ISSN-1996-918X

Pak. J. Anal. Environ. Chem. Vol. 26, No. 1 (2025) 15 – 26

http://doi.org/10.21743/pjaec/2025.06.02

# Modification of Carbon Paste Electrode with Imprinted Zeolite A as a Sensor for Potentiometric and Voltammetric Amitriptyline Analysis

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Received 31 January 2024, Revised 19 March 2025, Accepted 26 March 2025

Academic Editors: Amber R. Solangi and Huma Mudassar

## Abstract

Imprinted zeolite (IZ) has been used as a material to modify carbon paste electrodes and applied the modified electrode as a potentiometric and voltammetric sensor for amitriptyline (AMT). IZ was made from zeolite A, which is synthesized with an AMT/Si mole ratio of 0.03, then AMT was extracted from the zeolite framework to leave the active site that will recognize the AMT molecule selectively. Modified electrodes prepared with a mass ratio of paraffin, activated carbon, and IZ of 4:5:1 showed optimum performance as sensors in potentiometric analysis, which is expressed by a Nernst factor of 60.8 mV/decade, a detection limit of $9.85\times10^{-7}$ M, accuracy of 88-107%, recovery of 88.6% (n = 2), a response time of 60-89 s, and a life time longer than 18 weeks with more than 135 times of use. The presence of glucose, sucrose, and lactose did not interfere in AMT analysis. Measurement of the AMT using the modified electrode by voltammetry resulted in linearity of the calibration curve (R) of 0.9904, detection limit of $4.2\times10^{-8}$ M, precision of 82.9-97.7%, sensitivity of 552 nA/M, and recovery of 103.1% (n = 3). The modified electrode showed 2-4 times more selectiveness to AMT than the bare carbon paste electrode in the glucose matrix. Based on its advantages, the modified electrode is recommended for use in the pharmaceutical field to monitor AMT concentration in affordable antidepressant medicine, namely Amitriptyline Hydrochloride.

***Keywords:*** Carbon paste electrode, Imprinted zeolite, Electrode selectivity, Amitriptyline, Affordable medicine.

## Introduction

Amitriptyline (AMT) is an antidepressant drug in the tricyclic amine group that is commonly used to treat mental health disorders such as depression. AMT can inhibit the membrane pump mechanism responsible for the uptake of norepinephrine and serotonin in adrenergic and serotonergic neurons [1]. AMT is one of the more affordable medicines, so it is often prescribed by doctors for patients with depression. However, consuming the medicine in an excessive dose can cause serious side effects. Maximum daily intake of AMT is between 50 and 150 mg orally, leading to therapeutic blood concentration ranges between 0.01-0.16 mg/L daily and being considered toxic if the level in the blood >

0.50 mg/L [2]. Contraindications of consuming AMT are in patients with myocardial infarction, arrhythmia, bipolar disorder, severe liver disorders, and children aged <6 years. If people with depression consume the AMT in excessive doses, it can cause effects in part by anticholinergic effects such as coma, respiratory depression, and tachycardia [3]. The accuracy and consistency of AMT levels in medicine also need to be monitored by authorities to prevent carelessness by producers in compounding antidepressant medicine. Therefore, it is needed an accurate and economical method to determine the levels of AMT in medicine preparations.

Various methods have been developed to analyze AMT, such as spectrophotometry [4], high-performance liquid chromatography (HPLC) [5, 6], and gas chromatography-mass spectrometry (GC-MS) [7]. These methods have several limitations, including requiring a long time, complicated sample preparation, needing some chemicals, and being expensive.

Electrochemical methods such as voltammetry and potentiometry for drug analysis have attracted the attention of many researchers because these methods require short analysis time, are sensitive, accurate, simple in sample preparation, and are less expensive. The voltammetric method using graphite-screen-printed CuO nanoparticle electrodes [8], nafion-modified Au electrodes [9], plasticized polyvinyl chloride (PVC) membrane-coated glassy carbon [10], and $SiO_2/Al_2O_3/Nb_2O_5$/DNA-modified carbon paste electrodes [11] have been developed to analyze AMT. The method showed high accuracy and a low detection limit ($10^{-8}$ M). Potentiometric methods using dibutylphtalate (DBP)-coated graphite electrodes, molybdovanadate-based electrodes [12], and liquid carbon ionic nanoclay [13] have also been developed for AMT detection. The modified electrode showed the detection limit between $10^{-8}$ and $10^{-6}$ M.

