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ELECTROCHEMICAL STUDIES AND CYCLIC VOLTAMMETRY OF PARACETAMOL AT CLAY MODIFIED CARBON PASTE ELECTRODE

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Abstract: A Cyclic voltammetry (VC) method for the determination of trace amounts of paracetamol at carbon paste electrode modified with Clay (Clay-CPE) is proposed. The results showed that the Clay-CPE exhibited excellent electro catalytic activity to paracetamol. A quasi-reversible redox process of paracetamol at the modified electrode was obtained. The concentration of paracetamol and measuring solution pH was investigated. This electrochemical sensor shows an excellent performance for detecting paracetamol. The sensor was successfully applied to the determination of paracetamol in a real sample tablets with satisfactory results.
Keywords: Modified electrode; Cyclic voltammetry; Clay; Paracetamol.

INTRODUCTION

Paracetamol (I, N-acetyl-p-aminophenol, acetaminophen) is a long-established and one of the most extensively employed "over the counter" drugs in the world. It was first used in medicine by Von Mering in 1893. However, it was first discovered to have both analgesic and antipyretic properties in the late 19th century. It is noncarcinogenic and an effective substitute to aspirin for patients with sensitivity to aspirin [1]. Unlike aspirin, however, paracetamol s anti-inflammatory activity is considered weak and is, thus, not routinely used in inflammatory conditions such as rheumatoid arthritis. Nevertheless, it is used to reduce fever cough and cold, and reduce mild to moderate pain, including instances of tension headache, migraine headache, muscular aches, chronic pain, neuralgia, backache, joint pain, general pain and toothache [2–4]. It is also useful in osteoarthritis therapy [5] and it is sometimes used for management of cancer pain. Recent research suggests that paracetamol may help to protect from changes leading to hardening of arteries that cause cardiovascular disease [6]. It also remains the analgesic of choice for people with asthma [7]. There is also some evidence to suggest that paracetamol may offer some protection against ovarian

cancer [8]. Paracetamol shows no propensity to be addictive, even in people who use it frequently. When used in proper therapeutic dose, paracetamol is readily metabolized.

Overdoses of paracetamol produce toxic metabolite accumulation that causes acute hepatic necrosis, inducing morbidity and mortality in humans [9]. Thus, it is very important to have an analytical technique for the determination of paracetamol in pharmaceutical preparations.

Several analytical techniques such as titrimetry [10], spectrophotometry [11], spectrofluorometry [12], voltammetry [13], HPLC [14], TLC [15], colorimetry [16], Fourier transform infra red spectrometry [17], and many other methods are proposed for the determination of paracetamol. Since voltammetric techniques are more selective, less costly and less time-consuming, they are widely used for the determination of paracetamol in pharmaceutical preparations. Shuyan et al. described a relatively simple and rapid electrochemical method by cyclic voltammetry using glassy carbon electrode for the detection of paracetamol in 1.0 M HCl solution [18]. Voltammetric determination of paracetamol at chemically modified electrodes [19,20], boron doped diamond film electrode [21] and at other electrodes [22–25] have also attracted attention, however, the lowest detection limit of 1.2 lMis reported at nafion/ruthenium oxide pyrochlore chemically modified electrode. Owing to their novel optical, electronic, magnetic and catalytic properties gold nanoparticles are one of the most intensively studied and one of the most popular materials to be assembled on electrodes [26]. It has been reported that the small size of gold nanoparticles allow the conductive materials to come into the vicinity of the active process providing bioelectrocatalytic activity that can be utilized in the construction of biosensors [27]. It also provides some important functions for electroanalysis [28,33]. Gold nanoparticles-modified electrodes are used increasingly in many electrochemical applications since they have the ability to enhance the electrode conductivity and facilitate the electron transfer, thus, improving the analytical selectivity and sensitivity. Normally peculiar binding molecules are used to assemble gold nanoparticles on the electrode surfaces [29,30]

but this may alter the conducting properties of the modified electrode [31]. Recently, Oyama et al. [32] have presented a new method to fabricate a gold nanoparticles attached indium tin oxide (Au/ITO) electrode without using peculiar binding molecules. The present work reports the differential pulse voltammetric determination of paracetamol at a physiological pH of 7 using clay modified carbon paste electrode. The modified electrode shows a strong catalytic function towards the oxidation of paracetamol.

