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Analytical Determination of Paracetamol in Human Blood by Improving the Catalytic Effect of a Clay-Based Electrode

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Abstract- In this work, we investigated the applicability of the clay-modified carbon paste electrode (CPE-clay) in the detection of paracetamol (PAR), using two electrochemical methods: differential pulse voltammetry (DPV) and cyclic voltammetry (CV) in the range between 20 and 400 mV in a Britton Robinson buffer solution (pH 7). The voltammetric technical behavior of PAR is studied where a sensitive anodic and cathodic peak has been appeared at about 0.4 V and 0.2 V (vs. Ag/AgCl/3 M KCl) successively. These peaks were recorded from the reversible redox of PAR at the CPE-clay surface. The proposed technical (DPV, CV) exhibits remarkably an electro-catalytic success for PAR redox. The current response of the catalytic peaks obtained by DPV depended linearly on the concentration of PAR in the range between 1.0×10^{-6} and 1.0×10^{-3} mol L^{-1} with a detection limit of 5.27×10^{-9} mol L^{-1}. Subsequently, the relative standard deviation (RSD) at 1.0×10^{-4} mol L^{-1} PAR concentration was 3.8% for nine replicates. The proposed electrode has been successfully used for PAR detection in the human blood sample.

Keywords- Paracetamol; Clay; Human blood; Electroanalysis; Electrode

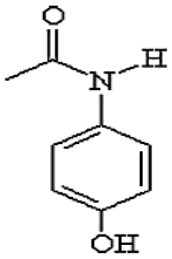
1. INTRODUCTION

A large number of PAR (scheme 1) is a strongly employed drug in the world. It was primarily employed in medicine in 1893. Nevertheless, it was primarily discovered as an antipyretic and analgesic in the 19th century. It is non-carcinogenic and is a powerful aspirin substitute for aspirin-sensitive patients [1]. Unlike aspirin, Nevertheless, PAR anti-inflammatory activity is considered feeble and is, therefore, not routinely employed in inflammatory. However, it is employed to diminish fever cough, and cold [2-4]. It is very useful in the treatment of osteoporosis [5] and it is sometimes employed for the treatment of cancer pain. New research proposes that PAR helps to protect against changes causing cardiovascular disease [6]. It also remains an analgesic preferably for people with asthma [7]. There is too certain evidence to propose that PAR proposes some protection against ovarian cancer [8].

Overdoses of PAR produce harmful metabolite accumulation that induces acute hepatic necrosis, resulting in mortality in humans [9]. Thus, it is important to have an analysis technique of PAR in pharmaceutical products. Different analytical methods such as quantitative titrimetry (Volumetry, Gravimetry, Coulometry) [10], spectrophotometry [11], spectrofluorometry [12], voltammetry [13], HPLC [14], TLC [15], colorimetry [16], FTIS [17], and several other techniques are suggested for the electroanalysis of the PAR. Shuyan et al. sufficiently describe the simple and rapid electrochemical techniques by the glassy carbon electrode for the detection of paracetamol in 1.0 M HCl [18]. Voltammetric analysis of PAR at electrochemically modified electrodes [19,20], boron-doped diamond film electrode [21-23], and other electrodes [24,25] also have an analytical determination by the modified electrodes. Nevertheless, the lower detection limit of 1.2 M was cited at the electrode electrochemically modified with Nafion pyrochlore oxide. Because of their new magnetic, optical, catalytic, and electronic properties gold nanoparticles are the more intensively suggested [26]. It was cited that the size of gold nanoparticles permits the conductive materials to come in the proximity of the adequate method furnishing bio-electrocatalytic activity which can be used in the preparation of biosensors [27]. It too furnishes some necessary functions for electrochemical analysis [28]. Modified electrodes by gold nanoparticles are utilized increasingly in several electroanalysis applications because they can ameliorate the conductivity of the electrode and favor the electron transfer, therefore, increasing the analytical sensitivity and selectivity. Usually, particular binding molecules are utilized to assembly gold nanoparticles at the electrode surfaces [29,30] nevertheless this may change the conducting characteristics of the modified electrode [31-33]. Lately, Oyama et al. [34] have shown a novel method to make a gold nanoparticle fixed indium tin oxide electrode without using particular binding molecules.

