Electroanalysis of Paracetamol by a Carbon Paste Electrode Modified by Zinc: Analytical Application in Human Blood

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The present work describes the catalytic effect of zinc particles for electroanalysis the paracetamol (PAR). The working electrode was prepared by mixing the zinc with the carbon powder. The voltammetric behavior of paracetamol was studied when an anodic peak to appear at 0.35 V in 0.1 M Na_2SO_4 solution (pH 12). The peak resulting from the irreversible oxidation of paracetamol on the zinc modified carbon paste electrode (Zn/CPE). The catalytic effect was evaluated by cyclic voltammetry (CV) and square wave voltammetry (SWV). The electrocatalytic behavior of the zinc particles is allotted to its chemical and physical properties. This electrode has a good performance for the electroanalysis of paracetamol. To obtain an electrochemical analysis of paracetamol oxidation at the surface of Zn/CPE, the voltammograms are used in a potential range of -1.5 V to 1.5 V. More, Zn/CPE can be utilized successfully to ameliorate the electroanalysis of paracetamol at very feeble concentration and with high detection sensitivity. The limit of detection (LD) and quantification (LQ) obtained are respectively $7.52 \cdot 10^{-8}$ mol L^{-1} and $2.6 \cdot 10^{-7}$ mol L^{-1}. Then the relative standard deviation (RSD) at $2.0 \cdot 10^{-5}$ mol L^{-1} PAR concentration was 2.88% for nine repetitions. Afterward, the presented method was used to electroanalysis paracetamol in human blood samples with satisfying results.

Keywords: cyclic voltammetry, electroanalysis, Zinc, paracetamol, detection, human blood

It's very important to develop a sensitive and precise technique for analyzing active ingredients to monitor the quality of drugs, which has a considerable impact on public health [1]. In 1893, paracetamol has been used in medicine as an antipyretic and analgesic by Von Mering. It is he is also taken as an analgesic for over 30 years for home medication. Paracetamol is acknowledged as the best performing treatment for pain relief and fever in children and adults. Paracetamol is the most generally prescribed after acetylsalicylic acid in the world as replacing aspirin [2]. The analgesic and antipyretic action of paracetamol are similar to that of aspirin [3]. The paracetamol is currently preferred, especially for the more sensitive ill in front of acetylsalicylic acid [4]. Excess of paracetamol causes an increase in toxic metabolites, resulting in acute hepatic necrosis, inducing death in humans [5-7]. The development of simple and more precise methods for the electroanalysis of paracetamol in the pharmaceutical field is more interesting [8, 9].

Many paracetamol analysis techniques have been cited in the bibliography: high-performance liquid-chromatography [10], Thin-layer chromatography [11], FTIR spectroscopy [12], and other techniques are cited for paracetamol analysis. Nevertheless, the analytical methods mentioned have certain drawbacks such as the high price, the long analysis time and the pretreatment of the samples, and in cases, the low sensitivity and selectivity render them ineffective for the analyzes. Paracetamol is an electroactive compound and most electro-analytical methods can be observed for paracetamol analysis as a good alternative to the methods mentioned. Electrochemical techniques use carbon-modified electrodes, such as graphite modified with cobalt hexacyanoferrate, glassy carbon electrodes modified with carbon nanotube film and single-walled diacetyl phosphate [13, 14], carbon-layer resistance electrode [15], modified vitreous carbon electrodes [16, 17], boron-doped diamond thin-film electrodes [18, 19], and glassy carbon electrodes modified with metalloporphyrin [20].

However, the carbon nanotubes modified electrodes have been utilized for the electroanalysis of various analytical targets [20-27]. The present work describes the scientific research and the exploitation of a new electrochemical electrode prepared by the modification of the carbon paste electrodes (CPE) by zinc particles (Zn/CPE), as well as the properties of electroanalysis of the electrode. The results obtained show that (Zn/CPE) present better performances for the electroanalysis of paracetamol. The proposed method was simple, fast and of high sensitivity.

Materials and methods

Chemicals and equipment

Paracetamol, Na_2SO_4, $ZnSO_4$, H_3PO_4 and NaOH were purchased from Sigma-Aldrich. The pH values of the electrolytic media were established by phosphoric acid or potassium hydroxide. The electrolytic solutions utilized in was prepared by distilled water. The experiments of the electroanalysis of paracetamol have been executed at 25 °C.