EXPERIMENTAL

Apparatus and software

Voltammetric experiments were performed using a voltalab potentiostat (model PGSTAT 100, Eco Chemie B.V., Utrecht, The Netherlands) driven by the general purpose electrochemical systems data processing software (voltalab master 4 software) run under windows 2007. The three electrode system consisted of a chemically modified carbon paste electrode as the working electrode a saturated calomel electrode (SCE) serving as reference electrode, and platinum as an auxiliary electrode.

Electrodes

Modified electrodes were prepared by mixing a carbon powder and the desired weight of clay. The body of the working electrode for voltammetric experiments was a PTFE cylinder that was tightly packed with carbon paste. The geometric area of this electrode was 0.1256cm2. Electrical contact was made at the back by means of a bare carbon.

Procedure

The initial working procedure consisted of measuring the electrochemical response at Clay-CPE at a fixed concentration of paracetamol. Standard solution of paracetamol was added into the electrochemical cell containing 100 mL of supporting electrolyte.

The mixture solution was kept for 20 s at open circuit and deoxygenated by bubbling pure nitrogen gas prior to each electrochemical measurement. The cyclic voltammetry was recorded in the range from -0,7 V to 1V. Optimum conditions were established by measuring the peak currents in dependence on all parameters. All experiments were carried out under ambient temperature.

RESULTS AND DISCUSSION

Surface characteristics

The morphology of the electrode surface of Clay was observed by scanning electron microscopy (Figure 1).

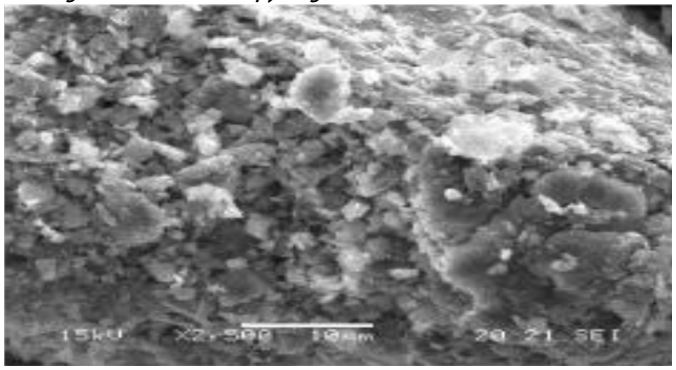


***Figure 1**: Scanning electron micrograph of Clay paste electrode.*

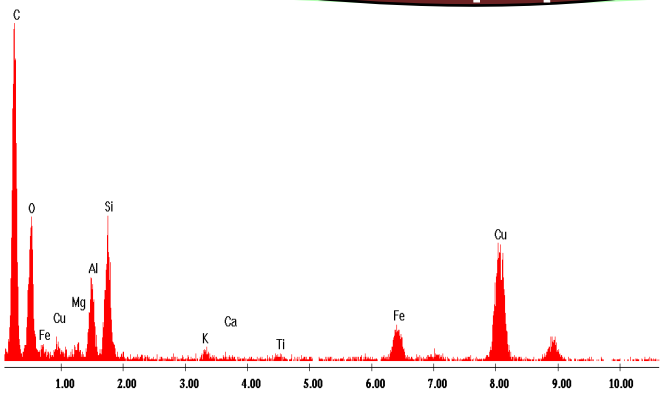


***Figure 2:** Chemical composition treated clay.*

We find that the matrix is formed by compact particles fractions between 1 and 15 µm. Clay treaty has the following chemical composition given by transmission electron microscopy (TEM): O (22%), Mg (5.4%), Al (22.4%), K (2.7%), Ca (1%), Ti (1.8%) Fe (17.1%), Si (27.8%) and more metals order ppm (Figure 2). An examination of clay modified carbon paste electrode indicates some kind of agglomeration.