In this work, we have studied the electrocatalytic studies of PAR redox and their sensitive detection at CPE-clay in the Britton Robinson solution buffer (pH 7). Its redox performance is compared with the carbon paste electrode. The success of the CPE-clay surface toward the electrochemical analysis of PAR is evaluated by CV and DPV techniques. So, the electrode has

been used to the sensitive electroanalysis of trace amounts of PAR in human blood based on its redox using CV.



Scheme 1. Structure of paracetamol

2. EXPERIMENTAL SECTION

2.1. Chemicals and reagents

PAR was bought from Sigma-Aldrich. Britton Robinson buffer solution (pH 7) was utilized as the supporting electrolyte and has been prepared by acetic acid, boric acid, and phosphoric acid, which were too from Sigma Aldrich. The pH has been adjusted by sulfuric acid or potassium hydroxide. All aqueous solutions utilized were prepared by distilled water. The natural red clay used comes from the region of Beni Mellal (Morocco). All experiments were realized at room temperature.

2.2. Apparatus

The electro-catalytic activity of the CPE-clay surface toward the redox of PAR was obtained by the CV and DPV connected to a computer for control, data acquisition, and storage. The software used was the Voltalab Potentiostat PGP100 fitted with the voltalab master 4 software. The paracetamol reaction was carried out in an analytical cell containing three electrodes. Ag/AgCl/KCl (3 M) was used as a reference electrode, a platinum wire as a counter electrode, and CPE-clay as a working electrode.

2.3 Electrodes preparation

The modified carbon paste electrode was prepared by mixing the clay with graphite powder in a small mortar until a smooth paste was obtained. Subsequently, the paste is manually inserted into the cylindrical cavity of the electrode body.

2.4 Procedure

Several buffer solutions were tested such as acetate buffer, phosphate buffer, and Britton Robinson buffer. The better electroanalysis response was recorded in the Britton Robinson buffer (pH 7). The working method consists of measuring the responses of the electroanalysis

on the CPE -clay for a fixed quantity of PAR. A known concentration of PAR solution has been prepared in 0.1 mol L^{-1} Britton Robinson buffer solution (pH 7) and 20 mL of the prepared solution has been transferred to the electroanalysis cell. The DPV and CV have been obtained between -0.4 and 1 V at 100 mV s^{-1}. Optimal conditions were determined by measuring the currents of the peaks for all the parameters.

3. RESULTS AND DISCUSSION

3.1 Electroanalytical behavior of PAR

The electroanalysis response of the CPE-clay surface toward PAR redox has been studied by its CV at CPE and CPE-clay (Figure 1A) in BR buffer (pH 7) containing 1.0×10^{-3} mol L^{-1} of PAR in the range between -0.4 and 1 V at a scanning rate of 100 mV s^{-1}. The anodic and cathodic peaks have appeared at Epa = 0.4 V and Epc = 0.2 V respectively. CPE-clay has been characterized by excellent electrocatalytic towards PAR than CPE. The sensitivity of this electrode was confirmed using the DPV method for the PAR oxidation peak (Figure 1B). According to this study, two protons have been transferred in the reaction. Paracetamol redox is a two-electron and two-proton mechanism in Scheme 2 given below [35,36].