All electroanalysis experiments of paracetamol were done by a potentiostat voltalab (model PGSTAT 100, Eco Chemie BV, Utrecht, Netherlands) controlled by a computer, this apparatus was piloted by the software (voltalab master 4) of electrochemical responses treatment. The electrochemical cell containing three electrodes: Zn/CPE as the working electrode, Ag/AgCl/Cl (3 mol L^{-1}) as a reference electrode and a platinum wire serving as the auxiliary electrode.

Preparation of the Zn/CPE and procedure

The Zn/CPE was prepared by mixing carbon and zinc powder. The body of this electrode was a cylinder tightly filled with the mixture of carbon paste and zinc. The surface of this electrode is 0.1256 cm^2. Electrical contact has been made using a carbon rod.

The surface of the electrode was smoothed by a filter paper and stabilized by recording cyclic voltammograms superimposed in 20 cycles in the electrolytic medium 0.1 M Na_2SO_4.

Different supporting electrolytes were tested such as Na_2SO_4, K_2SO_4, H_2SO_4, NaOH, KCl, and NaCl. The excellent electroanalysis responses were obtained by Na_2SO_4 (0.1 M, pH 12). The working procedure consists of measuring the electrochemical responses at the surface of Zn/CPE in the presence of the PAR concentration. An amount of PAR was added to the electroanalysis cell containing 20 ml of sodium sulfate as an electrolytic medium. The CV and SWV methods were obtained in the potential range between -1.5 V and 1.5 V. The excellent analysis conditions were determined by measuring the peak current oxidation as a function of the parameters. Electrochemical analyses were obtained at 25°C.

Results and discussion

Electrochemical identification of paracetamol

Voltammetric methods (SWV and CV)

Fig. 1 and 2 show the cyclic voltammograms (CVs) and the square wave voltammograms (SWVs) obtained in the potential range from -1.5 V to 1.5 V on the surface of CPE and Zn/CPE. The CVs and SWVs have different shapes, which shows that the surface of the CPE has been well modified by zinc. The electroanalysis responses of the CPE and Zn/CPE toward PAR oxidation were studied using CV and SWV in 0.1 M Na_2SO_4 (pH 12) containing $2.0 \cdot 10^{-5}$ mol L^{-1} of PAR. No peak appeared for the CPE (Fig. 3a and 4a). Fig. 3b and 4b show the oxidation peak at Epa = 0.35 V. The Zn/CPE exhibited excellent electrocatalytic oxidation of PAR compared to CPE.

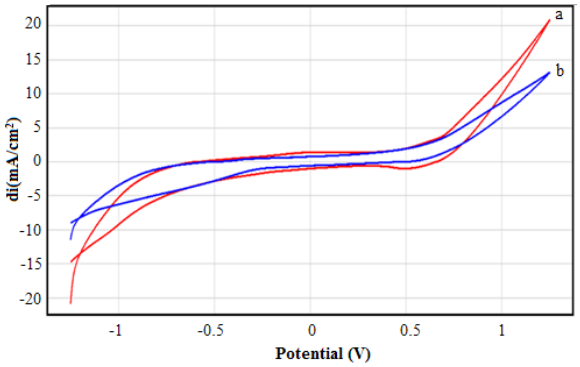


Fig. 1. CVs obtained for (a) CPE and (b) Zn/CPE, 0.1 M Na_2SO_4 (pH 12) at 100 mV s^{-1}.

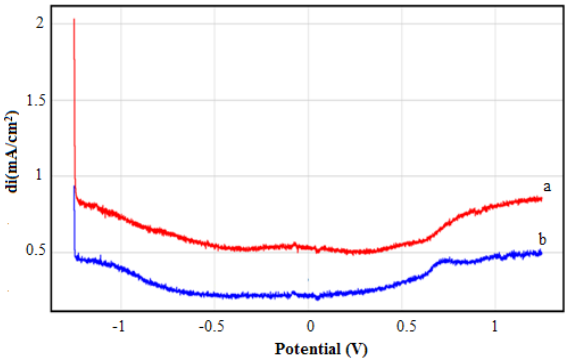


Fig. 2. SWVs obtained for (a) CPE and (b) Zn/CPE, 0.1 M Na_2SO_4 (pH 12).

