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Conductive Electrospun Nanofibers in The Electrochemical Sensor for Determination of Idarubicin

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ABSTRACT

The study reports the manufacturing of innovative electrochemical sensors using iron oxide ceramic nanofibers (Fe_3O_4 and Fe_2O_3) and polyether sulfone nanofibers (PES) to detect idarubicin in blood with sensitive and selective detection. The hybrid nanofiber matrix offers high surface area, excellent conductivity, and synergistic electrocatalytic properties, ideal for detecting idauricin in complex biological matrices. The sensor exhibits a wide linear detection range and remarkable sensitivity. The detection limit was suitable, indicating its ability to detect idarubicin at subclinical concentrations. The device showed excellent selectivity and minimal interference from biological analytes, ensuring reliable performance in blood samples. Repeated experiments measured a relative standard deviation (RSD) of 1.7%, while the repeatability of the independently manufactured sensor showed an RSD of 1.7%, demonstrating the robustness of the manufacturing process. Integrating Fe_3O_4/Fe_2O_3 ceramic nanofibers with PES offers a novel approach to overcoming the challenges of electrode and biofouling in blood. The sensor showed high recovery rates in human blood samples, confirming its application in clinical diagnostics. This paper presents a cost-effective and scalable method for constructing hybrid nanofiber electrochemical sensors with high sensitivity, selectivity, and repeatability. The result highlights the potential of Fe_3O_4/Fe_2O_3-PES nanofibers as a platform for developing next-generation point-of-care devices for monitoring chemotherapy drugs.

Keywords: Electrochemical, Idarubicin, Magnetic Nanofibers, Poly Ether Sulfone

1. INTRODUCTION

Despite the extensive efforts to treat cancer, the best therapeutic strategies have not yet been found. Chemotherapy remains the first line of cancer treatment [1]. Anthracycline (or anthracycline antibiotic) is a type of cancer chemotherapy drug. Idarubicin (IDA) is one of the most potent anthracycline chemotherapy drugs, approved to treat a wide range of acute and chronic malignant tumors [2-4]. Its strong anti-tumor effect is widely used in cancer treatments [5]. One of the disadvantages of idarubicin is its potential to cause cardiac damage, especially in cumulative doses. This can lead to heart failure or other heart problems. It can also cause cellular suppression and a decrease in blood cell counts. This can lead to anemia, increased risk of infection, and decreased platelet counts [6, 7]. Idarubicin is a 4-dimethoxy daunorubicin antibiotic with the formula $C_{26}H_{27}NO_9$ used in combination with other drugs as an anticancer agent (acute myelogenous leukemia (AML); a type of white blood cell cancer) [8]. IDA has a high lipophilic capacity due to its chemical structure (without a methyl group) and causes considerable cytotoxicity to healthy cells and tumor cells [9, 10]. By elucidating the mechanisms associated with IDA research, it can be

Volume 4, Number 2, December 2024, Page 55 - 66
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possible to unravel the path of action leading to cell toxicity and develop new drug molecules to target tumor cells selectively [11]. Traditional methods of detection of idarubicin, such as high-performance liquid chromatography (HPLC) and mass spectroscopy, are highly sensitive and accurate but require time, cost, and complex sample preparation [12]. These limitations have stimulated interest in developing quick, cost-effective, and portable alternatives, sensitivity, selectivity, and fast response time, including electrochemical sensors, which have emerged as a promising solution [13-15]. Integrating advanced nanomaterials into sensor design further enhances their performance [16]. Nanomaterials such as metal oxides, carbon nanostructures, and polymers improve electrode surface, conductivity, and catalytic activity, effectively detecting low concentrations of analytes in a complex matrix such as blood [17].

A biosensor is a device that measures biological or chemical reactions by producing concentration-proportional signals that are used using a Fe_3O_4 nanoparticle. These sensors can be used for non-invasive inspections and sensor scanning with high information accuracy [18, 19]. The electrospinning technology is considered the simplest method of preparing (nano) fibers. These fibers are beneficial in electrochemistry because nano-scale or micro-diameter pores increase surface area and have many applications [20, 21]. Because of their properties, specific structures, and simple interaction with materials such as biomolecules, enzymes, catalysts, and energy transformation particles, these fibers are suitable for electrochemical sensor synthesis and electrode surface modification [19, 22, 23].

Electrospun composites are a promising candidate for advanced technology development, influencing the production and commercialization of ultra-small and small materials due to their outstanding properties, synergy, new structures, composition, and exceptional mass transport [24].

One of the fascinating fields of chemically modified electrodes is cyclic and square-wave voltammetry (CPE), a simple preparation method with reproducible porous surfaces at low cost [3-4]. Nanoparticles with properties such as high surface, catalyst effect, high conductivity, etc., can be easily placed on CPE surfaces [25]. It is essential to find a simple, cost-effective, and high-performance way of producing the desired properties of nanomaterials [26].

