

Electrochemical Detection of Paracetamol Using Graphene Oxide -Modified Glassy Carbon Electrode

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A very sensitive electrochemical sensor has been developed by modification of glassy carbon electrode (GCE) with graphene oxide (GO). The electrochemical behavior of paracetamol was studied at GO/GCE using cyclic voltammetry (CV) and square-wave voltammetric techniques (SWV). A well defined oxidation peak was observed in 0.1 M KH₂PO₄ electrolyte solution by solid phase voltammetry. Under the CV techniques, it appears that the catalytic effect of the modification on graphene oxide GO/GCE shows higher current response as compared to bare GCE. Observed peak potential was shifted to less positive value by about 220 mV and current was significantly enhanced by about 2 folds. Square-wave voltammetry showed higher sensitive response than CV techniques, where current was significantly enhanced by more than 2 folds. Under the optimum conditions, the oxidation peak current of paracetamol varied linearly with concentration over a wide range of 5 × 10⁻⁸ mol L⁻¹ to 1 × 10⁻⁶ mol L⁻¹ and the detection limit of this method was as low as 4.9 × 10⁻⁸ M.

Keywords: graphene oxide (GO); Modified GC electrode; paracetamol; Cyclic Voltammetry(CV)

1. INTRODUCTION

Graphene is a one atom layer thick carbon sheet. Graphene exhibits many interesting electronic, optical and mechanical properties due to its two-dimensional (2D) crystal structure and possesses high conductivity despite it being an organic compound [1]. In general, chemical oxidation method produces graphene by first introducing functional groups such as carbonyl, hydroxyl and peroxy in between carbon layers of graphite. These functional groups weaken the Vander Waals bond between the carbon layers which cause the graphene layers to peel off layer by layer from graphite [2]. The resulting (GO) can be reduced to graphene by adding hydrazine into the GO solution. GO has a

similar layered structure to graphite, but the plane of carbon atoms in GO is heavily decorated by oxygen-containing groups, which not only expand the interlayer but also make the atomic-thick layers hydrophilic. As a result, these oxidized layers can be exfoliated in water under moderate ultrasonication. If the exfoliated sheets contain only one or few layers of carbon atoms like graphene, these sheets are named (GO) [3]. One of the alternative methods is chemical oxidation. In this work, (GO) was synthesized using the simplified Hummer's method, which would produce GO with large lateral dimension in scalable quantity [4]. Acetaminophen or paracetamol is one of the most commonly used analgesics in pharmaceutical formulations, for the reduction of fever and also as a painkiller for the relief of mild to moderate pain associated with headache, backache, arthritis and post-operative pain. Acetaminophen is electroactive and voltammetric mechanistic studies for the electrode processes of the acetaminophen /N-acetyl-p-quinoneimine redox system has been presented [5-8]. One of the most commonly used analgesics in pharmaceutical formulations is acetaminophen or paracetamol as a painkiller for the relief of pain associated with headache, backache, arthritis and post-operative pain. The fabrication of chemically modified electrode (CME) consisting of a mixture of carbon paste and modifying reagent have been widely used. They can be easily prepared and have a stable electrode response and important analytical properties of electrodes-sensitivity, selectivity, reproducibility [9-10]. Since there are very limited electrochemical studies on graphene oxide especially via (CV), here we report electrochemical method for the determination of paracetamol at modified electrode using SWV and CV. Glassy carbon electrode (GCE) modified with (GO) was studied to improve the sensitivity of electrode for electrochemical detection.

2. EXPERIMENTAL

2.1 Instrumentation and electroanalytical analysis methods

Electrochemical workstations of Bioanalytical System Inc. USA: Model BAS 50W with potentiostat driven by electroanalytical measuring softwares were connected to the computer to perform cyclic voltammetry (CV), and square-wave voltammetric techniques(SWV) An Ag/AgCl (3M NaCl) electrode and platinum wire were used as a reference and counter electrodes respectively. The working electrode used in this study was a 3 mm diameter glassy carbon (GC). Unless otherwise stated, the voltammetric experiments were carried out at $25 \pm 2^\circ\text{C}$ using 0.1 M NH₄Cl as supporting electrolyte. Solutions were degassed with nitrogen for ten minutes prior to recording the voltammogram. Scanning electron microscopy (SEM) was used to characterize the surface of the (GO) composites at 5 mm diameter basal plane paralytic graphite electrode (BPPGE) (Model JOEL, JSM-64000 machine).