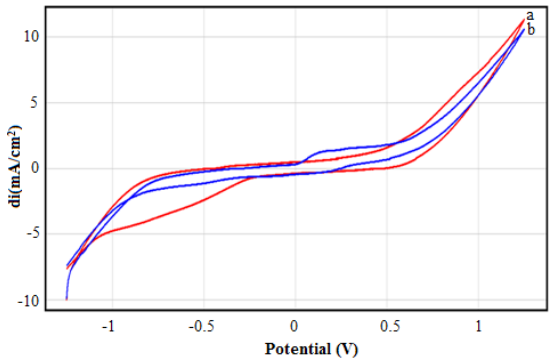


Fig. 3. CVs recorded for (a) CPE and (b) Zn/CPE in the presence of $2 \cdot 10^{-5}$ mol L^{-1} PAR, 100 mV s^{-1}.

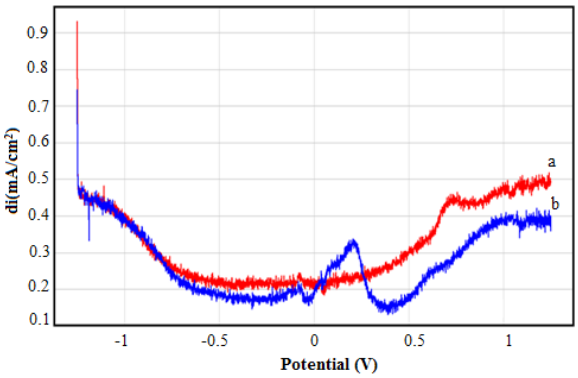
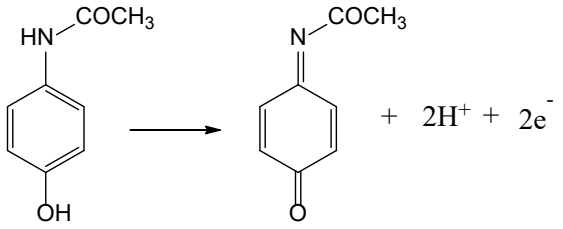


Fig. 4. SWVs recorded for (a) CPE and (b) Zn/CPE in the presence of $2 \cdot 10^{-5}$ mol L^{-1} PAR.

According to this study, scheme 1 shows the PAR oxidation.



Paracetamol N-acetyl-p-quinone imine

Scheme 1. Oxidation reaction of PAR.

Effect of accumulation time and % zinc

This electroanalysis study was realized by the CV method. The electrochemical parameters have been optimized in 0.1 M Na_2SO_4 (pH 12) containing $2.0 \cdot 10^{-5}$ mol L^{-1} of PAR. The increase of the modifier's loading (from 1 to 30 % by weight of carbon paste) affects the electrochemical analysis of PAR at the Zn/CPE surface (Fig. 5). The peak current of PAR increases with the increase of the zinc until 10 %, after this percentage the current decreases. Hence a 10 % of the ratio by weight has been used in all experiences.

The effect of preconcentration time on electrochemical responses has been studied. Fig. 6 represents an increase in the current intensity as a function of preconcentration time during the first 2 minutes.

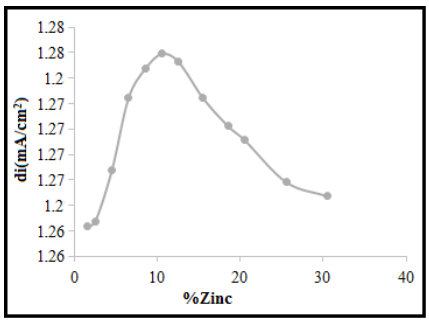


Fig. 5. Effect of % Zinc in presence of $2 \cdot 10^{-5}$ mol L^{-1} PAR in 0.1 M Na_2SO_4 at the Zn/CPE.

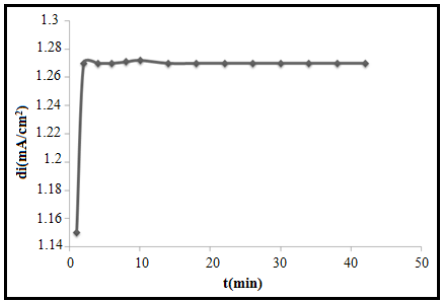


Fig. 6. Effect of the preconcentration time in presence of $2 \cdot 10^{-5}$ mol L^{-1} PAR at the Zn/CPE on the peak current oxidation.

Another increase in preconcentration time does not increase PAR at the surface of Zn/CPE, which produces stability in the peak current oxidation. This process is attributed to the saturation of the surface of Zn/CPE by adsorbed PAR. Hence 2 minutes has been used in all work.

