Bukti Korespondensi ABECHEM – 2018

Judul : Construction and Performance of Creatinine Selective Electrode based on Carbon Paste-Imprinting Zeolite

Penulis : Miratul Khasanah*, Usreg Sri Handajani, Alfa Akustia W, Abdulloh, Ria Risty Rindarti

Jurnal : Analytical and Bioanalytical Electrochemistry, 2018, 10(4), 429-438

miratul khasanah <miratul-k@fst.unair.ac.id>

Receipt ABEC-2018-115

abechem <abec@abechem.com>
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Cc: alfaakustia@fst.unair.ac.id

Tue, Jan 30, 2018 at 12:39 AM

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Thanks for choosing Anal. & Bioanal. Electrochem. to present the results of your research work.

Please find the receipt of your submission as an attachment. Your submitted manuscript has been assigned an editorial number of ABEC-2018-115.

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On Mon, Jan 29, 2018 at 6:23 AM, alfa akustia widati <alfaakustia@fst.unair.ac.id> wrote:

> Dear Editor-in-Chief
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> Herein,we would like to submit our article entitled "Construction and Performance Selective Electrode Based on Carbon Paste Imprinting Zeolite"
> ",
> We hope our aricle can be published as a research paper in Analytical and Bioanalytical Electrochemistry. In the clinical analysis, the commonly methods to analyze creatinine have some weakness, i.e. not specific, require long time, low precision, and short life time. This research successfully prepared the novel electrode that exposed good selectivity, reproducibility, accuracy, and long life time. The creatinine selective electrode based carbon paste imprinting zeolite has future prospect to be applied for analyzing creatinine in clinical laboratory. We hope that we can contribute our article in Analytical and Bioanalytical Electrochemistry, We are looking forward to hearing from you. Thanks for your kind cooperation.
>
> Sincerely,
> Alfa Akustia Widati,
> Lecturer of Inorganic Chemistry
> Department of Chemistry, Faculty of Science and Technology
> Universitas Airlangga
> Surabaya-Indonesia

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ANALYTICAL & BIOANALYTICAL ELECTROCHEMISTRY

Editor-in-Chief
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Professor in Analytical Chemistry

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January 29, 2018

Dear Dr. M. Khasanah,

This is to acknowledge the receipt of your manuscript submission entitled: “Construction and Performance of Creatinine Selective Electrode Based on Carbon Paste-Imprinting Zeolite”.

Please state the MS. No. **ABEC-2018-115** in any correspondence in connection with this manuscript.

Yours Sincerely,

M. R. Ganjali

M. R. Ganjali
Editor-in-Chief

miratul khasanah <miratul-k@fst.unair.ac.id>

Decision on ABEC-2018-115

---

abechem <abec@abechem.com> Sun, Mar 18, 2018 at 4:51 PM
To: miratul-k@fst.unair.ac.id

Dear Dr. M. Khasanah,

The reviewers have now commented on your manuscript ABEC-2018-115.

According to the comments, **Major Revision** has been considered.

You can find the acceptance and the referee's comments as attached files.

Best regards,
F. Faridbod
--
Dr. Farnoush Faridbod
Managing Editor
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On Mon, Jan 29, 2018 at 9:09 PM, abechem <abec@abechem.com> wrote:

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> Best regards,
> F. Faridbod
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> Dr. Farnoush Faridbod
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> On Mon, Jan 29, 2018 at 6:23 AM, alfa akustia widati <alfaakustia@fst.unair.ac.id> wrote:
>
>> Dear Editor-in-Chief
>> Analytical and Bioanalytical Electrochemistry

> > Herein,we would like to submit our article entitled "Construction and Performance Selective Electrode Based on Carbon Paste Imprinting Zeolite"
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> > We hope our aricle can be published as a research paper in Analytical and Bioanalytical Electrochemistry. In the clinical analysis, the commonly methods to analyze creatinine have some weakness, i.e. not specific, require long time, low precision, and short life time. This research successfully prepared the novel electrode that exposed good selectivity, reproducibility, accuracy, and long life time. The creatinine selective electrode based carbon paste imprinting zeolite has future prospect to be applied for analyzing creatinine in clinical laboratory. We hope that we can contribute our article in Analytical and Bioanalytical Electrochemistry, We are looking forward to hearing from you. Thanks for your kind cooperation.
> >
> > Sincerely,
> > Alfa Akustia Widati,
> > Lecturer of Inorganic Chemistry
> > Department of Chemistry, Faculty of Science and Technology
> > Universitas Airlangga
> > Surabaya-Indonesia

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ANALYTICAL & BIOANALYTICAL ELECTROCHEMISTRY

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Manuscript No.: ABEC-2018-115

Title of the manuscript: Construction and Performance of Creatinine Selective Electrode Based on Carbon Paste-Imprinting Zeolite

Author(s): Miratul Khasanah*, Usreg Sri Handajani, Alfa Akustia Widati, Abdulloh Abdulloh, Ria Risty Rindarti

No	Evaluation	Yes	No	See the comment
1	Novelty and originality of the manuscript	√		
2	Title of the manuscript is informative and suitable	√		
3	Abstract well summarizes the whole work	√		
4	Keywords is adequate and well selected		√	
5	Literature has been reviewed adequately	√		
6	The authors describes the aim of the work well	√		
7	The experimental section contains all the necessary data	√		
8	Results have been well presented	√		
9	Discussions on the results are acceptable	√		
10	Conclusions are supported the results	√		
11	The number of tables and figures are acceptable	√		
12	The figure qualities are acceptable		√	
13	The tables are well designed	√		
14	The references are adequate and related to the work	√		
15	The English level of the manuscript is acceptable		√	

Final Decision	**Accept as it is**	
	Minor Revision	
	Major Revision	√
	Resubmission	
	Reject	

Reviewer comments:

The prepared electrode had short life time (low stability).

The pH range was limited.

Authors had not written a method to calculate the value of detection limit.

ABEC-2018-115_revised manuscript

miratul khasanah <miratul-k@fst.unair.ac.id> Sat, Mar 24, 2018 at 10:09 PM
To: abechem <abec@abechem.com>

Dear **Dr. Farnoush Faridbod**
Managing Editor
Analytical & Bioanalytical Electrochemistry

Attached I sent the our revised manuscript (**ABEC-2018-115**) and response for reviewer comments.
We hope that our revised manuscript can be considered to publish in The Analytical and Bioanalytical Electrochemistry. Thank you for your attention.

Sincerely yours,
Dr. Miratul Khasanah
Analytical Chemistry,
Chemistry Department, FST, Universitas Airlangga
Kampus C, Jl. Ir. Sukarno, Mulyorejo
Surabaya 60115, INDONESIA

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9 attachments

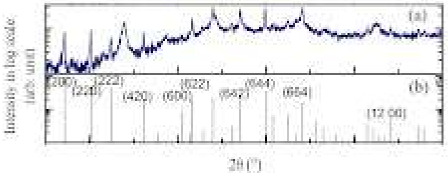

Fig 1.jpg
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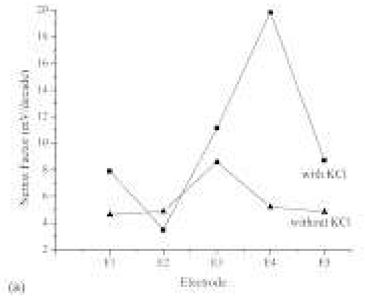

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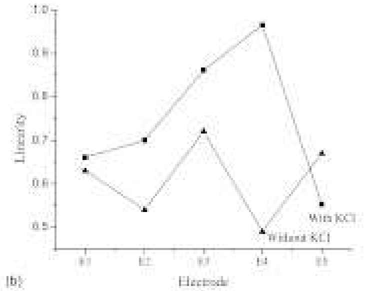

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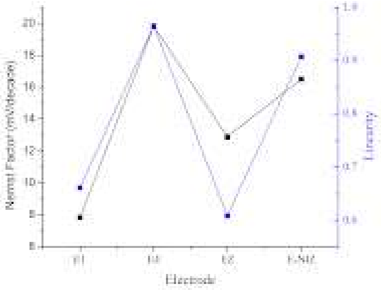

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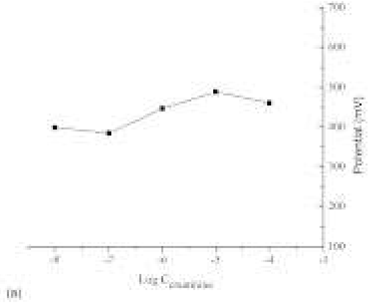

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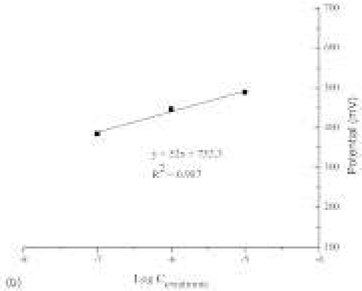

Fig. 4b.jpg
501K

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RESPONSES TO REFEREE'S COMMENTS

Manuscript No.: ABEC-2018-115

Title of the manuscript: Construction and Performance of Creatinine Selective Electrode Based on Carbon Paste-Imprinting Zeolite

Author(s): Miratul Khasanah*, Usreg Sri Handajani, Alfa Akustia Widati, Abdulloh Abdulloh, Ria Risty Rindarti

Dear Editor-in-Chief
Mohammad Reza Ganjali
Professor in Analytical Chemistry

We are very excited to have been given the opportunity to revise our manuscript. We have improved the quality of our manuscript based on the referee report. We give the blue colour for the further explanation to provide detail information about our work. Herein, we explain the responses to referee's comments:

No	Comments		Responses
1.	Evaluation from the table	Keywords is not adequate and well selected	Thank for this point correction. We have replaced the keyword with "creatinine selective electrode, imprinted zeolite, potentiometry"
		The figure qualities are not acceptable	We appreciate for your correction. We have increased the quality of figures. We also attached the file of figures (in the jpg format).
		The English level of the manuscript is notacceptable	We thank for this correction. We have improved the quality of English level using english editing service. In our email, we also attached the certificate of english editing.
2	Reviewer comments	The prepared electrode had short life time (low stability)	This is an interesting perspective. Most of researchers stated the term of lifetime using day/week/month, without specifiying how many times the electrode is used in thus periods. For the example, the provided table presents the lifetime of potentiometric sensor:

<table>
<tr>
<td></td>
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<td>
<table>
<tr><th>Analyte</th><th>Sensor</th><th>Lifetime</th><th>Author</th></tr>
<tr><td>Heparin</td><td>Carbon paste-MIP</td><td>2 months</td><td>Li <i>et al</i>. (2013)</td></tr>
<tr><td>Melamine</td><td>MIP-glass plate</td><td>2 months</td><td>Liang <i>et al</i>. (2009)</td></tr>
<tr><td>Azytromicine</td><td>MIP-graphite</td><td>4 weeks</td><td>Abu-Dalo <i>et al.</i> (2015)</td></tr>
<tr><td>Naphazoline hidrochloride</td><td>Carbon paste</td><td>30 days</td><td>Mohamed <i>et al</i>. (2013)</td></tr>
</table>

In this study, the electrode exposed the lifetime of about 7 weeks (used for 160 times). Compared with the other potentiometric sensors, we assumed that our developed electrode does not exposed low stability.