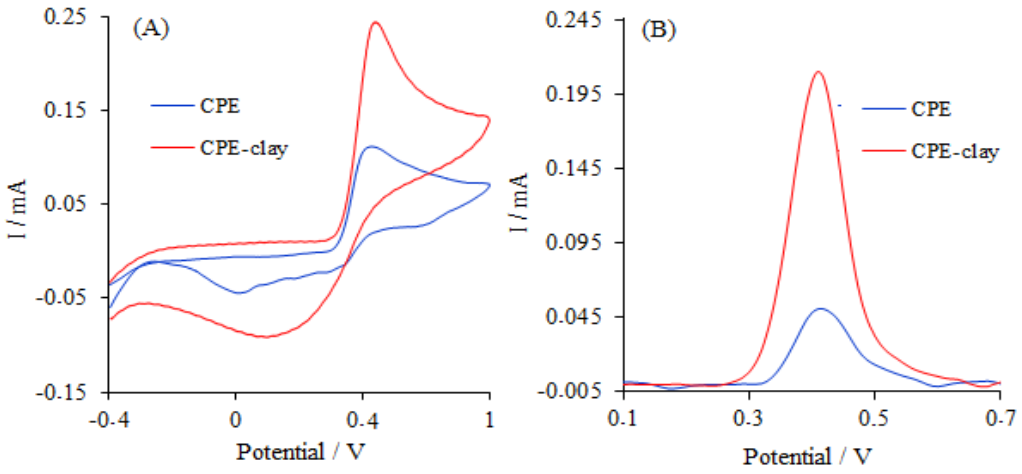
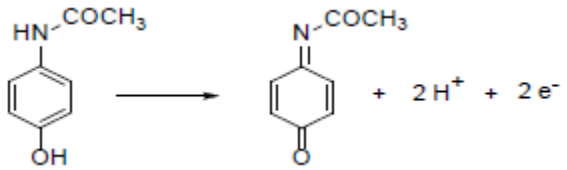


Fig. 1. (A) CV and (B) DPV of 10^{-3} mol L^{-1} PAR for CPE and CPE-clay in 10^{-1} mol L^{-1} BR buffer (pH 7).



Paracetamol N-acetyl-p-quinone imine

Scheme 2. Electrochemical redox of PAR at CPE-clay.

3.2. Effect of accumulation time and % clay

More to its electroanalytic properties, the CPE-clay indicates a good capacity for the detection of PAR. This electroanalysis investigate was perform by DPV, in BR buffer solution (pH 7) containing 1.0×10^{-3} mol L^{-1} of PAR. The effect of the accumulation time on the DPV measurements was illustrated (Figure 2A). Figure 2B shows a decrease in the anodic peak current according to the accumulation time after the 20 seconds. Then a 20 second was utilized in all analyses. The increasing of the clay loading between 3 to 50 % by weight of carbon influences the PAR determination at the CPE-clay represented by the DPV in Figure 3A. The anodic peak current of PAR increases with the increases in the clay until 50 % (Figure 3B). So, 50 % of the ratio by weight was used in all work.

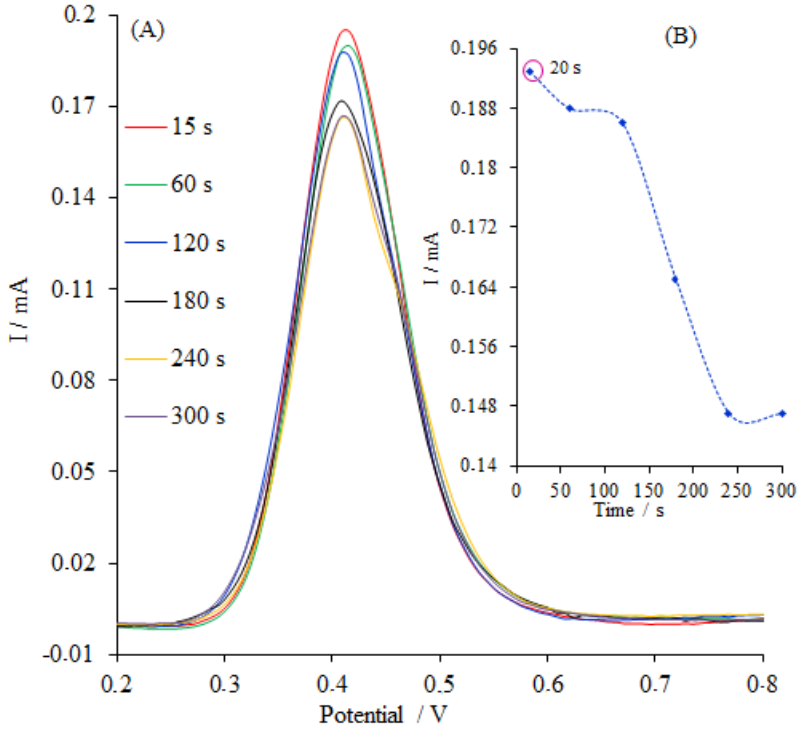


Fig. 2. Influence of the accumulation time recorded by the DPV method, 10^{-3} mol L^{-1} PAR in BR buffer solution (pH 7) at CPE-clay