Other experimental investigate, the optimal electrochemical analysis parameters to perform the detection of PAR has been found to be 20 mV s^{-1}, 100 ms, 140 mV, 220 ms for the step, pulse, width, and period, respectively.

Influence of scan rate and pH

The effect of the scan rate and pH on the anodic peak current of PAR have been studied on the surface of the Zn/CPE under the concentration of $1.5 \cdot 10^{-5}$ mol L^{-1} (PAR) in 0.1 M Na_2SO_4 (pH 12). The anodic peak current of PAR increased by increasing the scanning rate (Fig. 7). The relationship of oxidation peak current and scan rate was linear when the scan rate increased from 40 to 100 mV s^{-1} (Fig. 8). The adsorption phenomenon suggested an adsorption-controlled process at the Zn/CPE surface. The influence of buffer pH on the CV responses of the Zn/CPE was further studied in the pH range from 2 to 12 and well-defined CV curves were observed (Fig. 9). Therefore, pH=12 is the better electrocatalytic activity of the working electrode toward the oxidation of PAR (Fig. 10). Also, the increase in pH values moves the oxidation potentials towards the low values (Fig. 11).

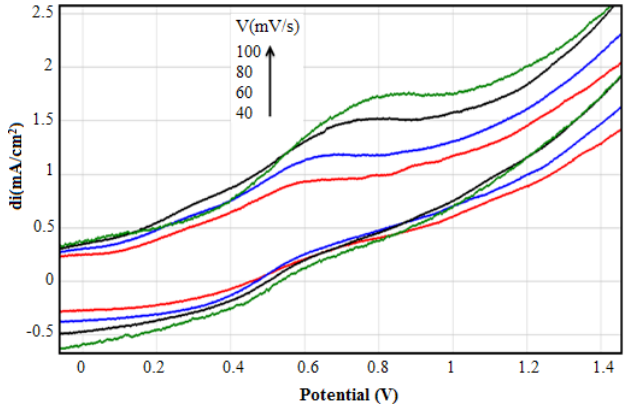


Fig. 7. CVs obtained at the Zn/CPE surface in presence of $1.5 \cdot 10^{-5}$ mol L^{-1} of PAR at different scan rates.

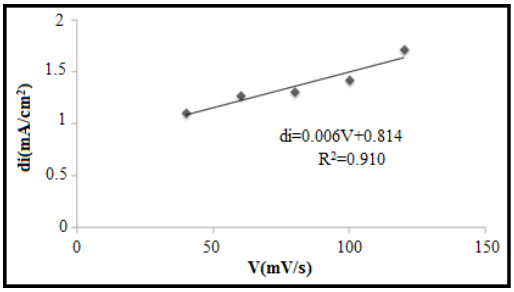


Fig. 8. Evolution of the current as a function of the scanning rates.

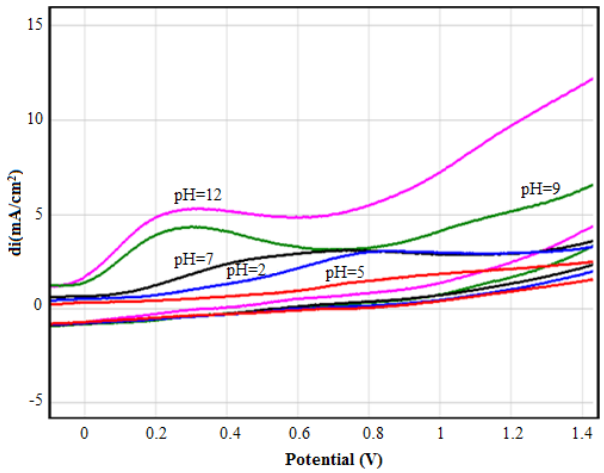


Fig. 9. CVs recorded for different pH values at the Zn/CPE surface.

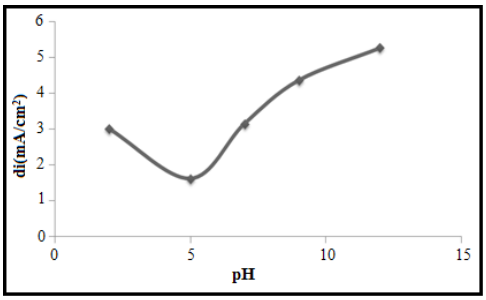


Fig. 10. The curve of variation of the current density as a function of the pH.