However, combining fibers with different nanoparticles using an electrical method and specific catalysts is relatively tricky, especially in simultaneous electrochemical processes. Many analytical methods have been used to determine the IDA in different media and samples, most of which are chromatographic tests [(27, 28]. These methods are considered time-consuming because of extraction methods, expensive instruments, and organic solvents. The redox-active properties of the anthracycline structure IDA are classified as electroactive molecules. Cyclic Voltammetry is a kinetic analysis technique used to study the reactions of electroactive compounds such as IDA [3].

This study focuses on the development of electrochemical sensors based on iron oxide ceramic nanofibers (Fe_3O_4 and Fe_2O_3) combined with polymers such as polyether sulfone (PES) for the detection of idarubicin in blood, which have shown great potential. These materials exhibit unique properties, including excellent biocompatibility, anti-fouling and electron transport capabilities, enhanced sensitivity, selectivity, reproducibility, and real-world applicability. They are suitable for detecting idarubicin in biological samples. Electrochemical technology provides a versatile platform for detecting idarubicin, allowing for better monitoring of its therapeutic effects and toxicity in clinical settings. Further research can focus on improving the selectivity and sensitivity for practical applications.

2. METHODS

2.1. Equipment/Tool/ Material.

2.1.1. Reagents

Idarubicin, Polyether sulfone, Graphite, Paraffin, Ascorbic acid, Uric acid, Glucose and Epirubicin from Merck (Germany). Dipotassium hydrogen phosphate and Potassium dihydrogen phosphate from Sigma Aldrich (USA).

Volume 4, Number 2, December 2024, Page 55 - 66
e-ISSN: 2776-4508; p-ISSN: 2776-1711
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2.2. Apparatus

2.2.1. Morphological study

SEM offers a high-resolution image of the sensor surface and shows the morphology of nanostructure material such as electrospun nanofibers, nanoparticles, and other functional layers. The surface's uniformity, porosity, and roughness can directly affect the sensor's interaction with the idarubicin.

2.2.2. Electrochemical behavior of modified electrodes

A modified electrode is coated with a thin layer of polymer, metal, metal oxide, carbon, or nanomaterial to improve its characteristics and introduce certain functionalities. The type, structure, and thickness of the material affect the conductivity and response of the electrodes directly [29, 30].

2.2.3. Electrochemical Behavior of IDA

IDA is an anthracycline antibiotic widely used in chemotherapy, so it is crucial to design effective chemical sensors for its detection. Understanding the redox properties of IDA, its interaction with electrode surfaces, and its behavior under different conditions will help optimize sensor performance.

Electrochemical sensors utilizing redox behavior can provide sensitive, selective, and rapid detection of idarubicin, making them valuable tools in pharmaceutical and clinical applications [31].

2.2.4. Potentiostat

Controls the voltage of electrochemical cells, measures the resulting current, and enables precise and reproducible characteristics of chemical sensors. Potentiostat records the relationship between the applied current and the resulting current (or other electrochemical reactions) and generates data for evaluating the performance of the sensor [32].

2.2.5. Cycle voltage measurement (CV)

CV is a process that scans the voltage of a working electrode between two voltage limits for information about the redox potential, motion, and thermodynamics of electrochemical reactions. Studying the reversible, quasi-reversible, and irreversible electrode processes is advantageous. It helps identify the presence of intermediates and side reactions [33, 34].

The choice of techniques depends on the specific purpose of the electrochemical investigation and the properties of the systems under study. CV is a widely used technology for qualitative and quantitative analysis; EIS provides detailed information on surface properties and kinetics [33, 35].

2.2.6. Quantitative Measurement of Idarubicin (IDA) Using a Carbon Paste Electrode Modified with Nanofibers (CF-CPE)

A carbon paste electrode (CPE) modified with electrospun nanofibers (INF) offers an effective platform for the quantitative detection of idarubicin (IDA). The INF layer enhances the electrode's surface area, electron transfer capability, and interaction with IDA molecules, improving sensitivity and selectivity.

By integrating electrospun nanofibers onto a carbon paste electrode, the CF-CPE system provides a robust and sensitive platform for the quantitative [36, 37].

2.3. Preparation of cyclic and square-wave voltammetry modified with conductive nanofibers

$FeCl_3$ and $FeCl_2$ salts were weighed respectively (1.2 gr and 0.6 gr), and water solvent (400 gr) was added to place on the stirrer for one hour to dissolve completely. In the next step, polyvinyl alcohol (0.9 gr) was added. The resulting solution was subjected to sonication for 30 min. The solution was electro-spun at 50 ° C for 24 h with a voltage of 17-18 kV at a distance of 20 cm between the needle and aluminum foil. Then, it was calcined in a furnace at 600 ° C for two hours, and the resulting nanoparticles were a mixture of Fe_2O_3 and Fe_3O_4 (Figure 1).