References :
1. Li, L., Liang, Y., Liu, Y., Analytical Biochemistry 434 (2013) 242–246
2. Liang, R., Zhang, R., Qin, W., Sensors and Actuators B 141 (2009) 544–550
3. Abu-Dalo, M.A., Nassory, N.S., Abdulla, N.I, Al-Mheidat, I. R., Journal of Electroanalytical Chemistry 751 (2015) 75–79
4. Mohamed, G. G., El-Dien, F. A. N., Frag, E. Y. Z., Moha, M.E, Journal of Pharmaceutical Analysis 3, 5 (2013) 367-375
</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The pH range was limited</td>
<td>We thank for the reviewer’s comment. We supposed that creatinine detection at pH 7 is advantageous and effective because it is similar to the blood and urine pH, and thus, does not require pH treatment in the sample preparation.
We have added this explanation on the text (on the page 9).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Authors had not written a method to calculate the value of</td>
<td>We thank for this correction. The limit of detection is derived from intersection of the linear and non-linear functions in the plot of log $C_{creatinine}$ vs. potential (mV).
We have suplemented this explanation in our</td>
</tr>
</table>

		detection limit	manuscript to reveals the detail description (on the page 9).

We appreciate the time and efforts by the editor and reviewers in review in this manuscript. Thank you so much for your kind cooperation. We hope that our revised manuscript can be considered to publish in The Analytical and Bioanalytical Electrochemistry. Thank you for your attention.

Fig 1

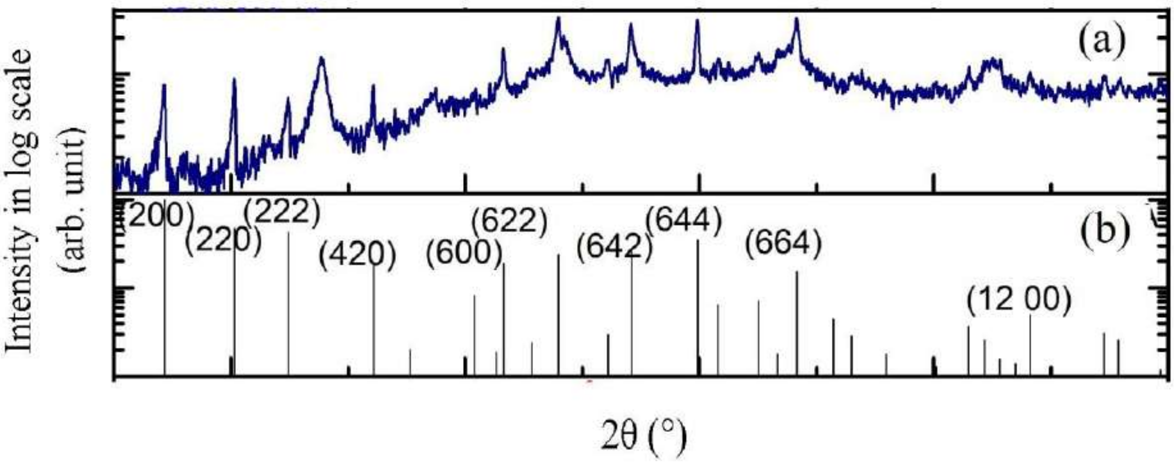

Intensity in log scale
(arb. unit)
(a)
(b)
(200)
(220)
(222)
(420)
(600)
(622)
(642)
(644)
(664)
(12 00)
2θ (°)

Fig 2a.

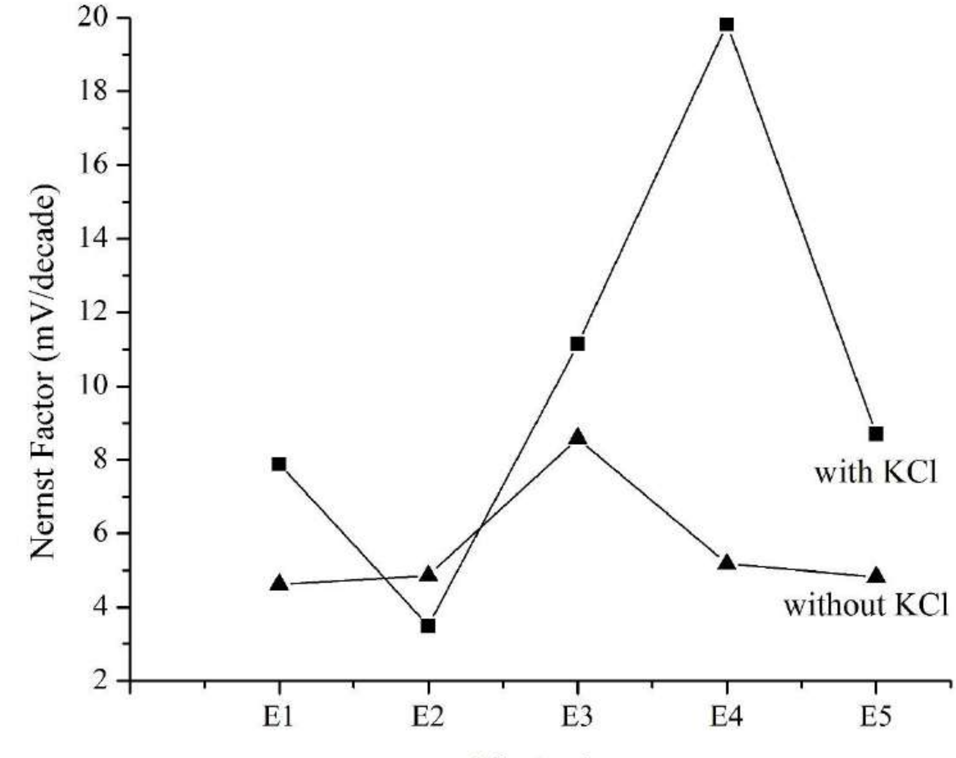

20
18
16
14
12
10
8
6
4
2
Nernst Factor (mV/decade)
E1
E2
E3
E4
E5
Electrode
with KCl
without KCl
(a)

Fig 2b.

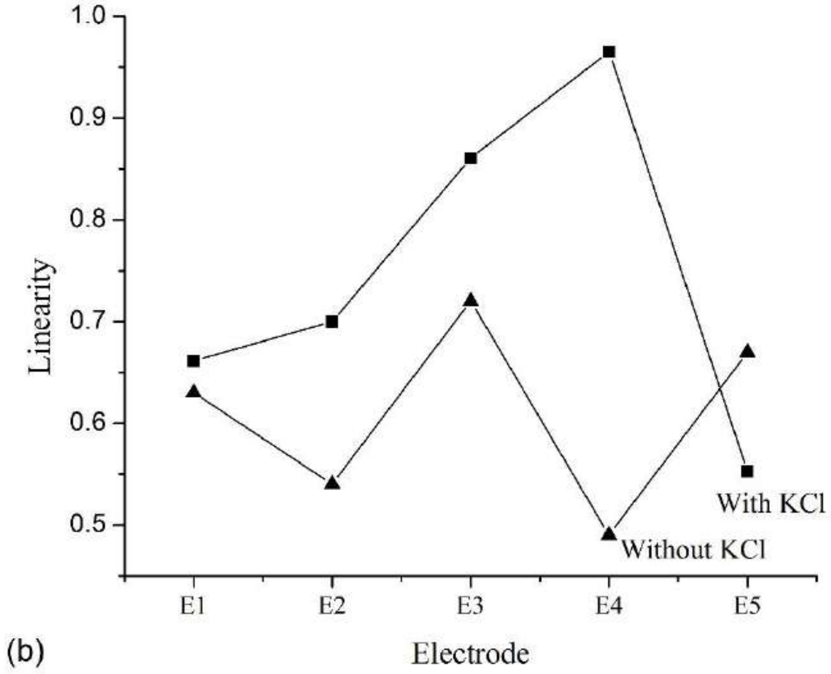

1.0
0.9
0.8
0.7
0.6
0.5
Linearity
With KCl
Without KCl
E1
E2
E3
E4
E5
(b)
Electrode

Fig 3

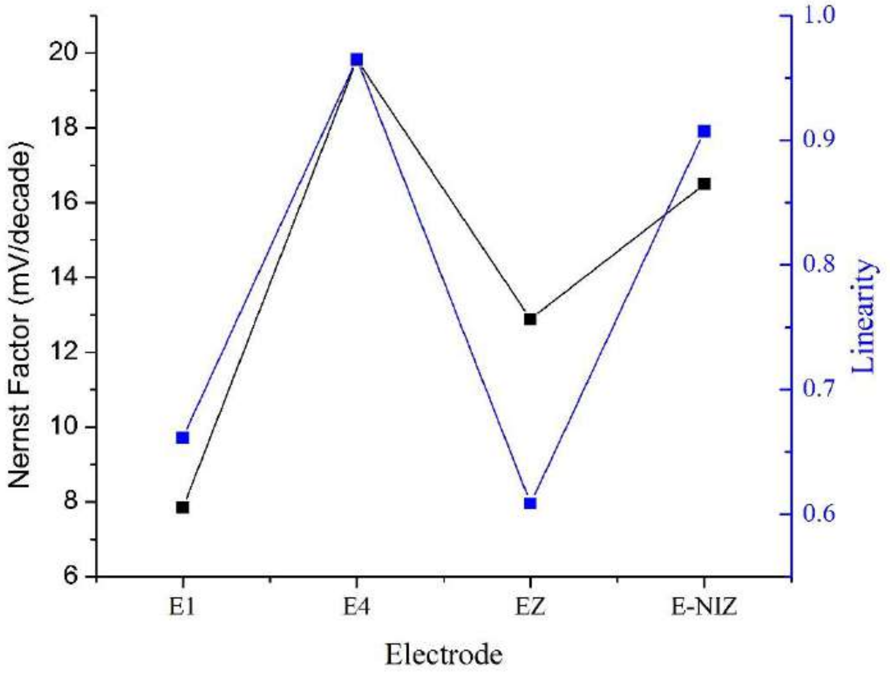
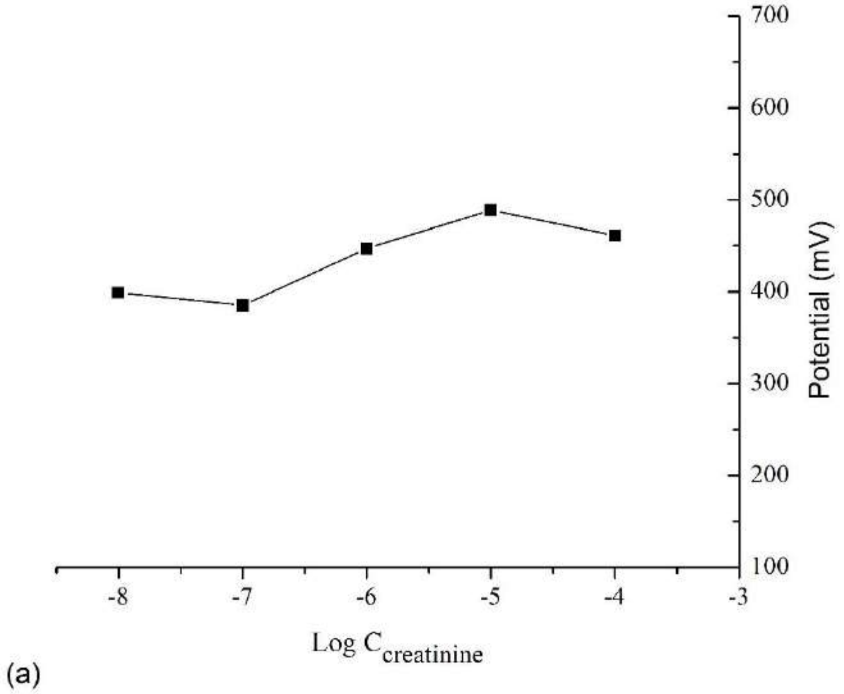
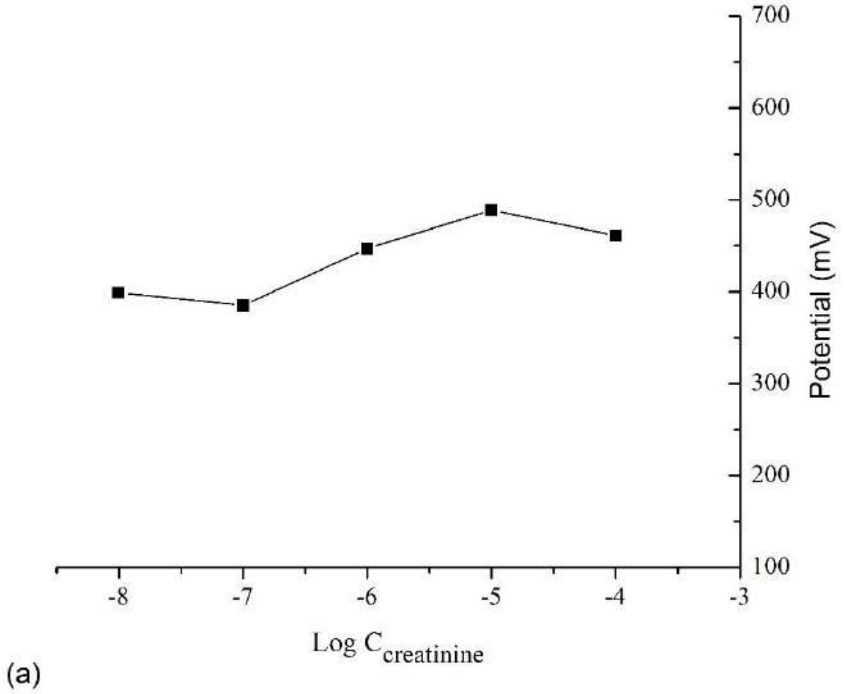