3.3. Effect of pH

The electroanalysis behavior of the PAR has been studied at different pH values using CV. Figure 4A presents the CV of the CPE-clay in solutions at different pH values ranging between 2 and 10. The good electrochemical responses were recorded at pH 7 on the CPE-clay toward PAR redox (Figure 4B). It appears that the peak potentials are shifted to negative values with the increase of pH values, involving those protons have been implied in the electrode process. An excellent linear relationship has been got between the pH values and peak potential (Ep) (Figure 4C).

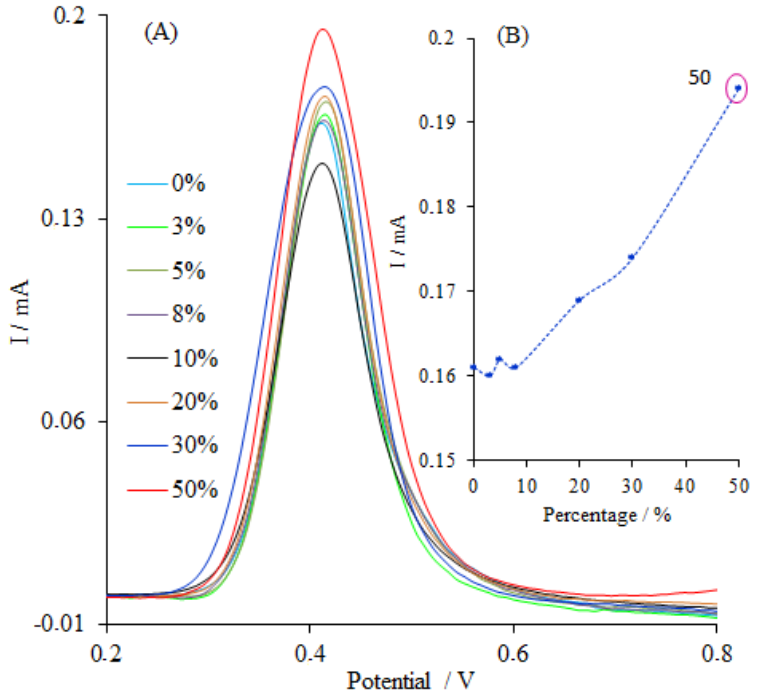


Fig. 3. Effect of the % clay recorded by the DPV, 1.0×10^{-3} mol L^{-1} PAR in BR buffer solution (pH 7) at CPE-clay