In the next step, polyether sulfone polymer with a weight percentage of 22% was mixed with 1% by weight of iron oxide nanoparticles (Fe_3O_4 and Fe_2O_3) and placed in an ultra-sonic device for one hour. Then, the final obtained solution, which includes polyether sulfone polymer and iron nanoparticles, was electro-spun again with the electrospinning method on the desired electrode at a speed of 0.2-0.6 mL/h. Then, the obtained product, which is electro-spun on the

Volume 4, Number 2, December 2024, Page 55 - 66
e-ISSN: 2776-4508; p-ISSN: 2776-1711
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surface of the electrode, is called iron oxide ceramic nanofibers and polyether sulfone nanofibers.

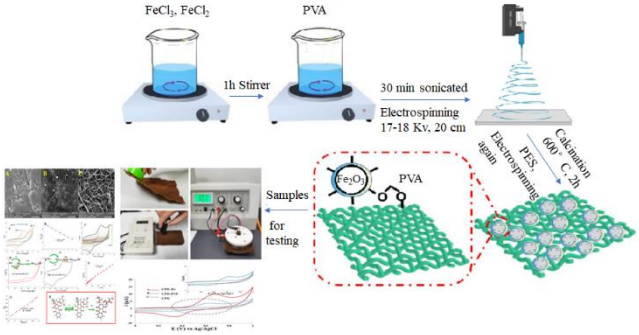

Figure. 1. The preparation steps of the Modified electrode.

2.4. Conductive nanofibers have modified the preparation of CPE and CPE nuclei

Two simple CPE electrodes and a modified CF (CPE- Fe) CPE electrode were prepared to compare the electrochemical behavior of CPE electrodes. The traditional CPE is manufactured by hand mixing graphite powder with paraffin oil at an agate mortar ratio of 85:15. Subsequently, CF, graphite powder, and paraffin oil (5:85:15 w/ w) were mixed (as CPE and modified electrodes). The electrode surface for the electrical connection is implemented by a silver wire placed in the tube. The resulting mixture was hand-mixed until a uniform paste was obtained. You get a new electrode surface by squeezing small parts of the paste and cleaning it with filter paper to get a smooth surface.

2.5. Sample preparation (CF-CPE)

Iron oxide nanofibers (Fe_3O_4 and Fe_2O_3) and electrode nanofibers modified with Polyether sulfone (PES) (CF-CPE) were combined with 0.2 M phosphate buffer at pH = 6.0 and subjected to cyclic voltage in the measurement range between 0 and 1.0 V in a scan at a speed of 100 mV/s were activated until a measurable voltage was obtained. When the current is fixed, they are transferred to a new cell with a specific concentration of 10 ml of supporting electrolytes and analyzers. For iron oxide nanofibers and modified electrode nanofibers, 6.5 mL of Carbon nanotubes (CNT) and 120 s of accumulation in 100 mV 0.1 m phosphate buffer were used to confirm IDA detection under pH 6.0 conditions and a stirring speed of 350 rpm. After 10 equilibration periods, a differential pulse voltmeter between 0.2 V and 1.2 V was recorded. All electrochemical test cycles were performed at room temperature.

2.6. Sample Preparation

The human plasma and urine sample was used to test the applicability of the electrode proposed in actual samples. The idarubicin powder (2.0 mg) is dissolved in 10.0 ml phosphate buffer (0.1 M, pH= 6.0), and a significant amount of this solution was chosen for analysis. Human plasma (from healthy volunteers) was added to 2.0 ml acetonitrile and centrifuged at 5000 rpm for 15 min to separate proteins from serum. This solution was transferred to a calibrated 10 ml bottle, added phosphate buffer, and the drug was spiked to mark. A urine sample was transferred to a volume glass of 10 ml of 2.0 murine, filled with phosphate buffer, and filled with different dosages of drugs.

2.7. Statistical analysis

The study statistically analyzes data obtained at a particular time during the drug's release using Excel software. The variation, standard deviation, and mean values obtained from drug concentrations were calculated by one-way analysis.

3. RESULTS AND DISCUSSION

3.1. Examining the structural morphology of nanofibers

As the SEM images of CPE, CPE-Fe, and CF-CPE electrodes show (Figure 2), the bare CPE electrode has graphite packing layers, while the CPE-Fe electrode shows no significant change in surface structure. The porous structure of the CF-CPE composite is significantly visible.

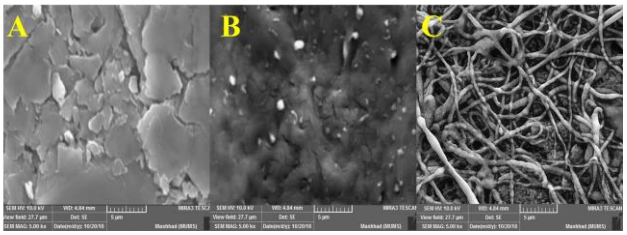

Figure 2. SEM images of (A) CPE, (B) CPE-Fe (CF), and (CF- CPE).