The working electrode is a very important component in electrochemical analysis. The widely used working electrode is a carbon-based electrode, such as graphite, glassy carbon, or carbon paste. The surface of the carbon paste electrode can be easily modified and produce a reproducible electrode [14]. The choice of modifier is very important in modifying the carbon paste electrode because it has a role in the reactivity of the electrode. The trend of using zeolite as a modifier is currently increasing. It is due to zeolite being a conductive material with a pore size that can be modified easily. Synthetic zeolite has a uniform pore size that can be used as an adsorbent, cation exchanger, and catalyst. Several synthetic zeolites are widely used as electrode modifiers because of their properties as an adsorbent with high conductivity, including zeolite types LTA (A), X, P, Y, ZSM-5, and TS-1. Zeolite A has been applied as an adsorbent for Cu and Ni [15], as a catalyst [16], and can be formed into an imprint.

Currently, many sensors based on imprinted materials have been developed for the electrochemical analysis of various compounds contained in the body fluid. The imprinting technique is a method for making specific recognition using template molecules, which makes its pore more selective. This technique has been used in traditional Chinese medicine studies due to the specificity and selectivity resulting from the printed material [17]. In previous studies, various imprinted zeolites have been developed as materials to modify carbon paste electrodes and applied the modified electrode to analyze uric acid [18], cholesterol [19], creatine [20], and glucose [21] in human serum or urine samples.

In this study, a carbon paste electrode modified with imprinted zeolite A (IZ-A) was used as an electrometric sensor for AMT analysis. This electrometric sensor acts as a medium for the transfer of electrons in the electrochemical process. The sensor works based on measuring changes in electrical properties (such as voltage and current) produced by the interaction of the sensor with an analyte. This sensor responds to changes in the concentration of AMT ions that undergo electrochemical reactions on the electrode surface. The more AMT ions detected, the higher the current response produced. The presence of an AMT imprint on the electrode material causes an increase in the catalytic reaction and specific recognition of AMT on the electrode surface. The sensor will interact with AMT only, even though there are many other ions in the complex solution.

## Materials and Methods

### *Materials*

Amitriptyline-HCl ($C_{20}H_{23}N.HCl$; (98%); Sigma Aldrich, St. Louis, MO, USA), glucose monohydrate ($C_6H_{12}O_6.H_2O$; (99.5%); Merck, Rahay, NJ, USA), sodium aluminate ($NaAlO_2$ (50%); Sigma Aldrich, St. Louis, MO, USA), tetraethyl orthosilicate (TEOS (99%); Merck, Rahay, NJ, USA), glacial acetic acid ($CH_3COOH$ (100%); Merck, Rahay, NJ, USA), sodium acetate trihydrate ($CH_3COONa.3H_2O$ (99.5%); Merck, Rahay, NJ, USA), sodium dihydrogenphospha-tedihydrate ($NaH_2PO_4.2H_2O$ (98%); Merck, Rahay, NJ, USA), sodium hydrogenphosphate dihydrate ($Na_2HPO_4.2H_2O$ (99%); Merck, Rahay, NJ, USA). Paraffin pellets (Sigma Aldrich, St. Louis, MO, USA) and activated carbon (Sigma Aldrich, St. Louis, MO, USA) as materials for fabricating electrodes. All chemicals were analytical grade. Distilled water was used as a solvent. AMT HCl was used as a sample. It was produced by Indofarma, Indonesia.

### *Instrumentations*

The instruments used were a ionmeter (Cyberscan 510, Frankfurt, Germany), a digital potentiostat (eDAQ ER 461 Echem), the proposed carbon paste electrode modified with IZ-A (CPE/IZ-A) as the working electrode, Ag/AgCl as reference electrode, and platinum wire as auxiliary electrode. Zeolite characterization was carried out using X-ray diffractometer (Shimadzu, Kyoto, Japan) and Fourier transform infrared spectrophotometer (Shimadzu Kyoto Japan in the range of 4000-400 $cm^{-1}$. A pH-meter (Cyberscan Eutech Instrument pH 510, Frankfurt, Germany) was used to measure the pH. Centrifuge (HITECH EBA 20, Westphalia, Germany), vacum oven (Model 5851, Amityville, NY, USA), agate mortar, polypropylene bottle and glassware commonly used in chemical laboratories.