20
18
16
14
12
10
8
6
Nernst Factor (mV/decade)
1.0
0.9
0.8
0.7
0.6
Linearity
E1
E4
EZ
E-NIZ
Electrode

Fig 4a.



700
600
500
400
300
200
100
Potential (mV)
-8
-7
-6
-5
-4
-3
Log $C_{creatinine}$
(a)

Fig 4b



700
600
500
400
300
200
100
Potential (mV)
-8
-7
-6
-5
-4
-3
Log $C_{creatinine}$
(a)

Construction and Performance of Creatinine Selective Electrode Based on Carbon Paste-Imprinting Zeolite

Miratul Khasanah*, Usreg Sri Handajani, Alfa Akustia Widati, Abdulloh Abdulloh, Ria Risty Rindarti

Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga
Mulyorejo Kampus C Universitas Airlangga, Surabaya 60115, Indonesia

[*] Corresponding author, miratul-k@fst.unair.ac.id

Abstract-Carbon paste-modified imprinted zeolite electrodes as a potentiometric sensor for creatinine detection have been constructed. The modified electrodes were fabricated by mixing activated carbon, imprinted zeolite, and paraffin. The electrode that was prepared with a respective mass ratio of 45:15:40 showed the best performance in creatinine detection. In addition, the electrode showed a fast response time (less than 50 s), a wide range of measurement (10^{-7}–10^{-5} M), and a low limit of detection (7.9×10^{-8} M). The presence of urea in the solution did not interfere in the detection of creatinine. The proposed creatinine-selective sensor exhibited good reproducibility, accuracy, and a long lifetime. The creatinine-selective electrode based on carbon paste-imprinted zeolite can be potentially used for creatinine detection in the medical field.

Keywords-creatinine selective electrode, imprinted zeolite, potentiometry

1. INTRODUCTION

Creatinine is a product of muscle metabolism, which is excreted through urine. The normal level of creatinine in blood is about 0.6 until 1.2 mg/dL. A lower than normal creatinine concentration may indicate poor nutrition [1], while a high level of creatinine can be a warning for kidney malfunction such as glomerulonephritis, tubular necrosis, and low filtration of glomerulus [2].

In clinical detection, creatinine concentration is commonly determined using the Jaffe method through reaction between creatinine and picric acid [3]. This method is not specific because not only creatinine, but also ketone, glucose, bilirubin, acetoacetic, and cephalosporin are detected [4]. Chromatography has also been used for creatinine detection; however, this method is time-consuming [5]. Other methods such as flow injection potentiometry [6] and voltammetry using a molecularly imprinted polymer (MIP)-modified hanging mercury drop electrode (HMDE) method [7, 8] have been developed creatinine detection. Detection of creatinine by voltammetry using an electrode based on poly(melamine-co-chloranil)-modified HMD exhibited high selectivity [7]. Unfortunately, this electrode had a short lifetime (can be used only once). The electrode preparation process also depends on polymer solubility. For a low-solubility polymer, electrode fabrication is difficult. A MIP synthesized from aniline as a monomer with ammonium peroxydisulfate as the initiator and creatinine as a template has been used to modify HMDE for voltammetric detection of creatinine. This method yielded high accuracy and sensitivity, but had low precision [9].

Potentiometry is one of the electrochemical methods that determines the difference in cell potential (EMF) between the working and reference electrodes under zero current. Some researchers have developed potentiometric sensors to analyze creatinine [10, 11]. However, not all the analytes yielded a high signal response because of the use of low-conductivity electrodes. In this research, a high-response and highly selective electrode is proposed for creatinine detection by potentiometry. A carbon paste electrode was modified with imprinted zeolite to construct the potentiometric electrode. The imprinted zeolite was used to increase the conductivity of the electrode, because of which a high signal response was obtained.

Zeolite is a crystalline TO_4 (T is a tetrahedral unit such as Al, Si, or Ti) with channels and three dimensional framework. The unique properties of zeolite as a porous material have been employed for pore selectivity. The shape and pore size of zeolite are designed to ensure conformity between zeolite pore and the target molecule. Our previous research had produced an imprinted zeolite, whose pores were selective toward uric acid. Titanium silicalite-1 and LTA zeolite have been proposed as selective materials for modification of carbon paste and glassy carbon electrode, which exhibited high selectivity in uric acid detection by potentiometry and voltammetry [12, 13].

In this work, we studied the optimum composition of carbon and imprinted zeolite in the preparation of an electrode for creatinine detection by potentiometry. The electrode properties were discussed with respect to response time, Nernst factor, limit of detection, range of measurement, selectivity, precision, and accuracy.

2. EXPERIMENTAL

2.1 Materials

Creatinine anhydrous (Sigma Aldrich, 98%), SiO_2 (Ludox, 40%), sodium aluminate (Sigma Aldrich, 50%), glacial acetic acid (Merck, 100%), sodium acetate (Merck, 99%), sodium dihydrogen phosphate dihydrate (Merck, 97%), urea (Merck, 98%), sodium hydrogen phosphate dihydrate (Merck, 99%), silver wires with 100% of purity, solid paraffin, carbon powder, and distilled water. All chemicals were used as received without any further purification.

2.2 Instruments

The potentiometric was performed on Cyberscan 510 using reference electrode Ag/AgCl.

The structure of zeolite was examined using XRD JEOL JDX-3530. The surface area and pore diameter of carbon was measured by N_2 adsorption-desorption using Quantachrome Instruments version 2.0.

2.3 Preparation of carbon paste electrode-imprinted zeolite

Firstly, we synthesized zeolite using mole ratio about 4 Na_2O : 1 Al_2O_3 : 1.8 SiO_2 : 270 H_2O [14]. Sodium aluminate as alumina source was mixed with water and SiO_2. The mixture was stirred and annealed at 100°C. After 45 hours, the obtained mixture was added creatinine with ratio creatinine: Si = 0.0306. The mixture was aged for 3 hours to trap the creatinine into zeolite pores. Moreover, the mixture was filtered using centrifugation with hot water till neutral. The purpose of this step was creatinine leave prints in the zeolite framework. The residue was dried at 80°C. The resulted powder was called imprinting zeolite.

Carbon paste electrode-imprinted zeolite was prepared using Ag wires as connector between electrode and potentiometer. A ¾ part of micropipette tube was filled using melted paraffin. After that, we mixed activated carbon-paraffin-imprinted zeolite, and heated at 50°C to result the paste texture. The formed paste was then filled into ¼ part of micropipette tube.

2.4 Optimization of electrode

To obtain the optimum condition of electrode, we investigated the composition of electrode and pH of creatinine sample. The variation of electrode composition was displayed in Table 1. The prepared electrodes were used to measure potential of electrode in the 10^{-2} – 10^{-8} M of creatinine standar solution. The optimum electrode was determined by value Nernst factor, linearity on EMF versus log concentration plot and range of concentration. The pH of creatinine solution was varied to study the influence of acidity/basicity towards electrode performance. The pH was varied pH of 4, 5, 6, 7, and 8 by adding buffer solution. The pH that performed constant potential was determined as optimum pH.

Table 1. The composition of activated carbon, imprinting zeolite and solid paraffin in the preparation of carbon paste electrode-imprinted zeolite

Electrode	Composition (%weight)		
	Activated carbon	Imprinted zeolite	Solid Parafin
E1	60	0	40
E2	55	5	40
E3	50	10	40
E4	45	15	40
E5	40	20	40

3. RESULTS AND DISCUSSION

3.1 Influence of electrode composition and pH on potentiometric response of the creatinine-selective electrode

To clarify the structure of zeolite, we characterized the obtained sample by XRD. The diffractogram of the synthesized zeolite is depicted in Figure 1. The XRD profile confirms the structure of zeolite LTA. The diffractogram shows peaks at $2\theta = 7.14$, 10.10, 12.40, 16.04, 21.58, 23.90, 27.02, 29.84, and 34.07°, among which the peak at 12.40° is associated with the cubic structure of zeolite LTA [15].