Electrochemical behavior of Clay-CPE

Figure 3 shows a cyclic voltammograms (CV) in the potential range -0.7 V to 1 V recorded, respectively, for carbon paste and clay modified carbon paste electrode at 100mV.s $^{-1}$. The voltammograms take different forms. No peak is observed in the case of Clay-CPE, it is recognized that carbon surface was effectively modified by clay.

Figure 4 shows, paracetamol exhibits a pair of redox waves on the Clay-CPE with Epa (anodic peak potential)=0.5V and Epc (cathodic peak potential)=0.15V.

Scheme shows the paracetamol undergone oxidation and reduction.

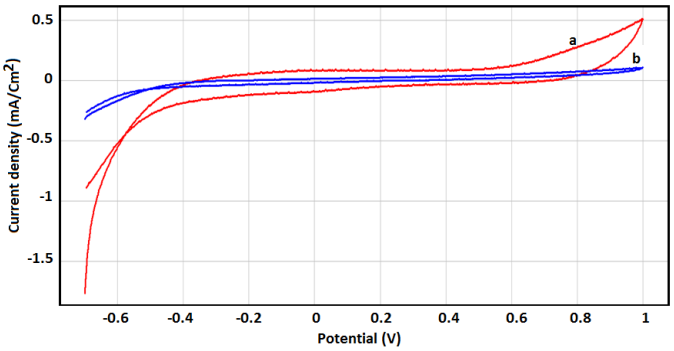


***Figure 3**: Cyclic voltammograms recorded for CPE (a) and bare Clay-CPE (b), in 0.1 M K_2SO_4 at 100 mV/s.*

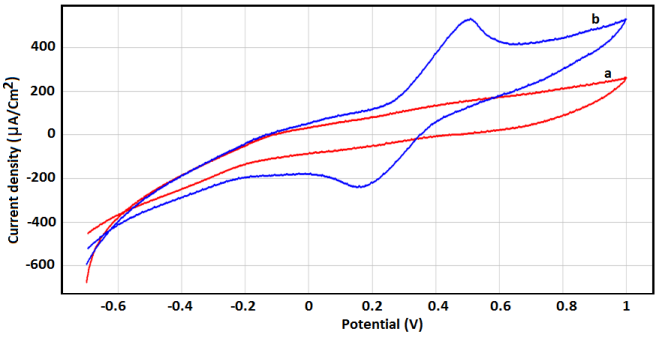
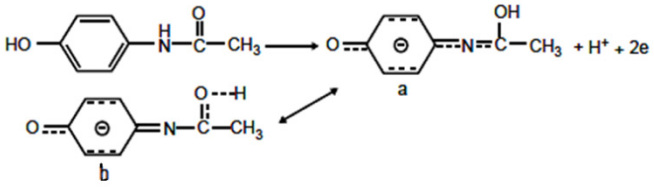


***Figure 4:** CVs recorded for 2.64 mM paracetamol at pH=7 at bare Clay-CPE (a) and Clay-CPE/paracetamol (b), scan rate 100 mV/s, preconcentration time (tp)= 3min.*



Scheme: *The redox mechanism of paracetamol.*

OPTIMIZATION OF EXPERIMENTAL CONDITIONS

Optimum conditions for the electrochemical response were established by measuring the peak current in dependence on all parameters.