### *Procedure*

#### *Synthesis of the IZ-A*

The IZ-A was synthesized by dissolving 8.2 g of $NaAlO_2$ into 113 mL of distilled water in a polypropylene bottle, adding 5.2 mL of TEOS solution drop by drop while stirring for 3 h with a magnetic stirrer. The mixture was heated in an oven at 100 °C for 45 h [22]. The one-third portion of the mixture was washed with distilled water using centrifugation and dried in an oven at 80 °C, resulting in zeolite A powder. The two-thirds other portions of the mixture were added to 0.108 g of AMT, which had been dissolved in distilled water, while stirring for 30 min. The mixture was kept for 3 h at room temperature. A half portion of the mixture was centrifuged, and then the precipitate (non-imprinted zeolite/NIZ) was dried using an oven. IZ was carried out by extracting amitriptilyne from the other half portion of the mixture with hot water at 80 °C with the centrifugation. Characterization of zeolite and IZ-A was carried out using X-ray diffraction (XRD) and

Fourier transform infrared (FTIR) spectroscopy.

### *Sensor Fabrication*

Sensors were prepared by mixing activated carbon, paraffin, and IZ-A with the composition shown in Table 1. The mixtures are heated using a hotplate at 60 °C until a homogeneous paste was formed. Inserted the paste into the micropipette tip, which has previously been pinned with Ag wire. The Ag wire must be ensured that it does not appear on the electrode surface. The remaining space in the micropipette tip was filled with melted paraffin. The pointed end of the micropipette tip was cut to obtain a certain surface area.

***Table 1.*** **Composition of activated carbon (C), paraffin (P), and IZ for preparing electrodes.**

| Electrode | Composition (% weight) | | |
|---|---|---|---|
| | P | C | IZ |
| E1 | 40 | 60 | 0 |
| E2 | 40 | 55 | 5 |
| E3 | 40 | 50 | 10 |
| E4 | 40 | 45 | 15 |
| E5 | 40 | 40 | 20 |

### ***Potentiometric Measurements***

The electrodes with variations in composition (E1-E5) were used to measure AMT $10^{-8}$ M–$10^{-2}$ M with a various pH. The electrode that has optimum performance was used to measure the AMT solution in the various concentrations to determine the response time, electrode lifetime, detection limit, and accuracy of the potentiometry method. The detection limit was determined by intersecting the linear and non-linear curve relationship the log [AMT] with the electrode potential and extrapolating it to the abscissa to yield the log [AMT] value. The accuracy value is calculated using equation (1).

$$Accuracy = \frac{Csp}{Ks} \times 100\% \quad (1)$$

where *Csp* is the found concentration and *Ks* is the true concentration of the AMT.

The selectivity of the electrode was studied by measuring the potential of a standard solution of AMT and an interfering solution. Glucose, lactose, and sucrose were used as interference matrixes. Electrode selectivity is expressed by the selectivity coefficient value ($K_{ij}$), which is calculated based on the matched potential method (MPM) according to equation 2.

$$K_{ij\,pot} = \frac{\Delta ai}{aj} \quad (2)$$

where the $\Delta ai$ is the main ion activity (AMT) and the $aj$ is the concentration of interfering ions/compound.

### ***Voltammetric Measurements***

In this study, the differential pulse stripping voltammetry (DPSV) technique was used to quantify the AMT concentration. Optimization of voltammetry method measurements as carried out using modified electrodes in AMT solution. The 100 mg/L amitriptyline solution was analysed with variations in deposition potential, deposition time, scan rate, and pH. AMT standard solution with a concentration of 20, 40, 60, 80, and 100 mg/L under optimum conditions was analysed using a modified electrode. Curves between AMT concentrations and currents for each concentration were constructed (n = 3). The linearity was expressed by the correlation coefficient (R) of the calibration curve. The limit of detection (LOD) was calculated using the data of the calibration curve according to equations (3) and (4) [23].

$$S_{y/x} = \sqrt{\frac{\Sigma\,(yi \quad \dot{y}i)^2}{n-2}} \quad (3)$$

$$Y_{LoD} = Yb + 3S_{y/x} \quad (4)$$

where $S_{y/x}$ is the standard deviation of the regression line and $Y_b$ is the blank response (intercept).