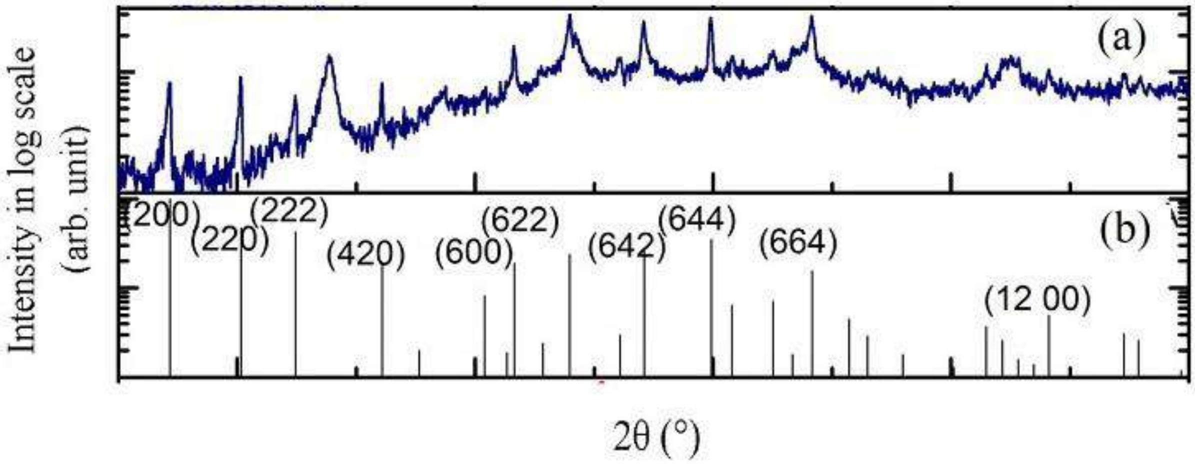


Fig. 1. XRD profile of (a) prepared zeolite LTA and (b) JCPDS of zeolite LTA (01-073-2340)

The working electrodes were prepared by mixing activated carbon, imprinted zeolite, and paraffin. Activated carbon was prepared by the activation method using 10^{-1} M H_3PO_4. It is well known that activated carbon exhibits high chemical stability and conductivity, and has a large surface area and pore diameter of about 877.463 m^2/g and 3.835 nm, respectively. Imprinted zeolites were used to increase the selectivity of the electrode because they present selective sites for creatinine molecules. Paraffin was added to bind the composite of carbon and imprinted zeolite.

The performance of the electrode was determined by the estimation of linearity, range of measurement, and Nernst factor. The Nernst factors of the resulting electrodes were 4.6–8.5 mV/dec, which were lower than the theoretical value. The obtained linearity was also lower than 1 at about 0.49–0.71. To increase the sensitivity of the method, KCl was added into the solution as it can ionize in water and improve the conductivity of the solution. After KCl addition, the Nernst factor and linearity increased, as can be seen in Figure 2. Among the synthesized electrodes, E4 displayed the highest Nernst factor and linearity. Therefore, for further study, E4 was used as the electrode.

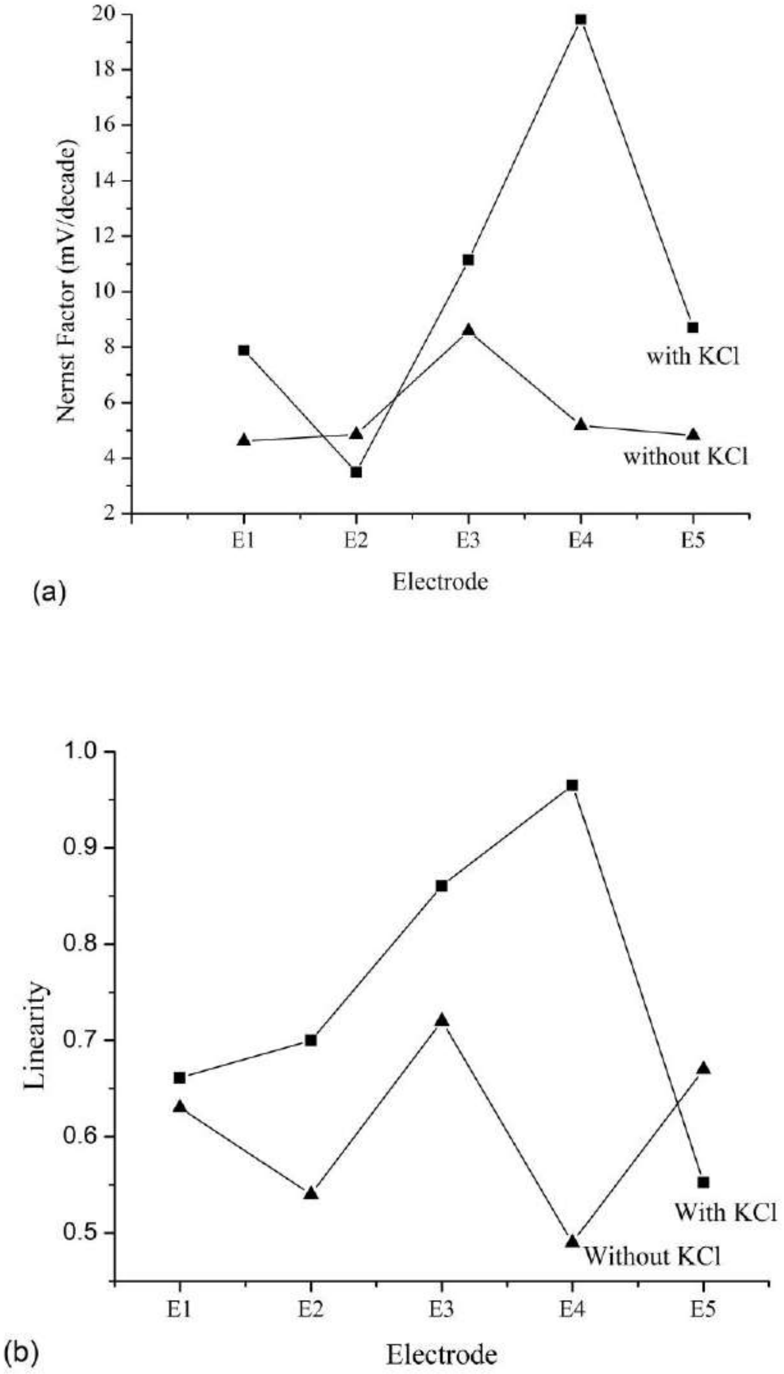


Fig. 2. (a) Nernst factor and (b) regression linearity of different electrode compositions

The concentration of imprinted zeolite affected the amount of active sites of the electrode. E4 with a carbon, imprinted zeolite, paraffin mass ratio of 45:15:40 showed the best performance as a sensor in creatinine detection by the potentiometry method, while E5 that contained a higher amount of imprinted zeolite exhibited a low Nernst factor and linearity. This is probably due to the formation of a rigid membrane, which resulted in the low response of the electrode toward the analyte.

To evaluate the effect of creatinine template on the performance of the electrode, we compared the working performances of E1 (without imprinted zeolite), E4, carbon paste-zeolite (EZ), and carbon paste-non-imprinted zeolite electrodes (E-NIZ). E4 exhibited better linearity and a higher Nernst factor than EZ and non E-NIZ did. This is because EZ did not have a creatinine-selective template, while in E-NIZ, creatinine was trapped in the zeolite framework and could not effectively move from the solution to the electrode. A comparison of the performances of these electrodes is displayed in Figure 3.

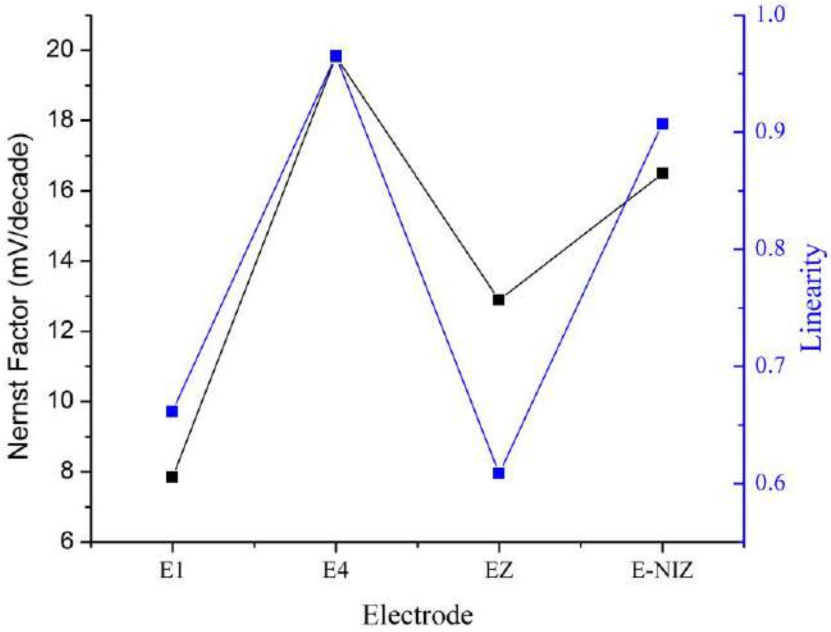


Fig. 3. Nernst factor and linearity of E1, E4, EZ, and E-NIZ electrodes

The electrode performance in H^+ sensing was also investigated. The performance of the optimal electrode was measured in solutions with varying pH (4, 5, 6, 7, and 8). The pH changed the Nernst factor. At pH 7, the resulting Nernst factor was about 52 mV/dec. Compared to other pH, the electrode showed a constant potential at pH 7. Creatinine has two dissociation constants, pKa_1 = 4.8 and pKa_2 = 9.2. However, since pKa_2 is less than 7, the second protonation of H^+ is difficult. It can be conclude that creatinine was analyzed as a monovalent molecule. Furthermore, creatinine detection at pH 7 is advantageous and effective because it is similar to the blood and urine pH, and thus, does not require pH treatment in the sample preparation.

3.2 Calibration graph of creatinine

A standard curve of creatinine was plotted from the electrode potential data of the creatinine measurements and log creatinine concentrations of 10^{-8}–10^{-4} M at pH 7 using the E4 electrode. From the data, we created the correlation curve of log of creatinine concentration (log $C_{creatinine}$) and potential (EMF) (Figure 4a). The log $C_{creatinine}$ from -5 to -7 displayed the regression equation $y = 52x + 752.3$, with $R^2 = 0.987$ (Figure 4b). From this equation, the obtained Nernst factor was 52 mV/dec, which is close to the theoretical Nernst factor of monovalent compound. In other words, the linear concentration range of the prepared electrode was 10^{-7}–10^{-5} M.

The limit of detection is derived from intersection of the linear ($y = 52x + 752.3$) and non-linear ($y = 38x^2 + 556x + 2415$) functions in the plot of log $C_{creatinine}$ vs. potential (mV). The limit of detection was calculated as 7.9×10^{-8} M, while the detection limit of the commonly used method for creatinine detection in the medical field (spectrophotometric method) is in the order of 10^{-5} M [16].

