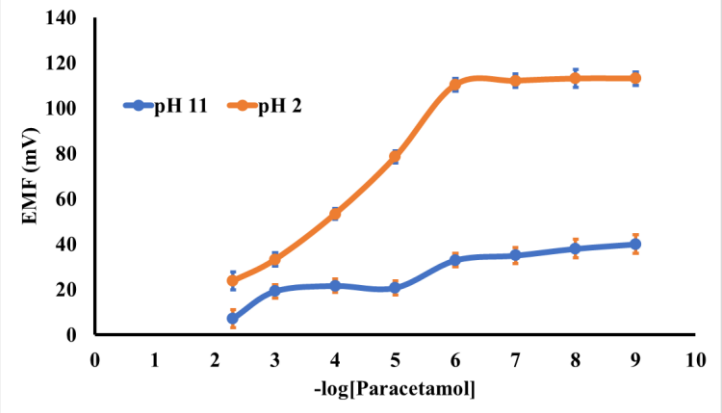

Figure 3. Relationship curve between -log[paracetamol] to EMF, for paracetamol sensor at pH 2 and pH 11

Performance of paracetamol sensor

The best paracetamol sensor performance was produced by a sensor made of chitosan-activated carbon membrane with 4% glutaraldehyde, as a recognizing agent was CTA-paracetamol, and an internal solution of 0.01 M paracetamol in phosphoric acid buffer pH 2.

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The accuracy of the paracetamol sensor was determined by standard addition to the herbal drug samples, Tabel 1. Both paracetamol solution and sample solution were determined under the same environmental conditions, with a response time of 2 minutes, repeated measurements were carried out 4 times on different days. Recovery in table 1 is the percentage of standard concentration of paracetamol from sensor measurements compared to the concentration of paracetamol added in herbal samples (40 µM). The percent recovery is one of accuracy parameter. The overall performance of the paracetamol sensor is shown in the Table 2.

Table 1. Average recovery data from four replications, standard addition with 40 µM of paracetamol into the herbal medicine samples

No	Sample Code	EMF (mV)		[paracetamol] (µM)		Recovery (%)
		Sample	Sample + standard	Sample	Sample + standard	
1	IB	108.7	69.9	0.8	36.9	90.34
2	JD	74.3	65.0	23.8	60.2	91.05
3	SM	112.1	69.9	0.5	36.9	90.89
4	MKD	67.5	61.4	46.9	82.9	89.94
5	PM	71.9	64.0	30.2	66.5	90.76

Table 2. Paracetamol sensor performance

No	Parameter	Performance
1	Response time	2 minutes
2	Concentration range	10^{-6} - 5 x 10^{-3} M
3	Linear equation	EMF = -30.05 - 22.6 log [paracetamol]
4	Sensitivity	(22.60 ± 0.01) mV/decade
5	Limit of detection	5.7 x 10^{-7} M
6	Accuracy	(90.60 ± 0.45) %

Table 3. Paracetamol (mg / pack) in the herbal sample determined by the paracetamol sensor were compared with the results of the DPV method.

Sample code	Volume per pack	Paracetamol levels (mg/pac)	
		Sensor	DPV
IB	6 g	0.1	Not detected
JD	600 mL	26.9	22.7
SM	7 g	0.1	Not detected
MKD	7 g	62.0	60.8
PM	9 g	51.3	49.2

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The levels of paracetamol in the herbal medicine samples were not only determined using a paracetamol sensor, but also by differential pulse voltammetry (DPV) as a comparator. The concentration of the standard paracetamol curve is 5 - 100 µM in phosphoric acid buffer pH 2. The levels of paracetamol in the samples are shown in Table 3. Paracetamol levels are expressed in mg of paracetamol per package. Table 3 shows that the level of paracetamol detected by the paracetamol sensor tends to be higher than the DPV method. However, the results from the paracetamol sensor are in line with the DPV method. This shows that the paracetamol sensor from this study can be applied to herbal medicine samples.

CONCLUSION

The paracetamol sensor electrode can be made with a mini tube type which is a modification of the membrane electrode model. The best paracetamol sensor electrode is made of a mixture of chitosan-activated carbon membrane, with CTA-paracetamol recognition agent, and an internal solution of 0.01 M paracetamol in pH 2 phosphoric acid buffer solution. The paracetamol sensor has an average sensitivity of 22.60 mV / decade with mean accuracy (90.6 ± 0.5) %. This paracetamol sensor can be applied to five samples of herbal medicine on the market, where the results of the determination of paracetamol in the five herbal samples by the sensor were higher than the results of the determination by DPV method.

ACKNOWLEDGMENT

The author would like to thank Brawijaya University for funding “Hibah Penelitian Unggulan 2020”

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