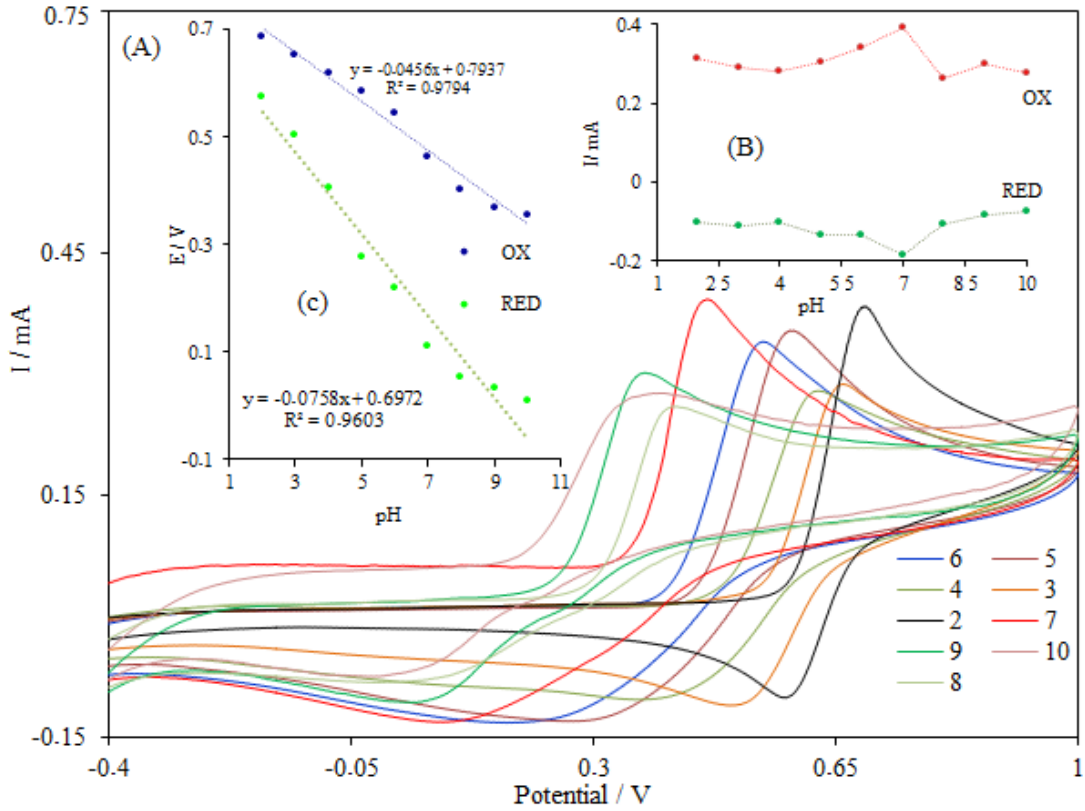


Fig. 4. (A) CV (at 100 mV s^{-1}) of 10^{-3} mol L^{-1} PAR at different pH; (B) plot of I_p versus pH; (C) plot of E_p versus pH

3.4. Catalytic study of CPE-clay on PAR redox

3.4.1. Effect of scanning rate

The scan rate effect on the redox peak current of PAR has been investigated at the CPE-clay surface under the concentration of 10^{-3} mol L^{-1} PAR in 0.1 M BR buffer solution (pH 7). Peak PAR currents increase with increasing slew rate (Figure 5A). The relationship between anode peak current and slew rate (20 and 400 mV s^{-1}) was linear with a correlation coefficient of 0.9894 (Figure 5B). This indicates that the kinetics of the oxidation reaction of paracetamol is controlled by adsorption because the current is right speed (R^2= 0.9894). The electrochemical redox of PAR at the CPE-clay surface has been reversible. The anodic peak potentials shifted toward the positive values with the logarithm of the scan rate (Figure 5D).