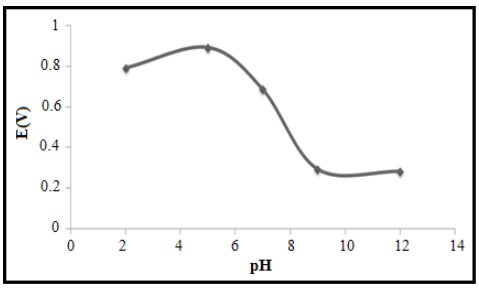


Fig. 11. The curve of variation of the oxidation potential of PAR as a function of the pH.

Effect of concentration

The effect of concentration was determined for PAR underneath optimum experimental conditions. Fig. 12 and 13 show the CVs and SWVs, respectively, recorded on the Zn/CPE surface in the range from $6.0 \cdot 10^{-5}$ to $7.0 \cdot 10^{-4}$ mol L^{-1} of PAR. The oxidation peaks current increases with the increase of PAR concentration. Fig. 14 indicates the linearity between the peak current versus the concentration of the PAR on the Zn/CPE. The reactivity of the Zn/CPE towards the electroanalysis of PAR is well-improved by the zinc. The limit of detection and quantification were calculated using the anodic peak current by the following equations: LD = 3 SD/M, LQ = 10 SD/M (SD: Standard deviation of the peak currents nine runs; M: Slope of the calibration curve).

$$SD = \frac{1}{(n-2)} \sum_{j=0}^{n} (i_j - I_j)^2$$

i_j: is the experimental value of the current calculated at manipulation j; I_j: is the corresponding value recalculated at the same concentration using the calibration equation; n = 5: number of experiments (C ($\cdot 10^{-4}$ mol L^{-1}) = 0.06; 1; 3; 5; 7).

The LD and LQ were calculated as $7.52 \cdot 10^{-8}$ mol L^{-1} and $2.6 \cdot 10^{-7}$ mol L^{-1}, respectively. The RSD for nine measurements was calculated as 2.88 % for PAR concentration of $2.0 \cdot 10^{-5}$ mol L^{-1}. The DL calculated by Zn/CPE is compared with the values of other electrodes (Table 1) [29-34].

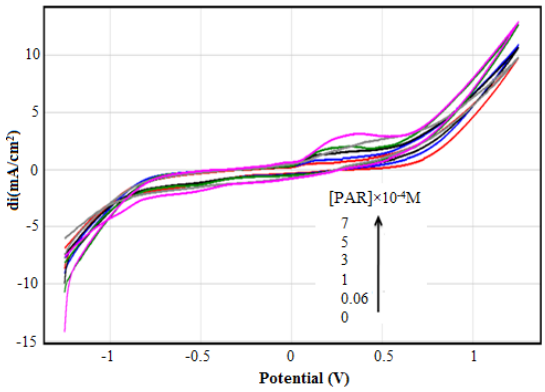


Fig. 12. CVs for different concentrations of PAR in 0.1 M Na_2SO_4 pH 12 at Zn/CPE, 100 mV s^{-1}.

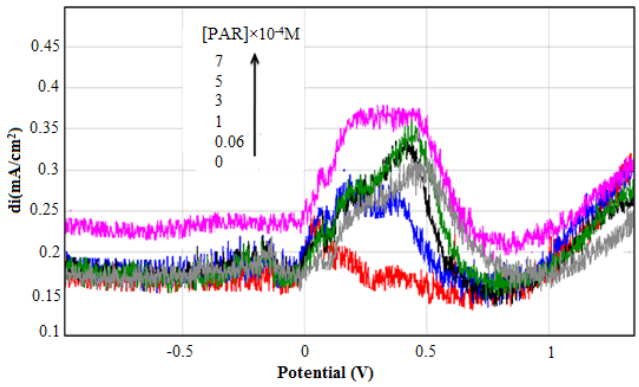


Fig. 13. SWVs for different concentrations of PAR at Zn/CPE in 0.1 M Na_2SO_4, pH 12.

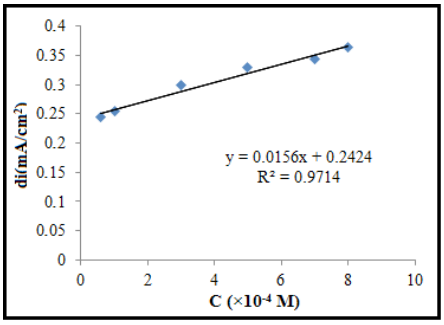


Fig. 14. The curve of peaks current versus the added concentration of PAR.

Table 1. Comparison of the different electrodes using for PAR detection.