Precision of the analytical method is expressed as relative standard deviation (RSD), which is calculated using equations (5) and (6).

$$SD = \sqrt{\frac{\sum_{i=1}^{n}(x_i-\bar{x})^2}{n-1}} \quad (5)$$

$$RSD = \frac{SD}{\bar{x}} \times 100\% \quad (6)$$

that $SD$ is the standard deviation, $x_i$ is the result of every $i$-th measurement, $\bar{x}$ is the average of the measurement results and $n$ is the number of repetitions of measurements. Sensor selectivity was studied by adding glucose at various concentrations and observing the deviation of the measured current between the AMT solution and the AMT containing glucose. The % recovery was determined using the standard addition method calculated by equation 7.

$$\%\, recovery = \frac{C1-C2}{C3} \times 100\% \quad (7)$$

with C1 is AMT concentration of sample solution spiked with standard solution, C2 is concentration AMT of sample solution, and C3 is concentration of AMT standard spiked to the sample solution.

## Results and Discussion

### *Synthesis and Characterization of IZ-A*

The zeolite A was synthesized by reacting $NaAlO_2$, TEOS, and $H_2O$ with a molar ratio of $Na_2O$: $Al_2O_3$: $SiO_2$: $H_2O$ of 1: 1.8: 3.9: 270 [22]. The mixture was then added with AMT as a template with a mole ratio of AMT /Si of 0.03. A white powder of zeolite A was obtained, which was further characterized by XRD to determine the peak of crystallinity and crystal lattice.

Characterization of zeolite A using XRD was carried out at position 2θ of 5-50◦. Based on the difractogram pattern in Fig. 1, it was observed the peak in the 2θ of 7.18◦; 10.17◦; 12.46◦; 16.11◦; 23.99◦; 26.11◦; 30.83◦; 34.18◦. The pattern is confirmed by the peak on standard zeolite A (7.25◦; 10.25◦; 12.50◦; 16.18◦; 21.72◦; 26.16◦; 30.87◦; 34.20◦) [24].

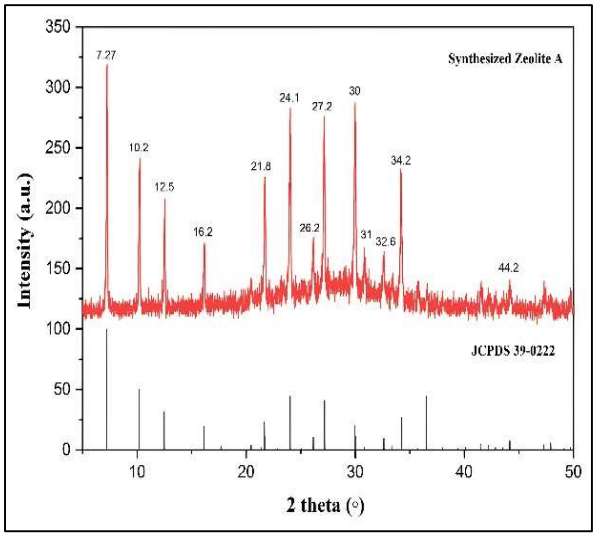


***Figure 1.*** **Diffractogram of synthesized zeolite A and JCPDS standar [24]**

Characterization of zeolite A, NIZ-A, IZ-A, and AMT with FTIR is shown in Fig. 2. It is observed the presence of Si-O and Al-O bonds (around 1000-1100 $cm^{-1}$, stretching vibration), which is characteristic of zeolites. The AMT spectra illustrates the presence of C-N (~1442 $cm^{-1}$, stretching vibrations). The FTIR spectra of NIZ-A shows characteristic C-N bonds (~1429 $cm^{-1}$, stretching vibration). The FTIR spectra of IZ-A shows the presence of a weak C-N bond (~ 1418 $cm^{-1}$, stretching vibration) with weak intensity. This proves that the amitriptyline molecule has been printed as a template on IZ-A.