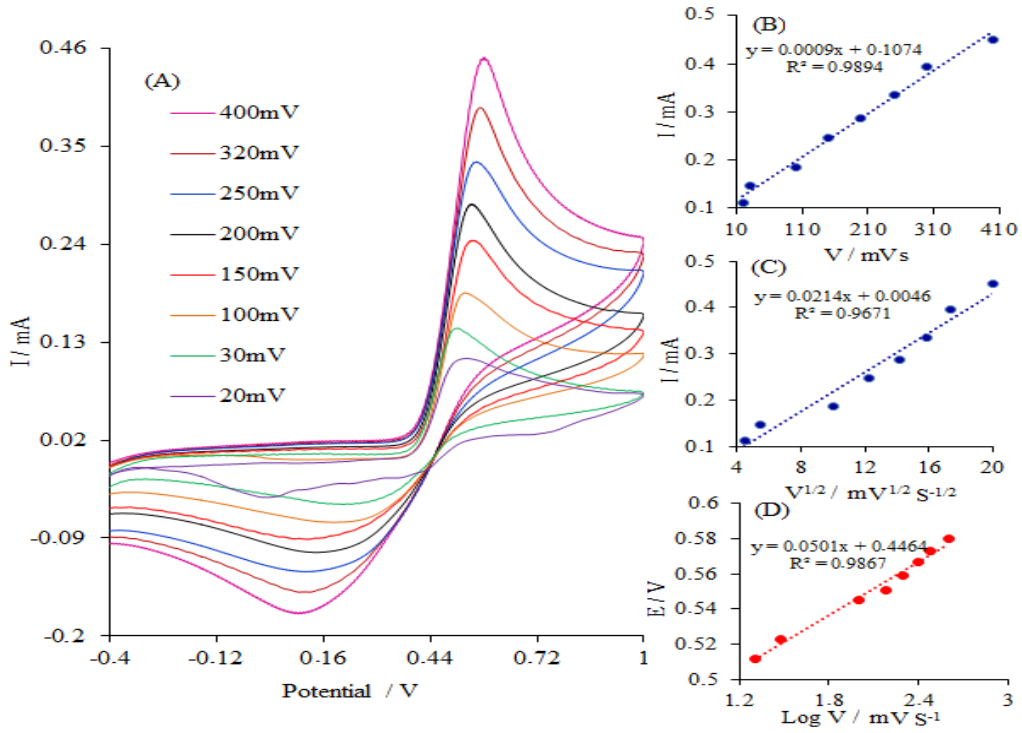


Fig. 5. (A) CVs at different scan rates of 10^{-3} mol L^{-1} PAR in 0.1 M BR buffer (pH 7); (B) variations of Ip with the V; (C) variations of Ip with the $V^{1/2}$; (D) variations of Ep with Log V.

3.4.2. Calibration curve

Before determining the calibration curve, we optimized the electrochemical parameters (pulse height, pulse width, amplitude) affecting the detection of PAR by CPE-clay using the DPV. The results obtained show that the good responses were recorded at 160 mV for the pulse height, 120 ms for the pulse width, and 20 mV for the amplitude, respectively. The calibration curve was obtained under optimal experimental conditions (160 mV, 120 ms, 20 mV). Figure 6A shows the DPV voltammograms obtained on the CPE-clay surface in the range from 1.0×10^{-6} to 1.0×10^{-3} mol L^{-1} of PAR. The intensity of the anode current increases with the concentration of PAR, we have divided the variation of the concentration current into two

curves: the part of low concentrations with a correlation coefficient of (R^2 = 0.8727) and the part of large concentrations with a correlation coefficient of (R^2 = 0.9927) (Figure 6B). The detection limit (DL) and quantification limit (QL) were calculated on the oxidation peak by the following equations: DL = 3 s/m, QL = 10 s /m (s: Standard deviation of the peak currents nine runs; m: Slope of the calibration curve), This is the minimum value detected by the electrochemical method. The DL and QL were calculated as 5.27×10^{-9} mol L^{-1} and 1.75×10^{-8} mol L^{-1} respectively. The RSD for nine measurements has been calculated as 3.8 % for the PAR concentration of 1.0×10^{-4} mol L^{-1}. The DL calculated by CPE-clay is compared by other electrodes (Table 1) [37-46].

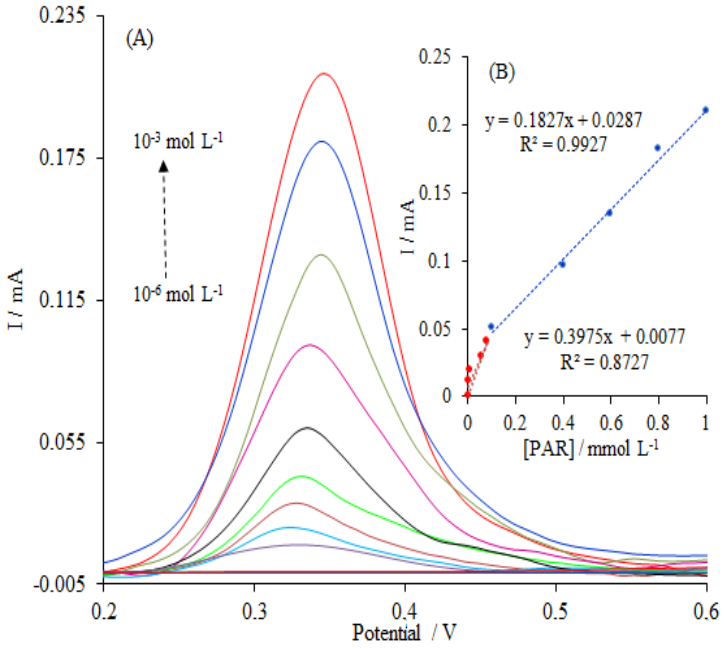


Fig. 6. (A) DPVs of PAR in 0.1 M BR (pH 7) 1.0×10^{-3}; 8.0×10^{-4}; 6.0×10^{-4}; 4.0×10^{-4}; 1.0×10^{-4}; 8.0×10^{-5}; 6.0×10^{-5}; 4.0×10^{-5}; 1.0×10^{-5}; 8.0×10^{-6}; 6.0×10^{-6}; 4.0×10^{-6}, 2.0×10^{-6} and 1.0×10^{-6} mol L^{-1}. (B) plots of peak current versus PAR concentration