Influence of accumulation time

The effect of the accumulation time is investigated (Figure 5); this significantly affects the oxidation peak current of paracetamol. The peak current of 3.96 mmol L^{-1} paracetamol increases greatly within the first 3 min. Further increase in accumulation time does not increase the amount of paracetamol at the electrode surface owing to surface saturation, and the peak current remains constant. This phenomenon is due to the cavity structure of clay-CPE that improves the ability of the electrode to adsorb electroactive paracetamol. Maybe this is attributed to the saturated adsorption of paracetamol on the Clay–CPE surface. Taking account of sensitivity and efficiency, accumulation time was 3 min in the following experiments.

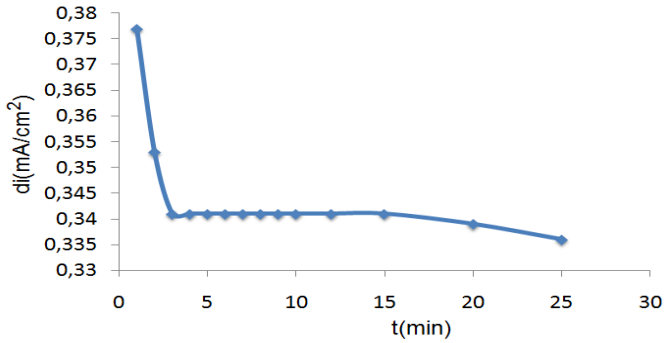


Figure 5: *Effects of accumulation time on oxidation peak currents of 3.96 mmol L^{-1} paracetamol at Clay-CPE, supporting electrolyte is K_2SO_4 0.1M (pH=7).*

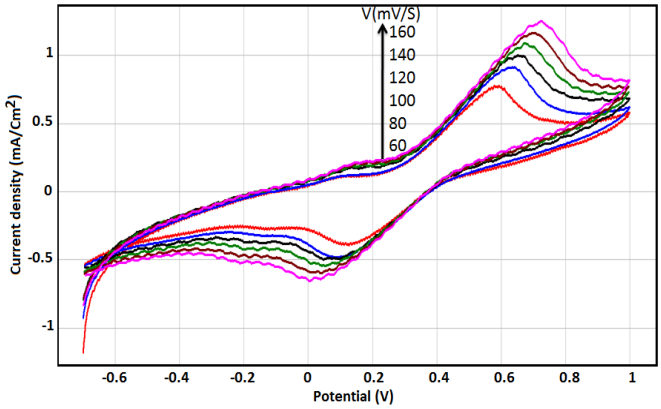


Figure 6: *CVs acquired on Clay-CPE with 5.28 mM paracetamol in the buffer solution at different scan rates from 60 to 160mV.s^{-1}. Inset is the plot of the peak current of paracetamol versus scan rate.*

Effect of scan rate

The effect of scan rates on the redox paracetamol at the clay modified carbon paste electrode was investigated by cyclic voltammetry (Figure 6). The redox peak currents increased linearly with the scan rate in the range from 60 to 160mV.s^{-1} indicating that paracetamol is adsorbed onto Clay-CPE surface.

The figure 7 shows the linear relationship between the scan rate anodic peak and cathodic peak currents of paracetamol at Clay/CPE. The linear regression equations:

$$I_{pa}=0.004V+0.514 \quad R^2=0.989$$
$$I_{pc}=-0.002V-0.217 \quad R^2=0.987$$

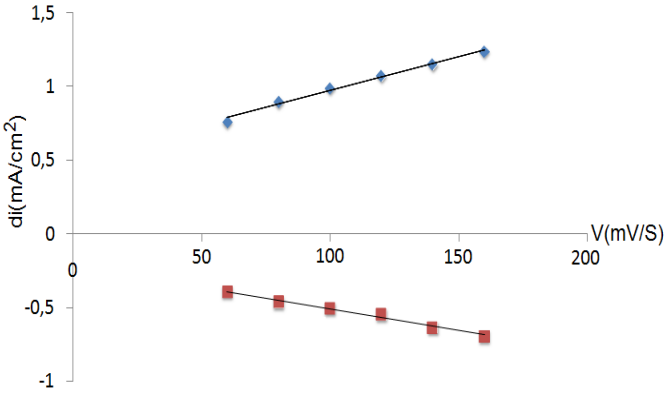


Figure 7: *Plot of peaks area versus scan rate*

Calibration graph

Figures (8,9) shows respectively the CV and SWV curves of different concentration of paracetamol at Clay/CPE was increased from 1.32 mM to 6.6 mM at pH 7. Both the anodic and cathodic peak current increases linearly with the concentration of paracetamol.