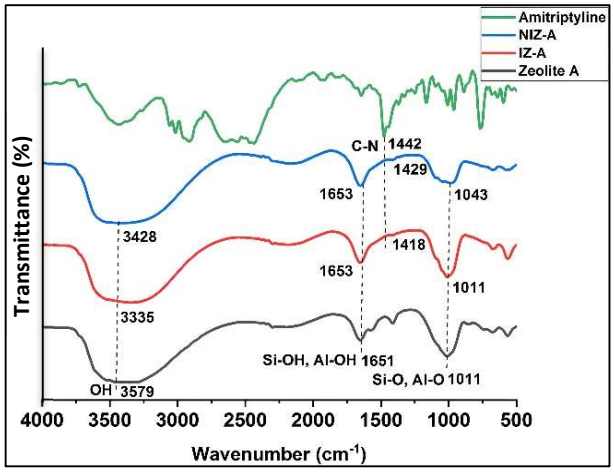


*Figure 2.* **FT-IR spectra of zeolite A, NIZ A, IZ A, and amitriptilyne**

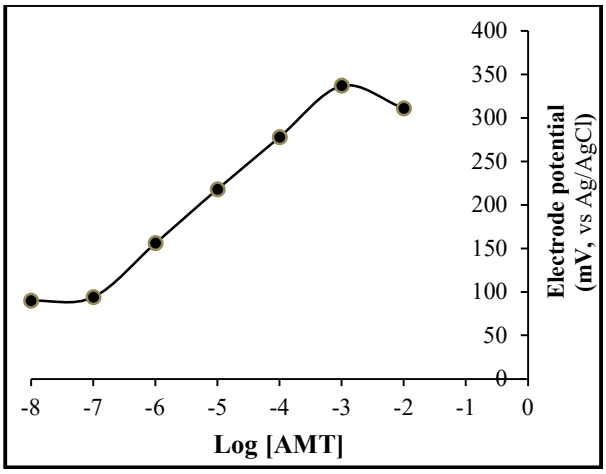


*Figure 3.* **The plot between log concentration of AMT and electrode potential using E3**

The absorption band of -CN functional group in IZ-A, which is increasingly shifted towards a shorter wavelength, namely from 1429 to 1418 $cm^{-1}$ (blue shift), is due to the breaking of the dipole-dipole interaction between the N atom in AMT and the O atom in IZ-A [25].

## *Performance of CPE/IZ-A*

**Effect of electrode composition and pH solution.** Before being used for analysis, the electrodes made with various compositions of activated carbon, paraffin, and IZ (Table 1) were soaked in an AMT solution to obtain an equilibrium of the AMT on the electrode surface. This equilibrium triggers the emergence of a potential difference in the working electrode. Each electrode was used to measure $10^{-8}$-$10^{-2}$ M AMT solution at pH 4, 5, 6, 7, and 8 by the potentiometric method. Data of measurement for AMT standard solutions were used to create a plot between the log [AMT] and the electrode potential. All electrodes express a measurement range of 1 $\times 10^{-7}$ – 1 $\times 10^{-3}$ M with varying Nernst factor value. Electrode E3 at pH 7 produces a Nernst factor of 60.8 mV/decade (Fig. 3), which is the closest to the theoretical value among other electrodes to determine AMT, a monovalent compound.

The potentiometric method using the developed electrode to measure AMT showed the lower detection limit of 9.8 $\times 10^{-7}$ M and accuracy of 88-107%. The detection limit in this study is lower than the previous study, which had a detection limit of 6.9 $\times 10^{-5}$ [12].

**Electrode response time.** Electrode response time is the time required for the electrode to respond to the analyte and provide a stable potential reading [26]. The response time of the carbon paste electrode-IZ (E3) to AMT solutions at pH 7 ranges from 60 to 89 s, for the concentration of $10^{-3}$ to $10^{-7}$ M. The higher the concentration of AMT, the shorter the time required for the electrode to respond to the AMT. This is caused by the higher the concentration, the faster the equilibrium occurs on the electrode surface.

**Lifetime of the electrode.** Electrode lifetime is one of the electrode performance criteria that describes electrode stability. Electrode lifetime is the period since the electrode provides good performance until a decrease in performance is observed, indicated by a decrease in the Nernst factor value. The E3 electrode showed stability in use up to 18 weeks (135 measurements). The life time is longer than the similar electrode previously developed to analyze blood glucose, namely 9 weeks [27].

**Application on real sample.** The usability of the electrode was studied by using it for the measurement of AMT concentration in real antidepressant tablets. The measurements were performed by potentiometry using the standard addition technique. The measurement results produce recovery as shown in Table 2.

***Table 2.*** **The % recovery in application of electrode to analyze AMT content in pharmaceutical sample.**

| Sample | Concentration (M) | | Recovery (%) |
|---|---|---|---|
| | Spiked | Found | |
| Tablet 1 | $3.28 \times 10^{-5}$ | $3.07 \times 10^{-5}$ | 93.60 |
| Tablet 2 | $3.28 \times 10^{-5}$ | $2.74 \times 10^{-5}$ | 83.54 |

The recovery value meets the range of value set by The Association of Official Analytical Chemists (AOAC) for concentration level $10^{-5}$ M, namely 80-110% [28]. Therefore, the developed electrode was qualified as an alternative sensor for potentiometric analysis of amitriptyline in pharmaceuticals.