Volume 4, Number 2, December 2024, Page 55 - 66
e-ISSN: 2776-4508; p-ISSN: 2776-1711
Publisher : Universitas Pakuan

3.2. Electrochemical behavior of modified electrodes

Shown the electrochemical behavior of the CPE, CPE- Fe, and CF-CPE electrodes in a solution of 5.0 mM $Fe(CN)_6]^{3-/4-}$ (Figure 3). CV of CPE shows a pair of peaks of the electrochemical probe at about 320 mV of ΔE. Although the CV of CPE- Fe electrodes is almost identical, the current increases lightly at ΔE 340 mV, and the iron oxide nanoparticles (Fe_3O_4 and Fe_2O_3) and graphite mixtures do not exhibit significant electrochemical improvement. Finally, CF-CPE proves that compared to two other electrodes, the redox probe electrochemical current increases while the ΔE is reduced to 240 mV, and the CF-CPE composite's electron transfer (ET) is greatly improved.

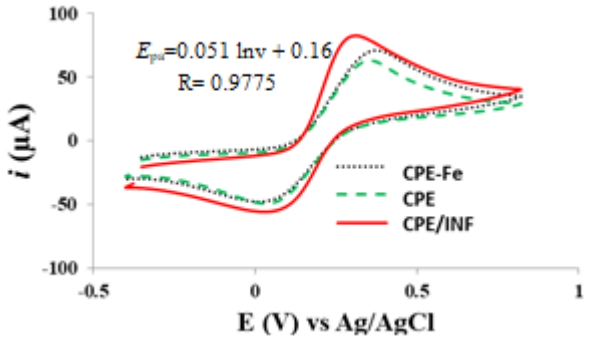

Figure 3. Electrochemical behavior of CPE-Fe, CPE, and CPE/INF in the presence of 5.0 mM of $Fe[(CN)_6]^{3-/4-}$ and 0.1 M KCl.

3.3. Electrochemical Behavior of IDA

Shows the IDA (1.0×10^5 M) electrochemical signal on the CF –CPE surface at pH = 6.0, varying from 0 to 50% of carbon fibers and iron oxide powder (Fe_3O_4 and Fe_2O_3) (Figure. 4). As CVs show, electrodes containing 1% iron oxide (Fe_3O_4 and Fe_2O_3) have the highest signal to IDA, whereas electrodes without CF (0%) do not have significant reactions to this analyzer concentration, proving the critical role of CF in CF –CPE electrodes. Other electrodes with higher CF percentages have lower electrochemical signals, which can contribute to lower iron oxide (Fe_3O_4 and Fe_2O_3) conductivity. Thus, the electrode with a 1% CF is chosen as the modified case.

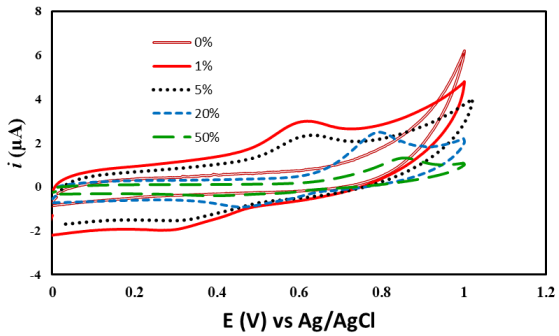

Figure 4. The electrochemical signal in pH=6.0 at the surface of CF-CPE with different iron oxide powders (Fe_3O_4 and Fe_2O_3): 0, 1, 5, 25, and 50%.

The cycle voltage of the bare and modified electrodes in IDA solution (5.0×10^{-6} M) was recorded in a 100 mV/ scan rate of pH=6.0 phosphate buffer (Figure 5).

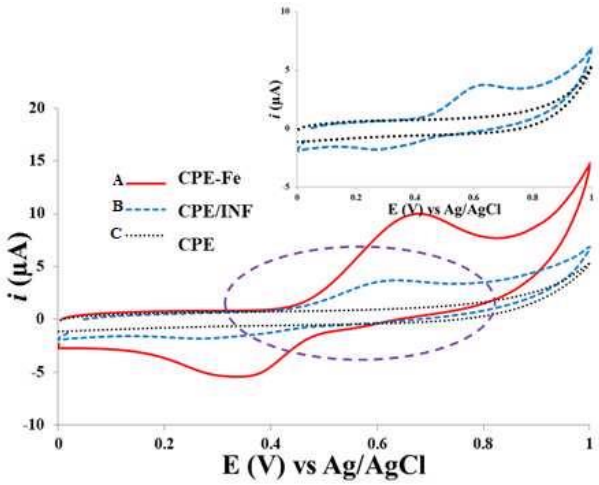

Figure 5. A) CPE-Fe, B) CF-CPE, and C) CPE 5 in 0.1 mol L-1 of phosphate buffer of pH 6, the scan rate is 100 mV s^{-1}.