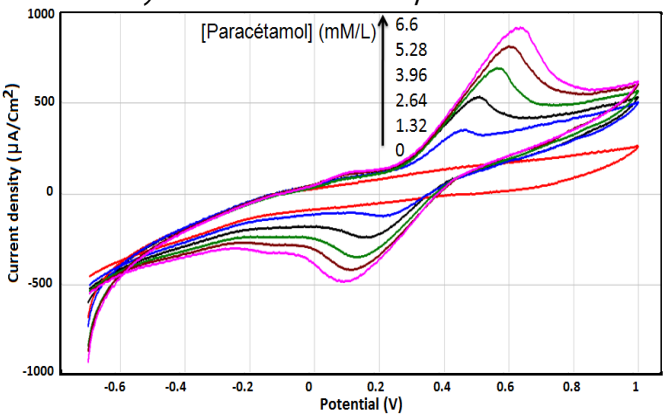


Figure 8: *Cyclic Voltammograms of different concentration of paracetamol (1.32mM to 6.6mM) at Clay/CPE in 0.1 M K_2SO_4 PH=7, Scan rate 100 mV/s.*

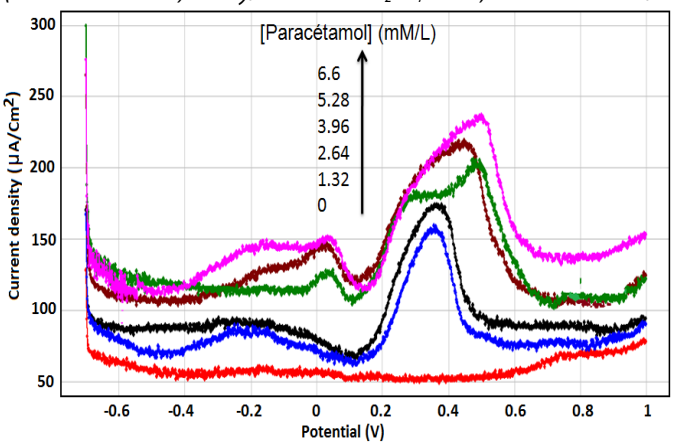


Figure 9: *Square Wave Voltammograms of different concentration of paracetamol (1.32mM to 6.6mM) at Clay/CPE in 0.1 M K_2SO_4 PH=7*

The calibration curve for the CV peak current for paracetamol oxidation and reduction vs. paracetamol concentration (Figure 10) shows excellent linearity.

The linear regression equations:

$$I_{pa}=0.144\,[Paracetamol]+0.112 \quad R^2=0.981$$

$$I_{pc}=-0.078\,[Paracetamol]-0.013 \quad R^2=0.989$$

The linear behavior of the calibration curve further indicates that the process is basically diffusion controlled within the studied concentration range.

Modification of carbon paste surface by clay remarkably improves the reactivity of Clay/CPE towards the oxidation and reduction of paracetamol.