**Selectivity of the electrode.** The electrode selectivity parameter describes the ability of a method to measure the analyte selectively in the presence of other compounds, which is expressed by the selectivity coefficient value. In this study, the selectivity coefficient was determined by measuring the potential of a standard solution of AMT with a concentration range of $10^{-7}$-$10^{-3}$ M, likewise the concentration of glucose, lactose, and sucrose used as interfering compounds. These three compounds are generally used as fillers or coating materials in AMT tablets. Data on Table 3 shows that glucose, lactose, and sucrose solutions do not interfere with the analysis of AMT using the carbon paste electrode modified IZ-A, due to the presence of specific binding sites for AMT in the IZ-A. The selectivity coefficient value of CPE/IZ-A (E3) is much smaller than the $K_{ij}$ value for bare CPE (E1). This shows that the addition of IZ to the carbon paste electrode can increase the selectivity of the electrode in AMT analysis.

***Table 3.*** **Selectivity coefficients of E1 (bare CPE) and E3 (CPE/IZ-A) to AMT in glucose, lactose, and sucrose matrices.**

| Matrix | Concentration (M) | $K_{ij}$ | |
|---|---|---|---|
| | | E1 | E3 |
| Glucose | $10^{-7}$ | 0.1327 | $0.44 \times 10^{-4}$ |
| | $10^{-6}$ | 1.4384 | $0.12 \times 10^{-4}$ |
| | $10^{-5}$ | 0.3360 | $0.37 \times 10^{-4}$ |
| | $10^{-4}$ | 0.5456 | $0.37 \times 10^{-5}$ |
| | $10^{-3}$ | 1.0000 | $0.96 \times 10^{-6}$ |
| Sucrose | $10^{-7}$ | 1.2238 | $0.38 \times 10^{-6}$ |
| | $10^{-6}$ | 1.1754 | $0.41 \times 10^{-5}$ |
| | $10^{-5}$ | 1.2743 | $0.78 \times 10^{-6}$ |
| | $10^{-4}$ | 2.1528 | $0.11 \times 10^{-6}$ |
| | $10^{-3}$ | 0.9224 | $0.12 \times 10^{-6}$ |
| Lactose | $10^{-7}$ | 0.1040 | $0.49 \times 10^{-6}$ |
| | $10^{-6}$ | 1.6907 | $0.54 \times 10^{-5}$ |
| | $10^{-5}$ | 0.2637 | $0.73 \times 10^{-6}$ |
| | $10^{-4}$ | 0.3949 | $0.13 \times 10^{-6}$ |
| | $10^{-3}$ | 1.0841 | $0.12 \times 10^{-6}$ |

**Voltammetric Measurement Studies.** The IZ-A modified carbon paste electrode was applied to measure the current generated by the electrochemical reaction of 100 µg/L AMT solution with pH 7 phosphate buffer using cyclic voltammetry. Cyclic voltammogram of AMT solution is shown in Fig. 4. There is an anodic peak indicating the transfer of electrons that occurs on the electrode surface. However, the adsorption properties of carbon and zeolite predominate, so that the oxidation peaks are not clearly visible. AMT-HCl is oxidized involving the transfer of one electron, this is in accordance with the reaction process that occurs in AMT [29].