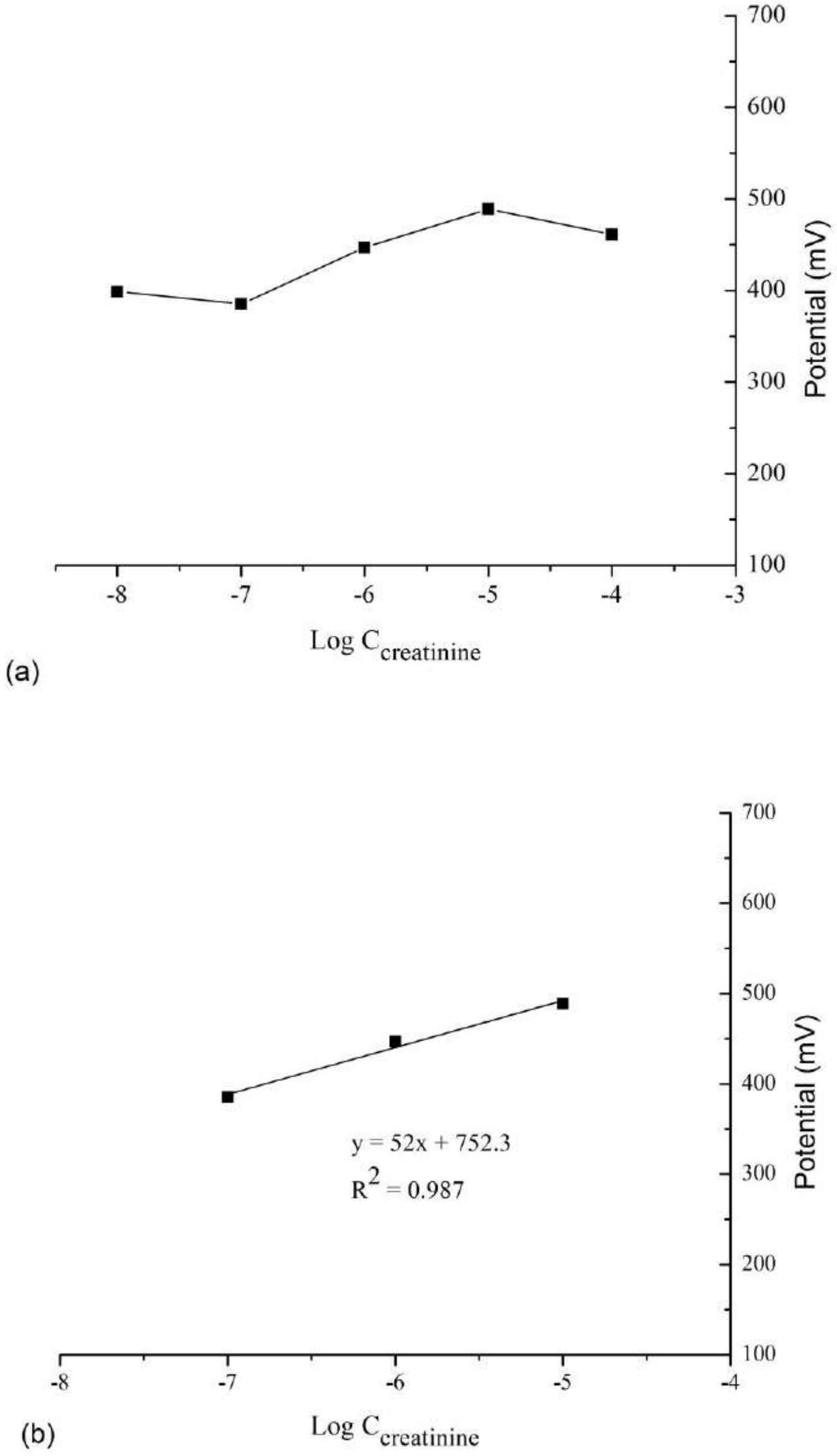


Fig. 4. (a) Plot of log $C_{creatinine}$ vs. electrode potential and (b) linear curve of creatinine-selective electrode for 10^{-7}–10^{-5} M creatinine solution

3.3 Performances of creatinine-selective electrode based on carbon paste and imprinted zeolite.

In this study, the response time, reproducibility, accuracy, selectivity, and lifetime of the fabricated electrode were investigated. The response time of an electrode is the time required by the electrode to detect an analyte, and is considered from the time of immersion of the electrode into the solution until the observation of a stable potential [17]. The response time increased with increase in creatinine concentration. At a higher concentration, molecules move faster from the solution to the electrode. Table 2 displays the variation in the response time of the electrode with creatinine concentration.

Table 2. The response time of electrode for 10^{-7}-10^{-5} M of creatinine

Concentration (M)	Response time (second)
10^{-7}	47
10^{-6}	38
10^{-5}	29

The reproducibility was determined by measuring the electrode performance in three creatinine solutions under the same conditions and concentration. The concentration of creatinine in the solution varied in the range of 10^{-7}–10^{-5} M. The proposed electrode demonstrated high reproducibility with a relative standard deviation less than 2.56%. The prepared electrodes also met the required sensor criteria of the Association of Official Analytical Chemists. It states that the maximum relative standard deviation of a sensor should not exceed 15% for concentrations ranging from 10^{-7} M to 10^{-5} M [18].

In clinical laboratories, spectrophotomertry is the commonly used method for creatinine detection. Table 3 shows the accuracies of the proposed potentiometric method using the carbon paste-imprinted zeolite electrode and the spectrophotometry method in the detection of creatinine solution. The developed electrode shows an accuracy of 80.3–100.4%, while the accuracy of the method that is acceptable for concentrations of the order of 10^{-7}–10^{-5} M is 80–120% [18]. Association of Official Analytical Chemists declares the criterions of analysis method. An analytical method is considered eligible for use in quantitative analysis if it meets certain criteria, including relative standard deviation and accuracy. According to the method accuracy and relative standard deviation, the developed carbon paste-modified imprinted zeolite electrode can be used as an alternative sensor for creatinine detection in the medical field.

Table 3. The accuracy of potentiometric method compared with spectrophotometry in the measurement of creatinine solution

Number of sample	Concentration (M)		Accuracy (%)
	Potentiometry	Spectrophotometry*)	
1	3.74×10^{-4}	4.66×10^{-4}	80.3
2	4.77×10^{-4}	5.05×10^{-4}	94.5
3	7.07×10^{-4}	7.04×10^{-4}	100.4
4	3.91×10^{-4}	4.55×10^{-4}	85.9
5	4.52×10^{-4}	4.97×10^{-4}	90.9

*) *data from local clinical laboratory*

Selectivity, expressed by the selectivity coefficient, Kij, is the main parameter for performance evaluation of the prepared electrode. The coefficient of selectivity was investigated to study the selectivity of the electrode in creatinine solution, which also contained urea, which has a similar structure as that of creatinine and is present in high concentrations in blood and urine. The calculated selectivity coefficient values are presented in Table 4. It can be seen that the carbon paste-imprinted zeolite electrode exhibits high selectivity toward creatinine (i) than toward urea (j), which is indicated by a K_{ij} value less than 1. The electrode lifetime was determined to investigate the stability of the electrode after being used several times. The electrodes demonstrated a long lifetime of about 7 weeks (used for 160 times).

Table 4. The selectivity coefficient of carbon paste-imprinting zeolite electrode in 10^{-5} M creatinine

Interference	Concentation (M)	K_{ij}
Urea	10^{-6}	0.085
	10^{-5}	0.126
	10^{-4}	0.106

4. CONCLUSION

Creatinine-selective electrodes demonstrated high repeatability in the concentration range of 10^{-7}–10^{-5} M. The lifetime of 7 weeks (used 160 times) indicated that the electrodes are suitable for routine detection of medical samples. The detection limit of the developed electrode was much lower than that of the spectrophotometric method, and no interference was observed by the presence of urea. Therefore, the potentiometric method using the developed electrode can be potentially used to determine creatinine levels. Further, the proposed electrode showed an accuracy of 80.3–100.4% (n=5). It can be concluded that the method can be applied for creatinine detection in urine or serum samples.

ACKNOWLEDGMENT

The authors thank the Ministry or Research, Technology and Higher Education, Indonesia for the financial support of this investigation through Universitas Airlangga RUPT Grant No. 597/UN3.14/LT/2017 and Chemistry Department, Faculty of Science and Technology, Universitas Airlangga for the laboratory facilities provided.

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Author(s): Miratul Khasanah*, Usreg Sri Handajani, Alfa Akustia Widati, Abdulloh Abdulloh, Ria Risty Rindarti

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Part	Written	Correction
Page 2, line 8	hanging mercury drop electrode (HMDE) method [7,8] have been developed creatinine	hanging mercury drop electrode (HMDE) method [7,8] have been developed for creatinine
Page 3, line 37	The pH was varied pH of 4, 5, 6, 7, and 8 by adding buffer solution.	The pH was varied of 4, 5, 6, 7, and 8 by adding buffer solution.
Page 7, line 18-19	The response time increased with increase in creatinine concentration.	The response time increases with decreasing in creatinine concentration.
Page 9, line 34-35	M. Khasanah, G. Supriyanto, and A. P. Azhar, Media Kimia FST 1 (2013) 7 M. Khasanah, G. Supriyanto, and A. P. Azhar, Media Kimia FST 1 (2013)	M. Khasanah, G. Supriyanto, A. P. Azhar, Media Kimia FST 1 (2013) 1

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Full Paper

Construction and Performance of Creatinine Selective Electrode based on Carbon Paste-Imprinting Zeolite

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Received: 29 January 2018 / Received in revised form: 24 March 2018 /
Accepted: 10 April 2018 / Published online: xxxx 2018

Abstract- Carbon paste-modified imprinted zeolite electrodes as a potentiometric sensor for creatinine detection have been constructed. The modified electrodes were fabricated by mixing activated carbon, imprinted zeolite, and paraffin. The electrode that was prepared with a respective mass ratio of 45:15:40 showed the best performance in creatinine detection. In addition, the electrode showed a fast response time (less than 50 s), a wide range of measurement (10^{-7}–10^{-5} M), and a low limit of detection (7.9×10^{-8} M). The presence of urea in the solution did not interfere in the detection of creatinine. The proposed creatinine-selective sensor exhibited good reproducibility, accuracy, and a long lifetime. The creatinine-selective electrode based on carbon paste-imprinted zeolite can be potentially used for creatinine detection in the medical field.

Keywords- Creatinine selective electrode, Imprinted zeolite, Potentiometry

1. INTRODUCTION

Creatinine is a product of muscle metabolism, which is excreted through urine. The normal level of creatinine in blood is about 0.6 until 1.2 mg/dL. A lower than normal creatinine concentration may indicate poor nutrition [1], while a high level of creatinine can be a warning for kidney malfunction such as glomerulonephritis, tubular necrosis, and low filtration of glomerulus [2].

In clinical detection, creatinine concentration is commonly determined using the Jaffe method through reaction between creatinine and picric acid [3]. This method is not specific because not only creatinine, but also ketone, glucose, bilirubin, acetoacetic, and cephalosporin are detected [4]. Chromatography has also been used for creatinine detection; however, this method is time-consuming [5]. Other methods such as flow injection potentiometry [6] and voltammetry using a molecularly imprinted polymer (MIP)-modified hanging mercury drop electrode (HMDE) method [7,8] have been developed creatinine detection. Detection of creatinine by voltammetry using an electrode based on poly(melamine-co-chloranil)-modified HMD exhibited high selectivity [7]. Unfortunately, this electrode had a short lifetime (can be used only once). The electrode preparation process also depends on polymer solubility. For a low-solubility polymer, electrode fabrication is difficult. A MIP synthesized from aniline as a monomer with ammonium peroxydisulfate as the initiator and creatinine as a template has been used to modify HMDE for voltammetric detection of creatinine. This method yielded high accuracy and sensitivity, but had low precision [9].