Modified electrode	Analytical technique	Detection limit	Epa (V)	pH	Ref.
A nanogold modified indium tin oxide electrode	Differential pulse voltammetry	$1.8 \cdot 10^{-7}$ mol L^{-1}	0.11	7.2	[29]
MgB_2 microparticles modified glassy carbon electrode	Cyclic voltammetry	$3 \cdot 10^{-7}$ mol L^{-1}	0.6	6	[30]
Nafion/TiO_2-graphene modified glassy carbon electrode	Cyclic voltammetry	$2.1 \cdot 10^{-7}$ mol L^{-1}	0.575	7	[31]
Glassy carbon electrode	Differential pulse voltammetry	$3.69 \cdot 10^{-7}$ mol L^{-1}	0.6	4.51	[32]
Boron-doped diamond electrode	Differential pulse voltammetry	$4.9 \cdot 10^{-7}$ mol L^{-1}	0.8	4.5	[33]
Aluminum electrode modified by thin layer of palladium	Cyclic voltammetry	$5 \cdot 10^{-5}$ mol L^{-1}	0.6	6	[34]
Zn/CPE	Square wave voltammetry	$7.52 \cdot 10^{-8}$ mol L^{-1}	0.35	12	Present work

Analytical application

In order to verify the applicability and validity of the analytical method, the zinc-modified carbon paste electrode was used for the detection of paracetamol in the human blood sample. The sample was prepared by adding 0.284 g of Na_2SO_4 (0.1 M Na_2SO_4, pH 12) to 20 ml of human blood, then enriched with appropriate amounts of paracetamol. The electroanalytical curves were recorded by the method of square wave voltammetry (Fig. 15). The peak oxidation currents have been shown to increase linearly with respect to the paracetamol added to the solution (R^2 = 0.988; di = 0.298 [PAR] + 0.477) (Fig. 16). Consequently, the limit of detection obtained is $9.24 \cdot 10^{-8}$ mol L^{-1}. The RSD calculated is 7.16 % after nine measurements in solutions of $2.0 \cdot 10^{-5}$ mol L^{-1}. This shows the possibility to determine PAR in human blood samples.

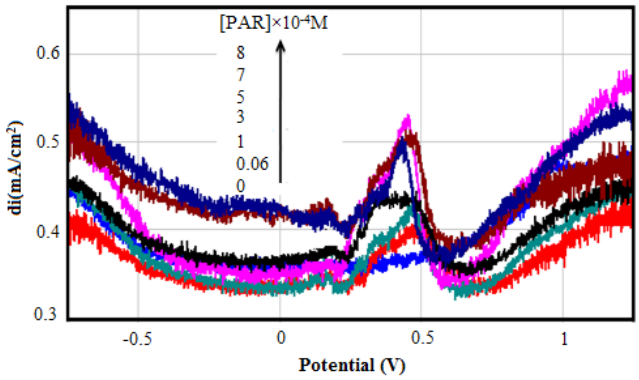


Fig. 15. SWVs for different concentrations of PAR at Zn/CPE in human blood under optimum conditions.

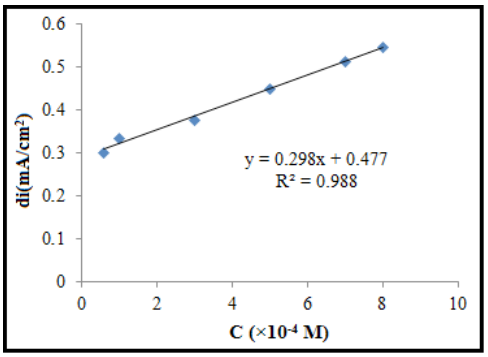


Fig. 16. Calibration curve between peak currents and PAR concentration under optimum conditions.

Conclusion

At the surface of the carbon paste electrode modified by the zinc, paracetamol undergoes an irreversible oxidation process of about 0.35 V in the solution. Zn/CPE is characterized by excellent adsorption of paracetamol. All the results are obtained by CV and SWV. The intensity evolution of the oxidation peaks of paracetamol between $6 \cdot 10^{-5}$ and $7 \cdot 10^{-4}$ mol L^{-1} is linear. The DL found is $7.52 \cdot 10^{-8}$ mol L^{-1}. This analytical technique was applied to detect the paracetamol in real samples. The technique is simple, fast, efficient, sensitive and repeatable.

Conflicts of interest

The authors declare no conflicts of interest.

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