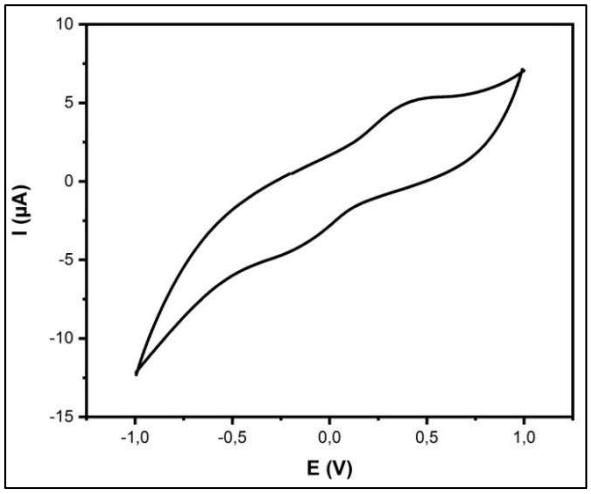


*Figure 4.* **Cyclic voltammogram of AMT 100 µg/L.**

## *Optimizations of the Measurement Paramete*

**Deposition potential.** AMT solution 100 µg/L was measured with various deposition potentials (0.1-1.0 V) using CPE/IZ-A. Deposition potential of 0.8 V was chosen for the optimum condition based on the high peak current and narrower peak width. In this study, the DPV stripping technique was used, which involved two steps, that is electrodeposition and stripping. During the electrodeposition step, the analyte in solution will be deposited (oxidized) on the surface of the electrode, while in the stripping step, the oxidized analyte will be reduced by providing a more negative potential than the deposition potential. The optimum deposition potential in this study was 0.8 V, and the stripping peak potential obtained was around 0.5-0.6 V.

**Deposition time.** The higher the deposition time, the more analyte will accumulate on the surface of the electrode, and then the amount of accumulated analyte will decrease with increasing deposition time [30]. At a deposition time 30 s, the surface of the electrode has been saturated and the redox reaction equilibrium has been reached, so that the reaction does not occur again when the time is added.

**Effect of pH.** The pH of the solution greatly affects the stability of certain species of an analyte when the measurement takes place. The effect of pH on the peak current indicates that changes in pH can cause a protonation reaction of a compound in solution. In AMT solution pH 8, AMT is surrounded by proton so it will easily reach the electrode in the form of a molecule [31], and the current is observed to be high within 33.13 nA.

**Voltammetric Analytical Performance.** Measurements by DPSV were carried out under previously optimal conditions to investigate the analytical performance of the CPE/IZ-A sensor for the determination of AMT. The voltammogram of measuring the standard solution and the calibration curve is shown in Fig. 5.

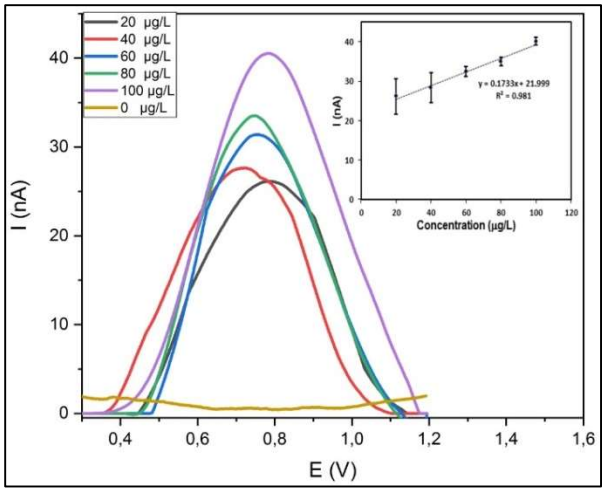


*Figure 5.* **Voltammogram of AMT (inset : calibration curve of AMT)**

A good linear correlation was found between the current and the concentration of AMT in the linear regression equation $Y = 0.1733x + 21.99$, with the correlation coefficient (R) of 0.9904. The developed sensor has a low detection limit, namely 13.21 µg/L ($4.2 \times 10^{-8}$ M). AMT solutions with the same concentration and under the same conditions were analyzed repeteadly, producing the RSD value of 2.3–17.1%. The

closeness between the found concentration and the true concentration in this study was expressed by an accuracy value of 90.8-119.5%.

**Application on real sample.** The analytical applications of the sensors were investigated by measuring AMT content in the generic pharmaceutical samples. The addition technique was used, which was carried out by measuring three solutions of sample, which were spiked with 35 µg/L AMT. The recovery value that resulted in measurement of the three sample solutions can be seen in Table 4.

The measurement with CPE/IZ-A has a $\bar{x}$ recovery of 103.1%, while according to the Association of Official Analytical Chemist (AOAC), the acceptable recovery of an analytical method to concentration of 100 µg/L is 80-110% [28]. Based on the recovery value, the developed sensor shows good accuracy and can be used as an alternative to measure and monitor AMT content in pharmaceutical preparations.