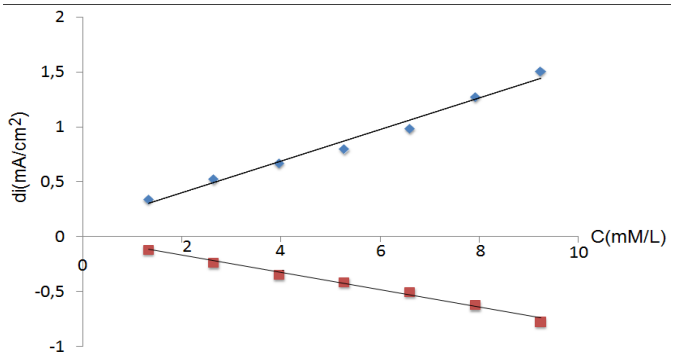


Figure 10: *Plot of peaks area versus added concentration of paracetamol.*

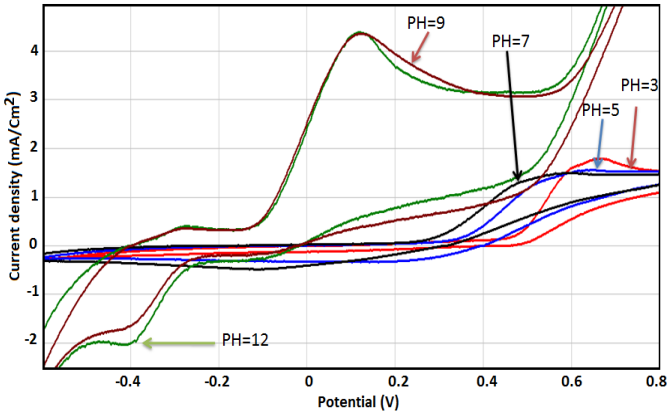


Figure 11: *Cyclic Voltammograms of different pH on the oxidation and the reduction of paracetamol at the Clay modified CPE.*

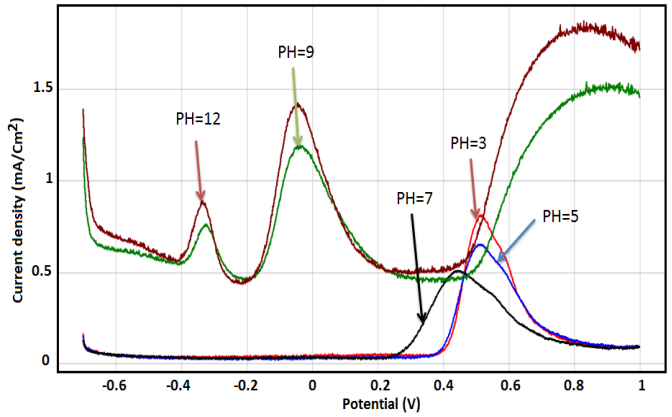


Figure 12: *SWV for the effect of pH on the oxidation and the reduction of paracetamol at the Clay modified CPE.*

Influences of pH

The effect of pH on the voltammetric response of paracetamol was studied in the range of pH 3-12. Figures (11,12) shows respectively the cyclic voltammograms and square wave voltammograms recorded at different values of pH to 6.24 mM paracetamol. The pH solution has a significant influence on the peak current and the peak potential of the catalytic oxidation peak and the reduction peak of paracetamol.

Figures (13,14) shows respectively the effect of pH on the current density and the peak potential for paracetamol oxidation and reduction.

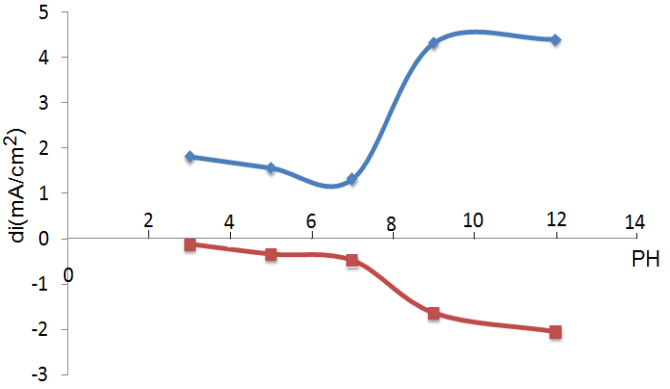


Figure 13: *Plot of the relationship between solution pH and the oxidation and reduction peak Current.*