The IDA does not show significant electrochemical signals on the surface of pure CPE, but CPE-Fe has visible quasi-reverse peaks of about 340 mV of ΔE. The IDA also has a reactive peak on the surface of the CF –CPE electrode, but with ΔE about 320 mV, the electrical current (signal) increases by more than 3.5 times, and the CPE/ towards the IDA is 320 mV, which indicates that the electron transfer reaction is not completely reversible. Some kinetic limitations or other factors may affect the relative magnitude of the oxidation and reduction peaks. In a quasi-reversible system, the Ipc/Ipa ratio can deviate from 1, with the exact value varying from the electron transfer kinetics, the scan rate, and other experimental

Volume 4, Number 2, December 2024, Page 55 - 66
e-ISSN: 2776-4508; p-ISSN: 2776-1711
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parameters. Generally, the Ipc/Ipa ratio is less than 1 in a quasi-reversible system, indicating that the reduction process is more complex than the oxidation process. Therefore, oxidation peak measurements were used to determine IDA. The higher performance of the CF–CPE electrode can be explained by two different roles of the INF composite: First, as shown in Figure. 3, the higher redox electrochemical current the composite in the CF–CPE electrode can be explained by the improved conductivity of the CF–CPE electrode. Second, if the electrochemical behavior of IDA on CPE, CPE- Fe, and CF –CPE proves that iron oxides (Fe_3O_4 and Fe_2O_3) can increase the electrochemical signal of IDA due to the high surface area and better conductivity of CF –CPE electrodes (as shown in the SEM experiment). Iron nanoparticles are generally not conductive materials and can obstruct further application in electrochemical sensors. Carbonization is a well-known method to increase the conductivity of composite containing metal oxides. The carbon fibers of the electric nozzle can increase the electrode conductivity here, thereby demonstrating the high electrochemical reaction of the CF –CPE electrode.

3.4. Potentiostat and Cyclic Voltammetry

Shows the CV of IDA (5.0×10^{-6} mol/ L^{-1}) at the pH range (2-9), which shows the behavior of IDA that depends on the pH (Figure. 5). The CV shows the increase in pH the voltage peak (Ep) moves to positive, and the graph of pH versus Ep (Figure. 5. B) gives a straight line with a slope of 60 mV/ pH, a typical electron one-proton conversion [38, 39].

This indicates that "C" represents the cyclic voltammogram (CV) of iminodiacetic acid (IDA) of pH= 6.0 PBS on the surface of the CF –CPE electrode at different scanning speeds (20 to 900 mVs^{-1}) (Figure. 6). As the figure shows, the redox current increases with the increase in scanning speed. However, at low scanning speeds, the anodic current disappears almost completely (Figure 6. D), but at high scanning speeds (Figure 6. E), a pair of peaks is distinguished. Cathodic products have sufficient time to undergo chemical reactions at low scan speeds, while oxidized IDA (IDAOx) has insufficient time to undergo chemical reactions at high scan speeds. By revising anodic potential to cathodic potential, related peaks appear. Ep and scanning rates are linearly connected (Figure 6. F), demonstrating that electro-directions are controlled under adsorption. Therefore, the data indicate that oxidation reactions have ECM mechanisms on the electrode surface and the adsorption processes. To calculate the apparent charge, transfer rate constant (Kapp), and charge transfer coefficient (CTC), the Lavrons theory (Eq) plots Epa (or EPC) to ln (v) (Figure 6. G): [27, 28].

$$E_{pa} = a + \frac{RT}{(1-\alpha)nF} \ln v \quad (1)$$

(Formula. 1)

$$log\ k_{app} = \alpha\ log(1-\alpha) + (1-\alpha) log\ \alpha - log\ \frac{RT}{nFv} - \frac{\alpha(1-\alpha)nF\Delta Ep}{2.3\ RT} \quad (2)$$

E_{pa} is the peak potential of the anodic and cathode. The calculated values of K_{app} are 0.7 and 1.4 $\times 10^{-2}$ s^{-1} (at 0.1 Vs^{-1}). Other reports in Figure 6. H illustrates and confirm the proposed electrochemical mechanism [39]. CV experiments have shown that anodic electrochemical reactions follow the EC mechanism. IDA first loses two electrodes at anodic power and forms active cations. This intermediate produces an anodic cation structure in chemical reactions that lose two H^+.

Specifically, the K_{app} (apparent rate constant) refers to a chemical reaction or process's observed or measured rate constant, which can be influenced by substrate concentration, pH, temperature, and other experimental conditions. In the logarithmic plot (log I - log α): The x-axis represents log α (the logarithm of the voltage). The y-axis represents log I (the logarithm of the current). The plot will be a straight line with a slope of n and a y-intercept of log k.

In the logarithmic plot, the dependence of I on α can be easily visualized and interpreted. The slope of the line represents the exponent n in the original I-α relationship, and the y-intercept represents the constant k.

Conducting proper experiments, particularly scan rate studies, you can determine the charge transfer coefficient (α) for the electrochemical reaction of IDA. Comparing the observed Ipa /Ipc ratios with previously reported data will confirm the quasi-reversible nature of the system and provide insight into the electron transfer kinetics.