3.4.3. DPV measurements of PAR in human blood samples

In order to determinate the analytical application of the CPE-clay, it has been utilized to determine PAR in human blood samples.

Human blood was prepared by adding acetic acid, boric acid and phosphoric acid to 20 ml of human blood.

The proposed technique has been used to analyze human blood samples contaminated with PAR at different concentrations. The oxidation peak of PAR has been well displayed. The linear calibration curve of PAR has been obtained in the concentration from 1.0×10^{-6} mol L^{-1} to 1.0×10^{-3} mol L^{-1} for human blood samples (Figure 7A). The coefficient of correlation of the curve has been (R^2 = 0.9908) (Figure 7B). The DL was found to be 8.29×10^{-9} mol L^{-1} with RSD of 3.07%.

Table 1. Comparison of CPE-clay results with different electrodes used in the detection paracetamol

Modified electrode	Analytical method	Detection limit	Ep_a (V)	pH	References
An indium tin oxide electrode modified by nanogold	DPV	1.8×10^{-7} mol L^{-1} 10^{-5} to 10^{-4} mol L^{-1}	0.11	7.2	[37]
Modified graphene glassy carbon electrodes	CV	3.2×10^{-8} mol L^{-1} 10^{-8} to 10^{-3} mol L^{-1}	0.368	9.3	[38]
MgB_2 microparticles modified glassy carbon electrode	CV	3×10^{-7} mol L^{-1} 10^{-7} to 10^{-3} mol L^{-1}	0.6	6	[39]
Nafion/TiO_2–graphene modified glassy carbon electrode	CV	2.1×10^{-7} mol L^{-1} 10^{-7} to 10^{-4} mol L^{-1}	0.575	7	[40]
Glassy carbon electrode	DPV	3.69×10^{-7} mol L^{-1} 10^{-6} to 10^{-4} mol L^{-1}	0.6	4.51	[41]
Boron-doped diamond electrode	DPV	4.9×10^{-7} mol L^{-1} 10^{-6} to 510^{-4} mol L^{-1}	0.8	4.5	[42]
Aluminum electrode modified with a thin layer of palladium	CV	5×10^{-5} mol L^{-1} 10^{-5} to 10^{-3} mol L^{-1}	0.6	6	[43]
Carbon paste electrode modified by the aluminum	CV	8.28×10^{-9} mol L^{-1} 6×10^{-5} to 8×10^{-4} mol L^{-1}	0.25	7	[44]
Carbon Paste Electrode Modified by Zinc	CV	7.52×10^{-8} mol L^{-1} 6×10^{-5} to 7×10^{-4} mol L^{-1}	0.35	12	[45]
Carbon Paste Electrode Modified with Heavy Metals	CV	10^{-9} mol L^{-1} 6×10^{-5} to 8×10^{-4} mol L^{-1}	0.27	12	[46]
CPE-clay	DPV	5.27×10^{-9} mol L^{-1} 10^{-6} to 10^{-3} mol L^{-1}	0.4	7	Present work

3.4.4. Effect of interferences

In order to determine the effect of different species with PAR on the CPE-clay response, a study implying these compounds has been performed. The selectivity of the studied detector has been investigated in electrolytic solution containing 1.0×10^{-4} mol L^{-1} of PAR add with resorcinol (RSC) (5.0×10^{-4} mol L^{-1}) and salicylic acid (As) (10^{-3} mol L^{-1}). The DPV measurements were studied in order to determine the effect of the interfering compounds on the intensity of the PAR oxidation current (Figure 8). The results recorded indicate that the presence of interfering compounds in solution containing PAR has no effect on the oxidation peak current.