Potentiometry is one of the electrochemical methods that determines the difference in cell potential (EMF) between the working and reference electrodes under zero current. Some researchers have developed potentiometric sensors to analyze creatinine [10,11]. However, not all the analytes yielded a high signal response because of the use of low-conductivity electrodes. In this research, a high-response and highly selective electrode is proposed for creatinine detection by potentiometry. A carbon paste electrode was modified with imprinted zeolite to construct the potentiometric electrode. The imprinted zeolite was used to increase the conductivity of the electrode, because of which a high signal response was obtained.

Zeolite is a crystalline TO_4 (T is a tetrahedral unit such as Al, Si, or Ti) with channels and three dimensional framework. The unique properties of zeolite as a porous material have been employed for pore selectivity. The shape and pore size of zeolite are designed to ensure conformity between zeolite pore and the target molecule. Our previous research had produced an imprinted zeolite, whose pores were selective toward uric acid. Titanium silicalite-1 and LTA zeolite have been proposed as selective materials for modification of carbon paste and glassy carbon electrode, which exhibited high selectivity in uric acid detection by potentiometry and voltammetry [12,13].

In this work, we studied the optimum composition of carbon and imprinted zeolite in the preparation of an electrode for creatinine detection by potentiometry. The electrode properties were discussed with respect to response time, Nernst factor, limit of detection, range of measurement, selectivity, precision, and accuracy.

2. EXPERIMENTAL

2.1. Materials

Creatinine anhydrous (Sigma Aldrich, 98%), SiO_2 (Ludox, 40%), sodium aluminate (Sigma Aldrich, 50%), glacial acetic acid (Merck, 100%), sodium acetate (Merck, 99%), sodium dihydrogen phosphate dihydrate (Merck, 97%), urea (Merck, 98%), sodium hydrogen phosphate dihydrate (Merck, 99%), silver wires with 100% of purity, solid paraffin, carbon powder, and distilled water. All chemicals were used as received without any further purification.

2.2. Instruments

The potentiometric was performed on Cyberscan 510 using reference electrode Ag/AgCl. The structure of zeolite was examined using XRD JEOL JDX-3530. The surface area and pore diameter of carbon was measured by N_2 adsorption-desorption using Quantachrome Instruments version 2.0.

2.3. Preparation of carbon paste electrode-imprinted zeolite

Firstly, we synthesized zeolite using mole ratio about 4 Na_2O: 1 Al_2O_3: 1.8 SiO_2: 270 H_2O [14]. Sodium aluminate as alumina source was mixed with water and SiO_2. The mixture was stirred and annealed at 100 °C. After 45 h, the obtained mixture was added creatinine with ratio creatinine: Si=0.0306. The mixture was aged for 3 h to trap the creatinine into zeolite pores. Moreover, the mixture was filtered using centrifugation with hot water till neutral. The purpose of this step was creatinine leave prints in the zeolite framework. The residue was dried at 80 °C. The resulted powder was called imprinting zeolite.

Carbon paste electrode-imprinted zeolite was prepared using Ag wires as connector between electrode and potentiometer. A ¾ part of micropipette tube was filled using melted paraffin. After that, we mixed activated carbon-paraffin-imprinted zeolite, and heated at 50 °C to result the paste texture. The formed paste was then filled into ¼ part of micropipette tube.

2.4. Optimization of electrode

To obtain the optimum condition of electrode, we investigated the composition of electrode and pH of creatinine sample. The variation of electrode composition was displayed in Table 1. The prepared electrodes were used to measure potential of electrode in the 10^{-2}–10^{-8} M of creatinine standard solution. The optimum electrode was determined by value Nernst factor, linearity on EMF versus log concentration plot and range of concentration. The pH of creatinine solution was varied to study the influence of acidity/basicity towards electrode performance. The pH was varied pH of 4, 5, 6, 7, and 8 by adding buffer solution.

The pH that performed constant potential was determined as optimum pH.

Table 1. The composition of activated carbon, imprinting zeolite and solid paraffin in the preparation of carbon paste electrode-imprinted zeolite

Electrode	**Composition (%weight)**		
	Activated carbon	**Imprinted zeolite**	**Solid Paraffin**
E1	60	0	40
E2	55	5	40
E3	50	10	40
E4	45	15	40
E5	40	20	40

3. RESULTS AND DISCUSSION

3.1. Influence of electrode composition and pH on potentiometric response of the creatinine-selective electrode

To clarify the structure of zeolite, we characterized the obtained sample by XRD. The diffractogram of the synthesized zeolite is depicted in Figure 1. The XRD profile confirms the structure of zeolite LTA. The diffractogram shows peaks at 2θ=7.14, 10.10, 12.40, 16.04, 21.58, 23.90, 27.02, 29.84, and 34.07°, among which the peak at 12.40° is associated with the cubic structure of zeolite LTA [15].

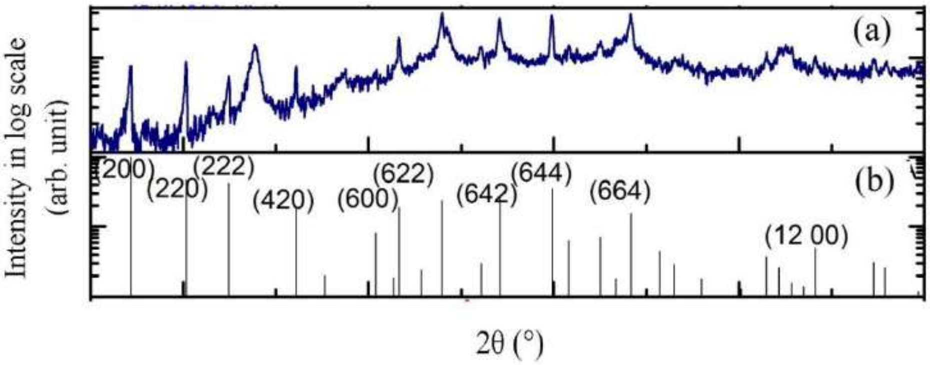

Fig. 1. XRD profile of (a) prepared zeolite LTA and (b) JCPDS of zeolite LTA (01-073-2340)

The working electrodes were prepared by mixing activated carbon, imprinted zeolite, and paraffin. Activated carbon was prepared by the activation method using 10^{-1} M H_3PO_4. It is well known that activated carbon exhibits high chemical stability and conductivity, and has a large surface area and pore diameter of about 877.463 m^2/g and 3.835 nm, respectively. Imprinted zeolites were used to increase the selectivity of the electrode because they present selective sites for creatinine molecules. Paraffin was added to bind the composite of carbon and imprinted zeolite

The performance of the electrode was determined by the estimation of linearity, range of measurement, and Nernst factor. The Nernst factors of the resulting electrodes were 4.6–8.5 mV/dec, which were lower than the theoretical value. The obtained linearity was also lower than 1 at about 0.49–0.71. To increase the sensitivity of the method, KCl was added into the solution as it can ionize in water and improve the conductivity of the solution. After KCl addition, the Nernst factor and linearity increased, as can be seen in Figure 2. Among the synthesized electrodes, E4 displayed the highest Nernst factor and linearity. Therefore, for further study, E4 was used as the electrode.

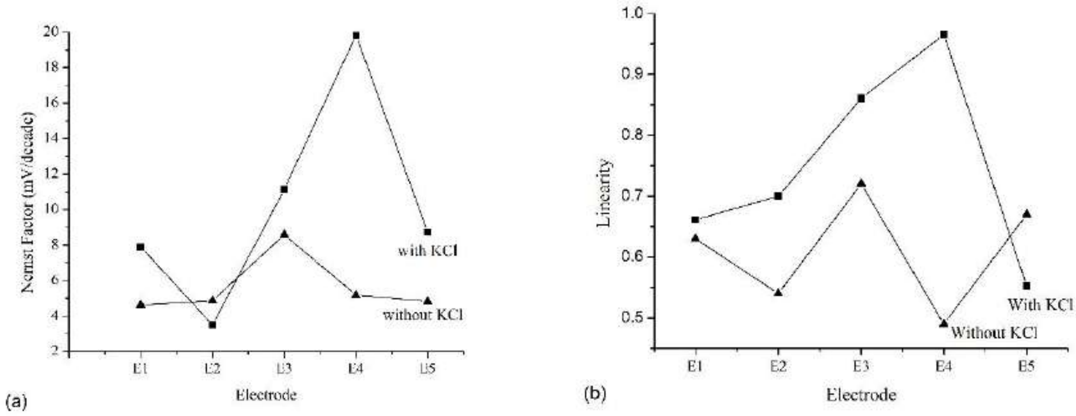

Fig. 2. (a) Nernst factor and (b) regression linearity of different electrode compositions

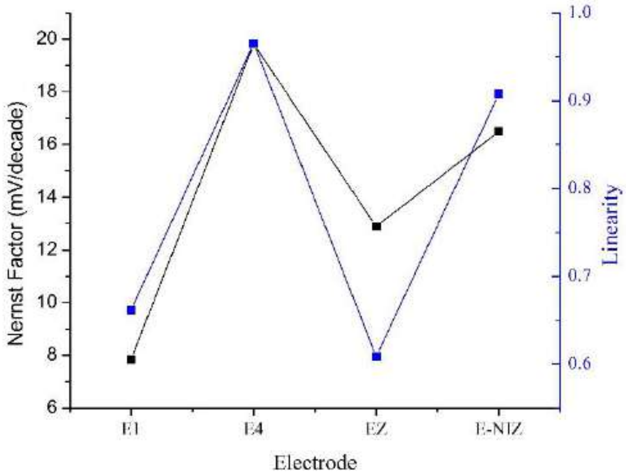

Fig. 3. Nernst factor and linearity of E1, E4, EZ, and E-NIZ electrodes

The concentration of imprinted zeolite affected the amount of active sites of the electrode. E4 with a carbon, imprinted zeolite, paraffin mass ratio of 45:15:40 showed the best performance as a sensor in creatinine detection by the potentiometry method, while E5 that contained a higher amount of imprinted zeolite exhibited a low Nernst factor and linearity.

This is probably due to the formation of a rigid membrane, which resulted in the low response of the electrode toward the analyte.

To evaluate the effect of creatinine template on the performance of the electrode, we compared the working performances of E1 (without imprinted zeolite), E4, carbon paste-zeolite (EZ), and carbon paste-non-imprinted zeolite electrodes (E-NIZ). E4 exhibited better linearity and a higher Nernst factor than EZ and non E-NIZ did. This is because EZ did not have a creatinine-selective template, while in E-NIZ, creatinine was trapped in the zeolite framework and could not effectively move from the solution to the electrode. A comparison of the performances of these electrodes is displayed in Figure 3.

The electrode performance in H^+ sensing was also investigated. The performance of the optimal electrode was measured in solutions with varying pH (4, 5, 6, 7, and 8). The pH changed the Nernst factor. At pH 7, the resulting Nernst factor was about 52 mV/dec. Compared to other pH, the electrode showed a constant potential at pH 7. Creatinine has two dissociation constants, pKa_1=4.8 and pKa_2=9.2. However, since pKa_2 is less than 7, the second protonation of H^+ is difficult. It can be conclude that creatinine was analyzed as a monovalent molecule. Furthermore, creatinine detection at pH 7 is advantageous and effective because it is similar to the blood and urine pH, and thus, does not require pH treatment in the sample preparation.