*Table 4.* **Recovery (%) in application of electrode to analyze AMT in AMT-HCl tablet.**

| Sample | Concentration (µg/L) | | Recovery (%) |
|---|---|---|---|
| | Spiked | Found | |
| Tablet 1 | 35.8 | 37.22 | 106.10 |
| Tablet 2 | 35.8 | 36.24 | 103.31 |
| Tablet 3 | 35.8 | 35.09 | 100.02 |

**The Selectivity of CPE/IZ-A.** Determination of selectivity in this study was necessary because in medicine tablets, AMT is present together with fillers, binders, and coating agents, which are generally simple carbohydrates or starch. Using the bare CPE, the presence of glucose decreased the current response of AMT by 28.27-94.28%.

*Table 5.* **Detection limit and measurement range using various electrode.**

| Methods | Electrode | LOD (M) | Measurement range (M) | Ref. |
|---|---|---|---|---|
| Potentiometry | Ion selective membrane-molybdovanadate and molybdotungstate | $6.9 \times 10^{-5}$ | $1 \times 10^{-4} – 1 \times 10^{-2}$ | [12] |
| | Liquid carbon ionic-nano clay | $2.4 \times 10^{-8}$ | $1 \times 10^{-7}$-$8 \times 10^{-6}$ | [13] |
| | DBP-coated graphite | $4.8 \times 10^{-7}$ | $1 \times 10^{-6} – 1 \times 10^{-1}$ | [32] |
| | Carbon paste IZ-A | $9.8 \times 10^{-7}$ | $1 \times 10^{-7} – 1 \times 10^{-3}$ | This study |
| Voltammetry | Graphite Screen Printed-CuO | $4.0 \times 10^{-7}$ | $1 \times 10^{-6}$-$2 \times 10^{-4}$ | [8] |
| | Nafion Aunps@Branched | $3.4 \times 10^{-8}$ | $1 \times 10^{-7}$-$7 \times 10^{-4}$ | [9] |
| | Plasticized PVC membrane-coated GC | $9.0 \times 10^{-8}$ | $1 \times 10^{-7} – 1 \times 10^{-4}$ | [10] |
| | $SiO_2/Al_2O_3/Nb_2O_5$/DNA-modified carbon paste | $1.2 \times 10^{-7}$ | $1 \times 10^{-5}$-$8 \times 10^{-5}$ | [11] |
| | Unmodified carbon nanotube | $1.6 \times 10^{-6}$ | $5 \times 10^{-6}$-$3 \times 10^{-5}$ | [29] |
| | MWCNT@cellulosa-glassy carbon | $8.4 \times 10^{-8}$ | $5 \times 10^{-7}$-$2 \times 10^{-5}$ | [33] |
| | Glassy carbon modified Fe(III)-exchanged clinoptioolite/graphite | $2.2 \times 10^{-7}$ | $5 \times 10^{-7}$-$5 \times 10^{-5}$ | [34] |
| | Carbon paste IZ-A | $4.2 \times 10^{-8}$ | $6.4 \times 10^{-8}$-$3.2 \times 10^{-8}$ | This study |

The high interference was caused by diffusion competition between AMT and glucose against the surface of the carbon paste electrode. Using CPE modified with IZ-A, the presence of glucose decreased the current response by 14.50-26.81%. Based on the decreasing in current due the presence of glucose in determining AMT using both electrode indicates that the presence of imprinted zeolite in the CPE makes the electrode more selective to the AMT than bare CPE. The glucose molecule has an H atom that can form hydrogen bonds with O atoms in the zeolite, so that both AMT and glucose can bind with the zeolite. The detection limit and measurement range of various analytical methods in the previous study for the analysis of AMT are shown in Table 5.

## Conclusion

Imprinted zeolite A modified carbon paste electrode (CPE/IZ-A) had shown good performance as a potentiometric and voltammetric sensor for AMT analysis. As a potentiometric sensor, CPE/IZ-A showed a Nernstian curve in the wide concentration range and was stable over a long period. The presence of glucose, lactose, and sucrose with various concentrations as carrier substances in the AMT tablet did not interfere with the analysis of AMT using the developed electrode. Aplication of the CPE/IZ-A to analyze AMT in the AMT medicine by potentiometry and voltammetry produces a recovery of 88.6 and 103.1%, respectively, so it is recommended for use by related institutions in monitoring AMT content in pharmaceutical preparations.

## Acknowledgement

This study was supported by the Directorate Research, Technology, and Community Development, Ministry of Education, Culture, Research, and Technology, Indonesia in the form of a PDUPT grant through Universitas Airlangga in accordance with contract number 776/UN3.15/PT/2022] for the research funding.

## Conflict of Interest

The authors declare that there is no conflict of interest related to the research work presented in this manuscript.

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