Volume 4, Number 2, December 2024, Page 55 - 66
e-ISSN: 2776-4508; p-ISSN: 2776-1711
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As shown in Figure 6, the presence of anodic and cathodic maximum potentials in phosphate buffer pH 6 using two modified electrodes shows that both electrode materials and electrochemical systems contribute to observed behavior.

The anode and cathode peaks of modified electrodes' pH 6 phosphate buffer may overlap partially with the IDA peaks, causing potential interference. However, with appropriate calibration, peak separation technology (such as DPV), and electrode optimization, this interference can be reduced, and reliable IDA detection can be achieved.

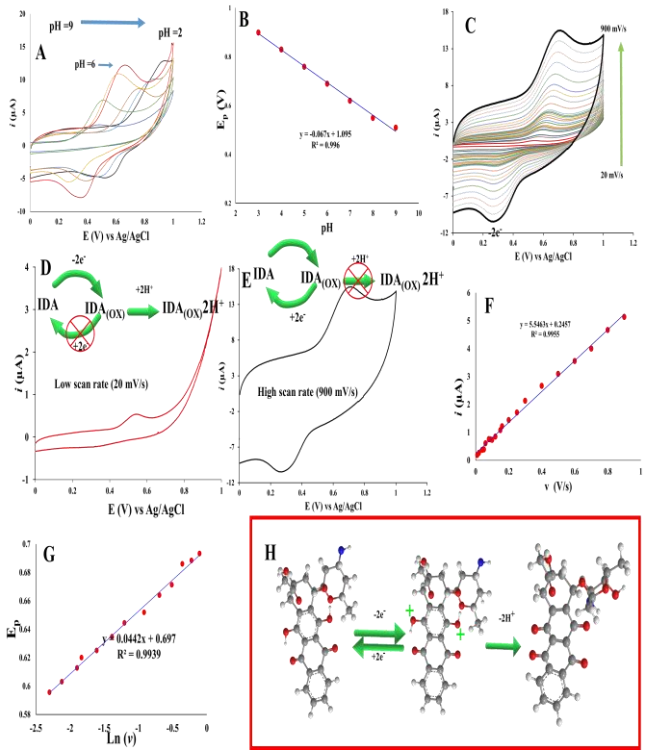

Figure 6. A) The CVs of 5.0 × 10^{-6} mol L^{-1} IDA at different pH (2-9), B) The plot of pH vs. the E_p, C) The CVs of 0.5 × 10^{-6} mol L^{-1} IDA in pH 6.0 PBS at on surface of CF –CPE electrode at different scan rates (20 to 900 mVs^{-1}), D&E are two selected CVs from Figure. 5. C at lower and higher scan rates with proposed reactions at each scan rate, F) The plot of E_p vs. scan rate, G) The plot of the E_{pa} against the ln (*v*), H) The proposed mechanism of electro-oxidation of IDA.

3.5. The quantitative measurement of IDA with CF- CPE electrode

Square wave voltage meters are a sensitive technique for measuring IDA quantitatively. As CV studies have shown, the adsorption process controls an electrochemical reaction, so the effects of the accumulation time of the analytical adsorption have been studied. The impact of accumulation time on signaling in the 1.90×10^{-5} M IDA was investigated after 10 to 600s. As shown in Figure. 7, the signal increases by increasing the time to 120s and then almost remains unchanged. Therefore, 120s has been selected as the optimal accumulation time.

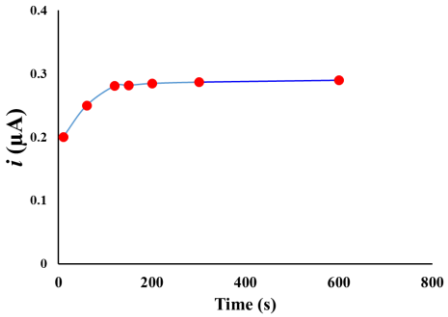

Figure 7. Accumulation time on the 1.90× 10-6 M IDA signal.

Lower detection limits are the lowest concentrations or signal levels that the analytical technology instrument can reliably measure or detect. A detection limit (LOD) is a more defined statistical parameter representing a low concentration or signal level detected with high confidence, usually 95 percent or higher. The main difference between the low detection limit and the LOD is that the low detection limit is practical and effective, while the LOD is derived and defined statistical parameters.

Suppose the lower limit of the detection range is 15.6 times greater than the LOD. In that case, this indicates that the analytical method or tool has a relatively lower limit of detection compared to the actual LOD. This may be due to various factors, including maintaining a higher signal-to-noise ratio for reliable measurements. 1) Limitations of measurement system or instrumentation. 2) Complexity of sample or analyte matrix. 3) Desire to achieve a wider dynamic range for the analytical method.