3.2. Calibration graph of creatinine

A standard curve of creatinine was plotted from the electrode potential data of the creatinine measurements and log creatinine concentrations of 10^{-8}–10^{-4} M at pH 7 using the E4 electrode.

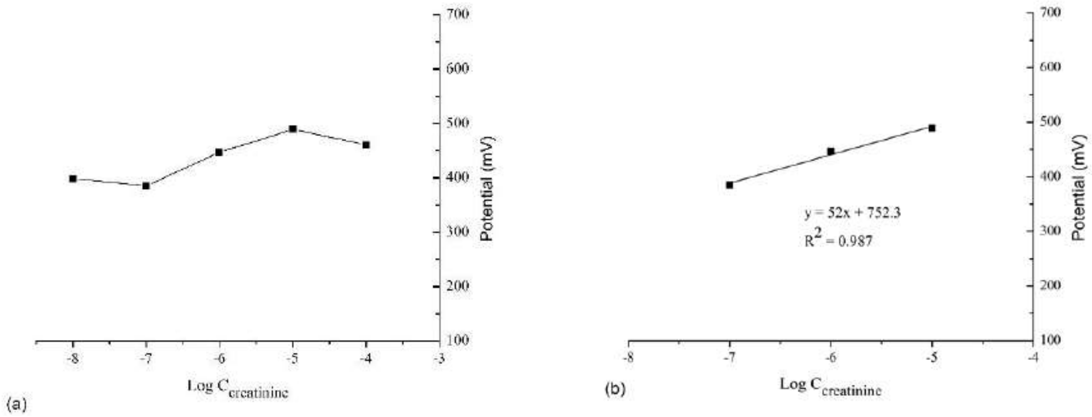

Fig. 4. (a) Plot of log $C_{creatinine}$ *vs.* electrode potential and (b) linear curve of creatinine-selective electrode for 10^{-7}–10^{-5} M creatinine solution

From the data, we created the correlation curve of log of creatinine concentration (log $C_{creatinine}$) and potential (EMF) (Figure 4a). The log $C_{creatinine}$ from -5 to -7 displayed the regression equation y=52x+752.3, with R^2=0.987 (Figure 4b). From this equation, the obtained Nernst factor was 52 mV/dec, which is close to the theoretical Nernst factor of monovalent compound. In other words, the linear concentration range of the prepared electrode was 10^{-7}–10^{-5} M.

The limit of detection is derived from intersection of the linear (y=52x+752.3) and non-linear ($y=38x^2+556x+2415$) functions in the plot of log $C_{creatinine}$ *vs*. potential (mV). The limit of detection was calculated as 7.9×10^{-8} M, while the detection limit of the commonly used method for creatinine detection in the medical field (spectrophotometric method) is in the order of 10^{-5} M [16].

3.3. Performances of creatinine-selective electrode based on carbon paste and imprinted zeolite

In this study, the response time, reproducibility, accuracy, selectivity, and lifetime of the fabricated electrode were investigated. The response time of an electrode is the time required by the electrode to detect an analyte, and is considered from the time of immersion of the electrode into the solution until the observation of a stable potential [17]. The response time increased with increase in creatinine concentration. At a higher concentration, molecules move faster from the solution to the electrode. Table 2 displays the variation in the response time of the electrode with creatinine concentration.

Table 2. The response time of electrode for 10^{-7}-10^{-5} M of creatinine

Concentration (M)	Response time (second)
10^{-7}	47
10^{-6}	38
10^{-5}	29

The reproducibility was determined by measuring the electrode performance in three creatinine solutions under the same conditions and concentration. The concentration of creatinine in the solution varied in the range of 10^{-7}–10^{-5} M. The proposed electrode demonstrated high reproducibility with a relative standard deviation less than 2.56%. The prepared electrodes also met the required sensor criteria of the Association of Official Analytical Chemists. It states that the maximum relative standard deviation of a sensor should not exceed 15% for concentrations ranging from 10^{-7} M to 10^{-5} M [18].

In clinical laboratories, spectrophotomertry is the commonly used method for creatinine detection. Table 3 shows the accuracies of the proposed potentiometric method using the carbon paste-imprinted zeolite electrode and the spectrophotometry method in the detection of creatinine solution. The developed electrode shows an accuracy of 80.3–100.4%, while the accuracy of the method that is acceptable for concentrations of the order of 10^{-7}–10^{-5} M is 80–120% [18]. Association of Official Analytical Chemists declares the criterions of analysis method. An analytical method is considered eligible for use in quantitative analysis if it meets certain criteria, including relative standard deviation and accuracy. According to the method accuracy and relative standard deviation, the developed carbon paste-modified imprinted zeolite electrode can be used as an alternative sensor for creatinine detection in the medical field.

Table 3. The accuracy of potentiometric method compared with spectrophotometry in the measurement of creatinine solution

Number of sample	**Concentration (M)**		**Accuracy (%)**
	Potentiometry	**Spectrophotometry***)	
1	3.74×10^{-4}	4.66×10^{-4}	80.3
2	4.77×10^{-4}	5.05×10^{-4}	94.5
3	7.07×10^{-4}	7.04×10^{-4}	100.4
4	3.91×10^{-4}	4.55×10^{-4}	85.9
5	4.52×10^{-4}	4.97×10^{-4}	90.9

*) data from local clinical laboratory

Selectivity, expressed by the selectivity coefficient, Kij, is the main parameter for performance evaluation of the prepared electrode. The coefficient of selectivity was investigated to study the selectivity of the electrode in creatinine solution, which also contained urea, which has a similar structure as that of creatinine and is present in high concentrations in blood and urine.

Table 4. The selectivity coefficient of carbon paste-imprinting zeolite electrode in 10^{-5} M creatinine

Interference	**Concentration (M)**	**K_{ij}**
Urea	10^{-6}	0.085
	10^{-5}	0.126
	10^{-4}	0.106

The calculated selectivity coefficient values are presented in Table 4. It can be seen that the carbon paste-imprinted zeolite electrode exhibits high selectivity toward creatinine (i) than toward urea (j), which is indicated by a K_{ij} value less than 1. The electrode lifetime was determined to investigate the stability of the electrode after being used several times. The electrodes demonstrated a long lifetime of about 7 weeks (used for 160 times).

4. CONCLUSION

Creatinine-selective electrodes demonstrated high repeatability in the concentration range of 10^{-7}–10^{-5} M. The lifetime of 7 weeks (used 160 times) indicated that the electrodes are suitable for routine detection of medical samples. The detection limit of the developed electrode was much lower than that of the spectrophotometric method, and no interference was observed by the presence of urea. Therefore, the potentiometric method using the developed electrode can be potentially used to determine creatinine levels. Further, the proposed electrode showed an accuracy of 80.3–100.4% (n=5). It can be concluded that the method can be applied for creatinine detection in urine or serum samples.

Acknowledgment

The authors thank the Ministry or Research, Technology and Higher Education, Indonesia for the financial support of this investigation through Universitas Airlangga RUPT Grant No. 597/UN3.14/LT/2017 and Chemistry Department, Faculty of Science and Technology, Universitas Airlangga for the laboratory facilities provided.

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Construction and Performance of Creatinine Selective Electrode based on Carbon Paste-Imprinting Zeolite

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Received: 29 January 2018 / Received in revised form: 24 March 2018 /
Accepted: 10 April 2018 / Published online: 30 April 2018

Abstract- Carbon paste-modified imprinted zeolite electrodes as a potentiometric sensor for creatinine detection have been constructed. The modified electrodes were fabricated by mixing activated carbon, imprinted zeolite, and paraffin. The electrode that was prepared with a respective mass ratio of 45:15:40 showed the best performance in creatinine detection. In addition, the electrode showed a fast response time (less than 50 s), a wide range of measurement (10^{-7}–10^{-5} M), and a low limit of detection (7.9×10^{-8} M). The presence of urea in the solution did not interfere in the detection of creatinine. The proposed creatinine-selective sensor exhibited good reproducibility, accuracy, and a long lifetime. The creatinine-selective electrode based on carbon paste-imprinted zeolite can be potentially used for creatinine detection in the medical field.

Keywords- Creatinine selective electrode, Imprinted zeolite, Potentiometry

1. INTRODUCTION

Creatinine is a product of muscle metabolism, which is excreted through urine. The normal level of creatinine in blood is about 0.6 until 1.2 mg/dL. A lower than normal creatinine concentration may indicate poor nutrition [1], while a high level of creatinine can be a warning for kidney malfunction such as glomerulonephritis, tubular necrosis, and low filtration of glomerulus [2].

In clinical detection, creatinine concentration is commonly determined using the Jaffe method through reaction between creatinine and picric acid [3]. This method is not specific because not only creatinine, but also ketone, glucose, bilirubin, acetoacetic, and cephalosporin are detected [4]. Chromatography has also been used for creatinine detection; however, this method is time-consuming [5]. Other methods such as flow injection potentiometry [6] and voltammetry using a molecularly imprinted polymer (MIP)-modified hanging mercury drop electrode (HMDE) method [7,8] have been developed for creatinine detection. Detection of creatinine by voltammetry using an electrode based on poly(melamine-co-chloranil)-modified HMD exhibited high selectivity [7]. Unfortunately, this electrode had a short lifetime (can be used only once). The electrode preparation process also depends on polymer solubility. For a low-solubility polymer, electrode fabrication is difficult. A MIP synthesized from aniline as a monomer with ammonium peroxydisulfate as the initiator and creatinine as a template has been used to modify HMDE for voltammetric detection of creatinine. This method yielded high accuracy and sensitivity, but had low precision [9].

Potentiometry is one of the electrochemical methods that determines the difference in cell potential (EMF) between the working and reference electrodes under zero current. Some researchers have developed potentiometric sensors to analyze creatinine [10,11]. However, not all the analytes yielded a high signal response because of the use of low-conductivity electrodes. In this research, a high-response and highly selective electrode is proposed for creatinine detection by potentiometry. A carbon paste electrode was modified with imprinted zeolite to construct the potentiometric electrode. The imprinted zeolite was used to increase the conductivity of the electrode, because of which a high signal response was obtained.

Zeolite is a crystalline TO_4 (T is a tetrahedral unit such as Al, Si, or Ti) with channels and three dimensional framework. The unique properties of zeolite as a porous material have been employed for pore selectivity. The shape and pore size of zeolite are designed to ensure conformity between zeolite pore and the target molecule. Our previous research had produced an imprinted zeolite, whose pores were selective toward uric acid. Titanium silicalite-1 and LTA zeolite have been proposed as selective materials for modification of carbon paste and glassy carbon electrode, which exhibited high selectivity in uric acid detection by potentiometry and voltammetry [12,13].

In this work, we studied the optimum composition of carbon and imprinted zeolite in the preparation of an electrode for creatinine detection by potentiometry. The electrode properties were discussed with respect to response time, Nernst factor, limit of detection, range of measurement, selectivity, precision, and accuracy.

2. EXPERIMENTAL

2.1. Materials

Creatinine anhydrous (Sigma Aldrich, 98%), SiO_2 (Ludox, 40%), sodium aluminate (Sigma Aldrich, 50%), glacial acetic acid (Merck, 100%), sodium acetate (Merck, 99%), sodium dihydrogen phosphate dihydrate (Merck, 97%), urea (Merck, 98%), sodium hydrogen phosphate dihydrate (Merck, 99%), silver wires with 100% of purity, solid paraffin, carbon powder, and distilled water. All chemicals were used as received without any further purification.