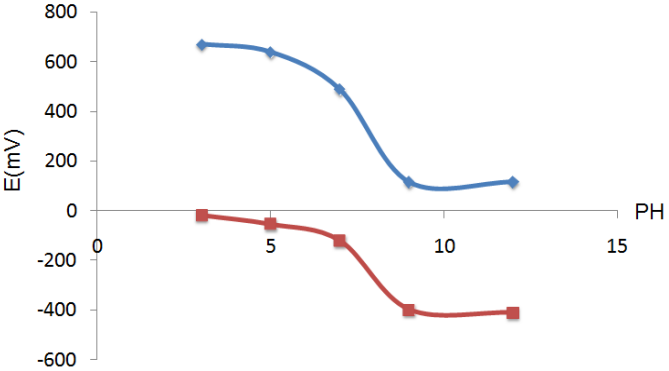


Figure 14: *Plot of mid-potential of paracetamol peaks versus pH values*

ANALYSIS OF COMMERCIAL SAMPLES

In order to evaluate the performance of the analytical methodology described above, the determination of paracetamol at Clay-CPE was carried out in commercial sample. The analytical curves were obtained by CV experiments in supporting electrode (Figure 15). It was founded that the peaks currents increase linearly versus paracetamol added into the buffer solutions (Figure 16).

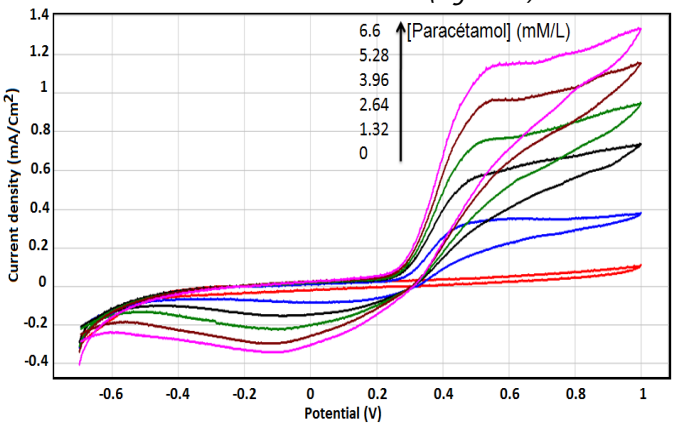


Figure 15: *Cyclic Voltammograms of different concentration of paracetamol (1.32mM to 6.6mM) at Clay/CPE, Scan rate 100 mV/s.*

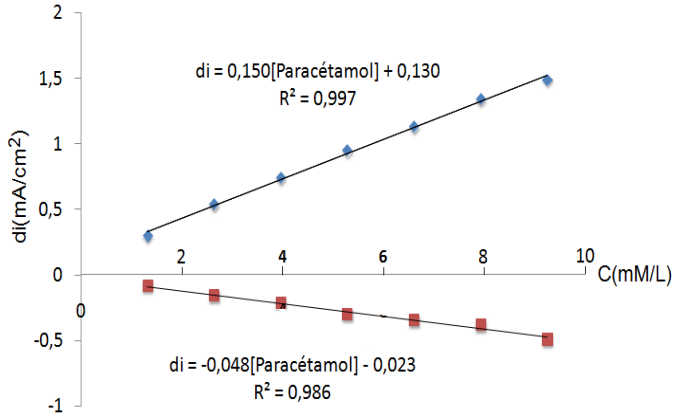


Figure 16: *Plot of peaks area versus added concentration of paracetamol.*

CONCLUSION

In this work, electrochemical behavior of paracetamol was evaluated using the voltammetric measurements. A novel method is described for the determination of paracetamol which is simple, quick and sensitive with a low cost of analysis.

The method has been satisfactorily applied to the determination of paracetamol in pharmaceutical formulations. The clay modified carbon paste electrode exhibited a stable and reproducible response for paracetamol. The modifier is not soluble in water, non-toxic, and not a pollutant.

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