Volume 4, Number 2, December 2024, Page 55 - 66
e-ISSN: 2776-4508; p-ISSN: 2776-1711
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SWV was used at different analysis concentrations to determine the linear range and the analytical performance of CF- CPE electrodes (Figure 8. A). The CF- CPE electrodes have linear IDA correlation in concentrations ranging from 3.9×10^{-6} to 1.4×10^{-4} M and regression equations of Ip (A)= 0.0257 C_{IDA} (M) – 0.117 (Figure. 7. B), correlation coefficients $R^2 = 0.987$, and detection limits 2.5×10^{-7} M (based on S/ N=3) the reproducibility of CF- CPE electrodes were investigated by detecting IDA 2.0 $\times10^{-5}$ M on three different electrodes. Based on these data, the CF- CPE electrode's relative standard deviation (RSD %) is approximately 1.7%, which indicates our sensor's high precision and reproducibility. Furthermore, the sensor stability was monitored for 2 weeks (every day) at 2.0 $\times10^{-5}$ M IDA, and later, the electrochemical sensor retained 97% of the initial signal, demonstrating good storage stability. The effects of potential interferences such as glucose (50 µM), ascorbic acid (50 µM), doxorubicin (50 µM), epirubicin HCl (40 µM), and urine (0.1 mM) have an IDA value of 5.0×10^{-6}. IDA signal showed significant changes in the presence of drugs, indicating the sensor's selectivity. The ability of the sensor to accurately detect and measure the target analyte in the presence of other potentially interfering substances. The sensitivity of a sensor with high selectivity is lower due to the less important effects of the presence of other compounds. Thus, more reliable and precise measurements are performed to investigate the ability of electrodes to detect different concentrations of IDA in actual samples; the CF-CPE electrode was used to measure concentrations in serum, urine, and tablets. Under the optimal conditions (pH = 6.0, 120s accumulation time), analytical data were collected, and the results are shown in Table 1. As shown in Table 1, the sensor has 96.5 to 102.5% recovery and about 1 to 3 percent RSD, indicating the sensor's excellent practical application for IDA determination in actual samples.

In cancer patients, the level of IDA in serum and urine can be significantly increased, with 2-20 µmol/L or even higher for serum and urine from 2-50 µmol/L or higher depending on the type and it has cancer stage.

The increase in serum IDA is due to the rise in the metabolism and circulation of specific biomolecules, such as amino acids in cancer cells, which leads to the increase in the production and release of IDA in the bloodstream. Urinary IDA is due to increased production and excretion of IDA by cancer cells, as well as impaired kidney function, which can occur in some cancer patients. An increase in urine IDA levels has been observed in various types of cancer, including liver, kidney, bladder, and prostate cancer.

The increase of IDA concentration in the serum and urine of cancer patients is related to the change in the metabolism and physiology of cancer cells. IDA is a metabolic product of various processes, and its high levels in cancer patients may reflect increased activity and turnover of specific biomolecules associated with the disease. Moreover, kidney dysfunction in some cancer patients may also contribute to the accumulation of IDA in the body and increase its excretion through urine.

Other pH has also been tested, but according to studies and results, the IDA redox reaction is most efficient at pH = 6, with a clear peak and minimal interference. This slightly acidic pH helps maintain IDA structure integrity.

Table. 1. Determination of IDA in human serum, urine, and tablet samples with the proposed method.

Sample	Spiked amount (µM)	Founded amount (µM)	Recovery (%)	RSD (%)	Average ±S.D
Serum	10.0	9.65	96.5	3.0	53.075
Urine	10.0	10.25	102.5	2.5	56.375
	Reported amount (mg)	Founded amount (mg)	Recovery (%)	RSD (%)	Average ±S.D
Tablet	40.0	39.59	99.0	1.0	59.295

Iron oxide ceramic nanofibers, especially Fe_3O_4 (magnetite) and Fe_2O_3 (hemicellulose), together with polyether sulfate nanofibers (PES), have shown significant potential for chemical detection. Its ability to detect idarubicin, a chemical therapy agent, is due to its synergistic properties, high surface, adaptability, and enhanced chemical reactivity [36, 37].

Volume 4, Number 2, December 2024, Page 55 - 66
e-ISSN: 2776-4508; p-ISSN: 2776-1711
Publisher : Universitas Pakuan

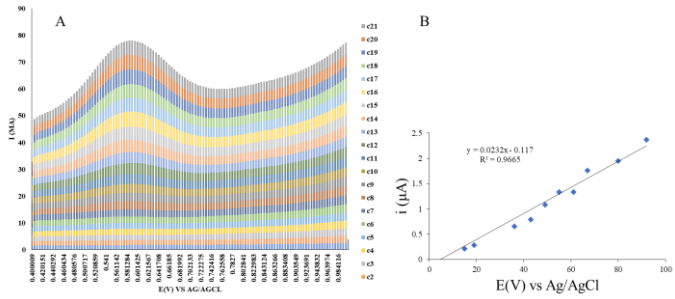

Figure 8. A) SWVs of the CF-CPE at different IDA concentrations (0, 2.5, 3.5, 5.0, 7.4, 9.8, 14.6, 19.2 28.3 37.0 45.5 69.0 83.3 96.8 112.0, 130.0 and 143 µM) B) the Calibration curve for the quantification of IDA.