2.2. Instruments

The potentiometric was performed on Cyberscan 510 using reference electrode Ag/AgCl. The structure of zeolite was examined using XRD JEOL JDX-3530. The surface area and pore diameter of carbon was measured by N_2 adsorption-desorption using Quantachrome Instruments version 2.0.

2.3. Preparation of carbon paste electrode-imprinted zeolite

Firstly, we synthesized zeolite using mole ratio about 4 Na_2O: 1 Al_2O_3: 1.8 SiO_2: 270 H_2O [14]. Sodium aluminate as alumina source was mixed with water and SiO_2. The mixture was stirred and annealed at 100 °C. After 45 h, the obtained mixture was added creatinine with ratio creatinine: Si=0.0306. The mixture was aged for 3 h to trap the creatinine into zeolite pores. Moreover, the mixture was filtered using centrifugation with hot water till neutral. The purpose of this step was creatinine leave prints in the zeolite framework. The residue was dried at 80 °C. The resulted powder was called imprinting zeolite.

Carbon paste electrode-imprinted zeolite was prepared using Ag wires as connector between electrode and potentiometer. A ¾ part of micropipette tube was filled using melted paraffin. After that, we mixed activated carbon-paraffin-imprinted zeolite, and heated at 50 °C to result the paste texture. The formed paste was then filled into ¼ part of micropipette tube.

2.4. Optimization of electrode

To obtain the optimum condition of electrode, we investigated the composition of electrode and pH of creatinine sample. The variation of electrode composition was displayed in Table 1. The prepared electrodes were used to measure potential of electrode in the 10^{-2}–10^{-8} M of creatinine standard solution. The optimum electrode was determined by value Nernst factor, linearity on EMF versus log concentration plot and range of concentration. The pH of creatinine solution was varied to study the influence of acidity/basicity towards electrode performance. The pH was varied of 4, 5, 6, 7, and 8 by adding buffer solution. The pH that performed constant potential was determined as optimum pH.

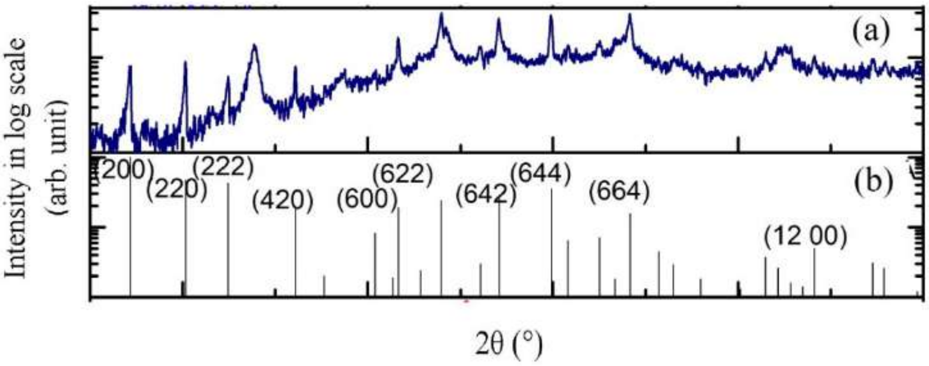
Table 1. The composition of activated carbon, imprinting zeolite and solid paraffin in the preparation of carbon paste electrode-imprinted zeolite

Electrode	**Composition (%weight)**		
	Activated carbon	**Imprinted zeolite**	**Solid Paraffin**
E1	60	0	40
E2	55	5	40
E3	50	10	40
E4	45	15	40
E5	40	20	40

3. RESULTS AND DISCUSSION

3.1. Influence of electrode composition and pH on potentiometric response of the creatinine-selective electrode

To clarify the structure of zeolite, we characterized the obtained sample by XRD. The diffractogram of the synthesized zeolite is depicted in Figure 1. The XRD profile confirms the structure of zeolite LTA. The diffractogram shows peaks at 2θ=7.14, 10.10, 12.40, 16.04, 21.58, 23.90, 27.02, 29.84, and 34.07°, among which the peak at 12.40° is associated with the cubic structure of zeolite LTA [15].



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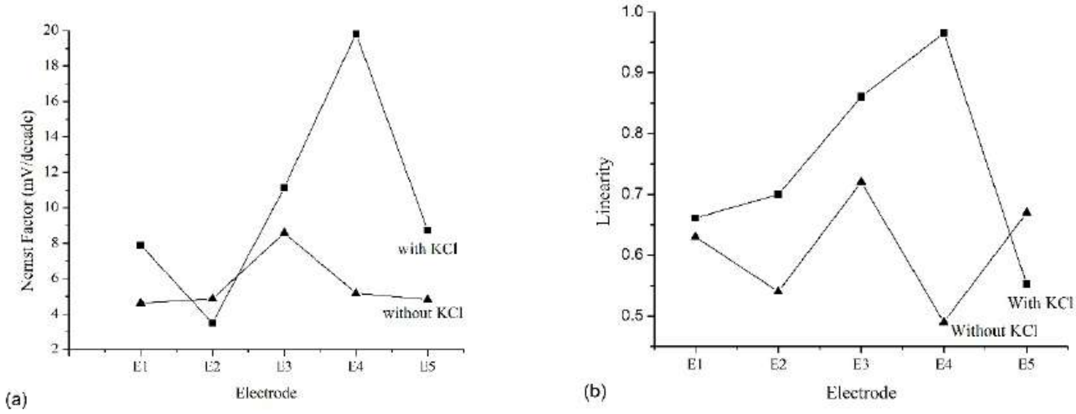
The performance of the electrode was determined by the estimation of linearity, range of measurement, and Nernst factor. The Nernst factors of the resulting electrodes were 4.6–8.5 mV/dec, which were lower than the theoretical value. The obtained linearity was also lower than 1 at about 0.49–0.71. To increase the sensitivity of the method, KCl was added into the solution as it can ionize in water and improve the conductivity of the solution. After KCl addition, the Nernst factor and linearity increased, as can be seen in Figure 2. Among the synthesized electrodes, E4 displayed the highest Nernst factor and linearity. Therefore, for further study, E4 was used as the electrode.



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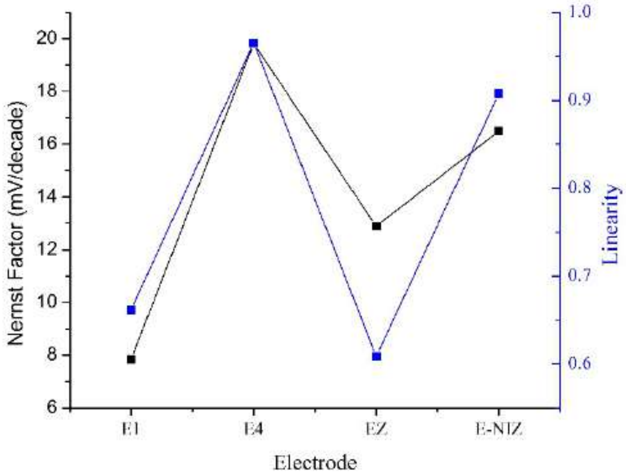

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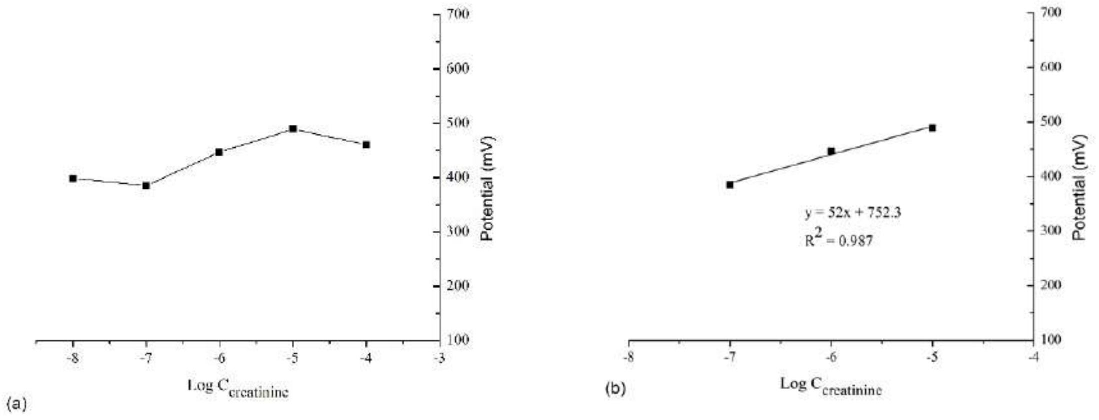

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The limit of detection is derived from intersection of the linear ($y=52x+752.3$) and non-linear ($y=38x^2+556x+2415$) functions in the plot of log $C_{creatinine}$ *vs*. potential (mV). The limit of detection was calculated as 7.9×10^{-8} M, while the detection limit of the commonly used method for creatinine detection in the medical field (spectrophotometric method) is in the order of 10^{-5} M [16].

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Concentration (M)	Response time (second)
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Table 3. The accuracy of potentiometric method compared with spectrophotometry in the measurement of creatinine solution

Number of sample	**Concentration (M)**		**Accuracy (%)**
	Potentiometry	**Spectrophotometry***)	
1	3.74×10^{-4}	4.66×10^{-4}	80.3
2	4.77×10^{-4}	5.05×10^{-4}	94.5
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4	3.91×10^{-4}	4.55×10^{-4}	85.9
5	4.52×10^{-4}	4.97×10^{-4}	90.9

*) data from local clinical laboratory

Selectivity, expressed by the selectivity coefficient, Kij, is the main parameter for performance evaluation of the prepared electrode. The coefficient of selectivity was investigated to study the selectivity of the electrode in creatinine solution, which also contained urea, which has a similar structure as that of creatinine and is present in high concentrations in blood and urine.

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The calculated selectivity coefficient values are presented in Table 4. It can be seen that the carbon paste-imprinted zeolite electrode exhibits high selectivity toward creatinine (i) than toward urea (j), which is indicated by a K_{ij} value less than 1. The electrode lifetime was determined to investigate the stability of the electrode after being used several times. The electrodes demonstrated a long lifetime of about 7 weeks (used for 160 times).

4. CONCLUSION

Creatinine-selective electrodes demonstrated high repeatability in the concentration range of 10^{-7}–10^{-5} M. The lifetime of 7 weeks (used 160 times) indicated that the electrodes are suitable for routine detection of medical samples. The detection limit of the developed electrode was much lower than that of the spectrophotometric method, and no interference was observed by the presence of urea. Therefore, the potentiometric method using the developed electrode can be potentially used to determine creatinine levels. Further, the proposed electrode showed an accuracy of 80.3–100.4% (n=5). It can be concluded that the method can be applied for creatinine detection in urine or serum samples.

Acknowledgment

The authors thank the Ministry or Research, Technology and Higher Education, Indonesia for the financial support of this investigation through Universitas Airlangga RUPT Grant No. 597/UN3.14/LT/2017 and Chemistry Department, Faculty of Science and Technology, Universitas Airlangga for the laboratory facilities provided.

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