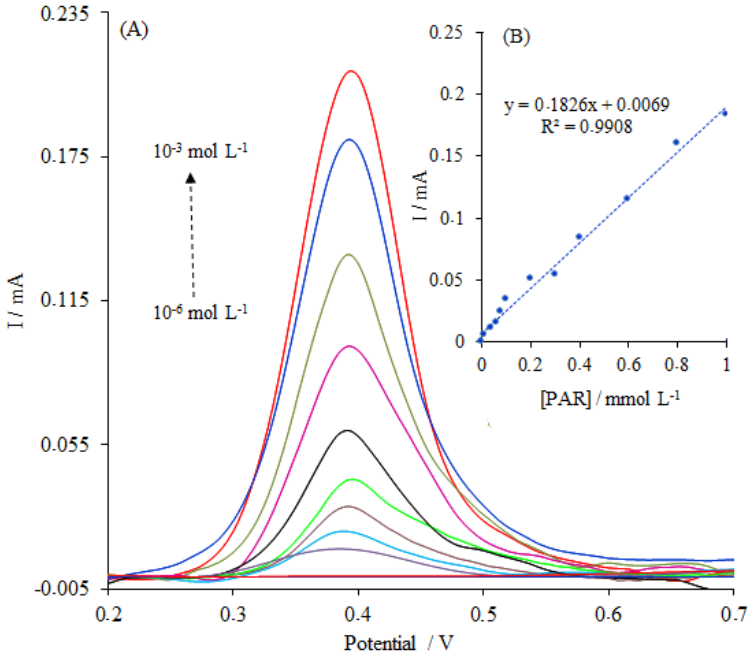


Fig. 7. (A) DPV of PAR from 10^{-6} to 10^{-3} mol L^{-1} in human blood samples under optimized conditions, (B) plot of peak current versus PAR concentration

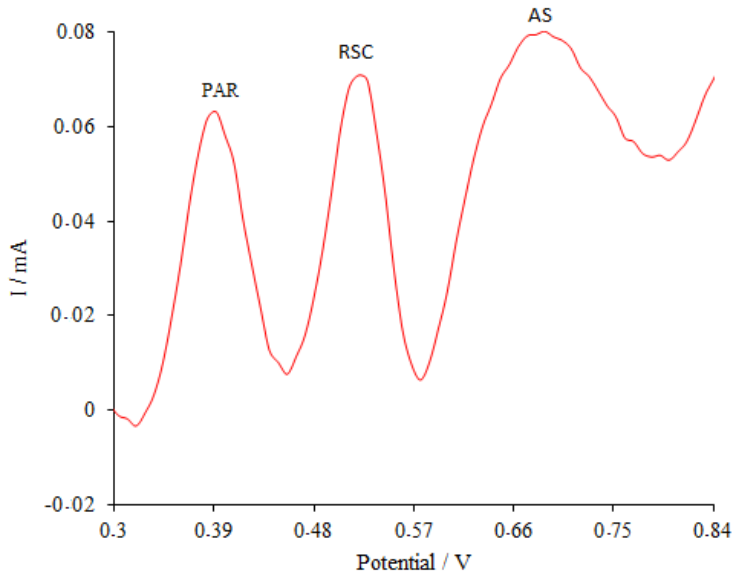


Fig. 8. DPV of a mixture of molecules containing paracetamol (PAR), resorcinol (RSC), Salicylic acid (As)

4. CONCLUSION

The CPE-clay has been used to detect PAR in BR buffer solution (pH 7). The electrochemical reaction of PAR has been followed using CV and DPV. The present study has shown that CPE clay exhibits excellent electro-catalytic activity with respect to PAR redox. DPV measurements show a linear relationship in the range of 10^{-6} to 10^{-3} mol L^{-1} mol L^{-1} and

DL of 5.27×10^{-9} mol L^{-1} for PAR oxidation. Finally, the clay-modified carbon paste electrode has been successfully applied for the electroanalysis of PAR in human blood samples. The simplicity of preparation, reproducibility, repeatability, low cost, and low limit of detection are the important advantages of CPE-clay.

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