The intrinsic properties of Fe_3O_4 and Fe_2O_3 nanofibers, including electronic conductivity and catalytic activity, enable the effective detection of idarubicin. PES is added to improve mechanical stability and provide a biocompatible platform for sensor performance [40].

Fe_3O_4 nanofiber has strong magnetic properties that can promote electron transmission processes and enhance detection signals [40, 41]. Fe_2O_3 nanofibers contribute to the interaction of oxidation-reduction with idarubicin molecules with their semiconducting behavior. PES is a support matrix that promotes efficient dispersion of iron oxide nanofibers and ensures consistent sensor performance [41].

The electrospinning technology used to manufacture these nanofibers guarantees a uniform morphology and high surface, a key factor in adequate chemical sensitivity [42].

These sensors provide a non-invasive, fast, and cost-effective method for monitoring the levels of idarubicin in clinical and pharmaceutical environments. The integration into portable devices improves the functionality of real-time drug surveillance [43]. SEM is crucial in analyzing the sensor's surface morphology, structure, and material distribution. These properties significantly impact the sensor's performance, including sensitivity and selectivity [44]. Quantitative measurement of IDA with a CPE or CF-CPE electrode provides a rapid and cost-effective way to assess IDA concentrations in various samples, including pharmaceutical formulations, biological fluids, and environmental samples [45].

CPE electrodes have graphite-packing layers, while CPE-Fe electrodes do not show significant surface structure changes. The electrolytes containing 1% iron oxide (Fe_3O_4 and Fe_2O_3) CF-CPE have the highest IDA signal, and the electrolytes without CF (0%) do not show a significant reaction to this analysis concentration. Other electrodes with higher percentages of CF have lower electrical chemical signals that may contribute to the lower conductivity of iron oxide (Fe_3O_4 and Fe_2O_3) [46]. When the electrochemical behavior of the IDA on the pure CPE surface is established, iron oxides (Fe_3O_4 and Fe_2O_3) can improve the electrochemical signals of the IDA due to the high surface and better conductivity of the CF-CPE electrode. Redox current increases with the speed of scanning. Ep and scanning rates are linearly linked, indicating the electrical direction of the absorption process. Absorption processes control electrochemical reactions, and the effects of absorption accumulation time are studied analytically. The signal increases with the increase in time to 120 seconds and then remains almost unchanged. The CF-CPE electrodes' relative standard deviation (RSD) is about 1.7%, indicating high accuracy and reproducibility. To detect IDA concentrations in actual samples, CF-CPE electrodes were used to measure serum, urine, and tablet concentrations [47, 48].

Hybrid Fe_3O_4/Fe_2O_3-PES (CF-CPE) nanofibers are more sensitive, have faster response time, and are more stable than conventional chemical sensors. The high surface-volume ratio of the nanofiber guarantees greater interaction with the idarubicin molecule, and the PES chemical stability extends the sensor's lifetime. Thus, this is a robust and innovative chemical sensing platform.

4. CONCLUSION

The sensors developed in this study demonstrate significant promise in the electrochemical detection of idarubicin, particularly in biological samples such as blood serum and urine from leukemia patients. The integration of iron oxide ceramic nanofibers (Fe_3O_4 and Fe_2O_3) and polyether sulfone (PES) nanofibers notably enhanced the electrocatalytic oxidation process, resulting in improved sensitivity, selectivity, and quantification accuracy for idarubicin detection. These modifications enable the sensors to offer higher current responses, making them an effective tool for measuring low drug concentrations in complex biological matrices.

Volume 4, Number 2, December 2024, Page 55 - 66
e-ISSN: 2776-4508; p-ISSN: 2776-1711
Publisher : Universitas Pakuan

The proposed sensors' cost-effective and more straightforward fabrication process further enhances their appeal, positioning them as a practical alternative to more expensive and intricate methods such as HPLC and LC-MS/MS. Moreover, the higher surface-to-volume ratio of the electrodes contributes to better electron transfer and quicker responses, addressing one of the key challenges in electrochemical analysis: increasing sensitivity while maintaining practical usability in a clinical setting.

From a clinical perspective, these sensors present a promising real-time diagnostic tool for personalized chemotherapy. They enable clinicians to accurately monitor and adjust idarubicin levels in patients to optimize therapeutic outcomes. With further advancements and potential integration into point-of-care testing devices, this approach could become invaluable for optimizing treatment regimens and minimizing adverse side effects in leukemia and liver cancer patients.

Future developments may improve sensor stability and reduce interference from complex biological components such as proteins and other drugs. Further optimization of the nanofiber modifications and electrode materials may also expand the applicability of this sensor to different chemotherapy agents, paving the way for broader clinical adoption. Research into multiplexed sensors for simultaneous drug monitoring could provide clinicians with the tools to manage combination chemotherapy more effectively.

This expanded conclusion emphasizes the study's positive findings and aligns them with real-world clinical applications. It also provides insights into future research directions that could enhance the sensor’s effectiveness and applicability.

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Volume 4, Number 2, December 2024, Page 55 - 66
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