2.2 Reagents

Graphite flakes were purchased from Asbury Graphite Mills, Inc (Asbury, N J). Sulfuric acid (H₂SO₄, 98%), potassium permanganate (KMnO₄, 99.9%) and hydrogen peroxide (H₂O₂, 30%) were

purchased from Merck (Darmstadt, Germany). Paracetamol tablet brand named Tempol from Pharmaceuticals Ltd in (Malaysia) was used. Deionized water from reverse osmosis (RO) water model Elken (BIO PURE) was used. Unless otherwise specified, the supporting electrolyte was 0.1 M KH₂PO₄ in aqueous media at room temperature. All solutions were desiccated with oxygen-free nitrogen gas for 15 minutes prior to making the measurement.

2.3 Procedures

2.3.1 Preparation of graphene -modified glassy carbon electrode

A bare GCE was polished with alumina powder, rinsed ultrasonically with deionized water and dried at room temperature before use. Approximately 1 mg of graphene and graphene oxide were dispersed in 1 mL of DMF and ultrasonicated for 30 min. GO modified electrode was fabricated using 10 μ L of the graphene oxide and graphene suspension by casting it on the surface of GCE before drying it in air. Prior to use, the modified electrode was carefully rinsed with water to remove the loosely attached graphene on the electrode surface.

3. RESULTS AND DISCUSSION

3.1 Enhancement Study.

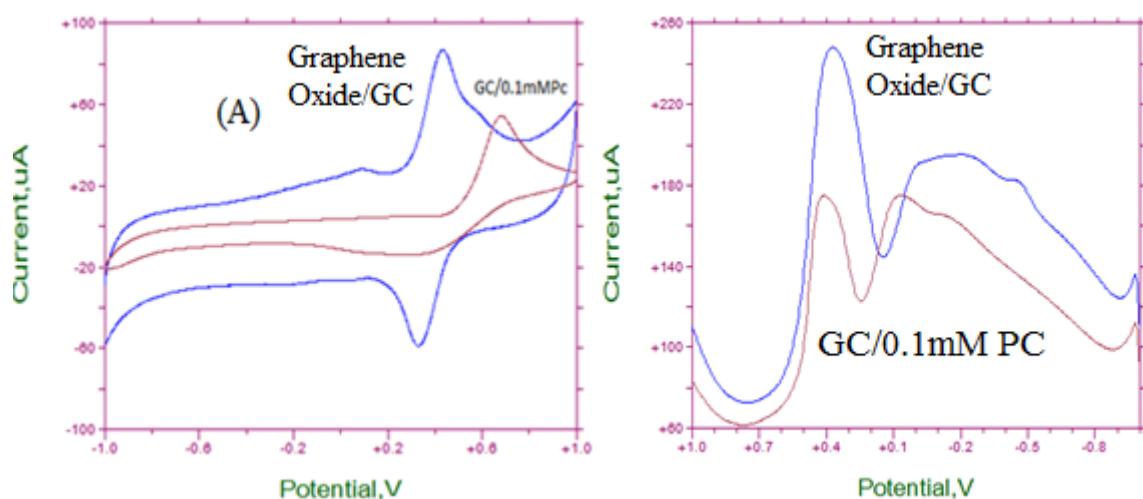


Figure 1. Cyclic voltammograms for oxidation of 0.1 mM paracetamol obtained in 0.1M KH₂PO₄ (pH 4.2), with potential scanning in the positive direction from -1000 to +1000 mV vs Ag/AgCl at a scan rate of 100mV/s at 25°C at (a) bare GC electrode and (b) modified GO/GC.

Figure 1 shows cyclic voltammograms obtained for the oxidation of paracetamol in 0.1 M KH₂PO₄ supporting electrolyte at pH 4.2 at modified GC electrode (a), and modified electrode with Graphene oxide (b). The observation on the oxidation potential of paracetamol shows an absence of

electroactivity on the reverse scan or reduction, indicating the irreversibility of the oxidation process. The electrocatalytic performance of GO/GCE was advantageous over that observed at the bare GCE. The enhancement of oxidation peak current at graphene-modified GCE reveals that graphene exhibit electro-catalytic behavior towards the electrochemical oxidation of paracetamol due to its fast electron transfer capability (see figure 1(a) and (b)). Peak potential was observed to shift slightly to less positive value by about 220 mV and current was significantly enhanced by about 2 folds. Square-wave voltammetry showed a higher sensitive response compared to CV techniques, where current was significantly enhanced by more than 2 folds

3.2 Effect of varying pH

The solution was varied from pH 2.0 to 11 to determine its effect on the catalytic oxidation of 0.1 mM paracetamol at the GO/GC modified electrode. Figure 2. shows that the optimum peak current was achieved at pH 4.2. With the rise in pH, the peak current decreased due to pH dependency of half wave potential which indicate involvement of protons in the electrode process and finally descended as we moved towards more alkaline pH due to lower number of available protons. With the increasing pH from 4.2 to 9.0, peak current is shifted to more negative potentials.

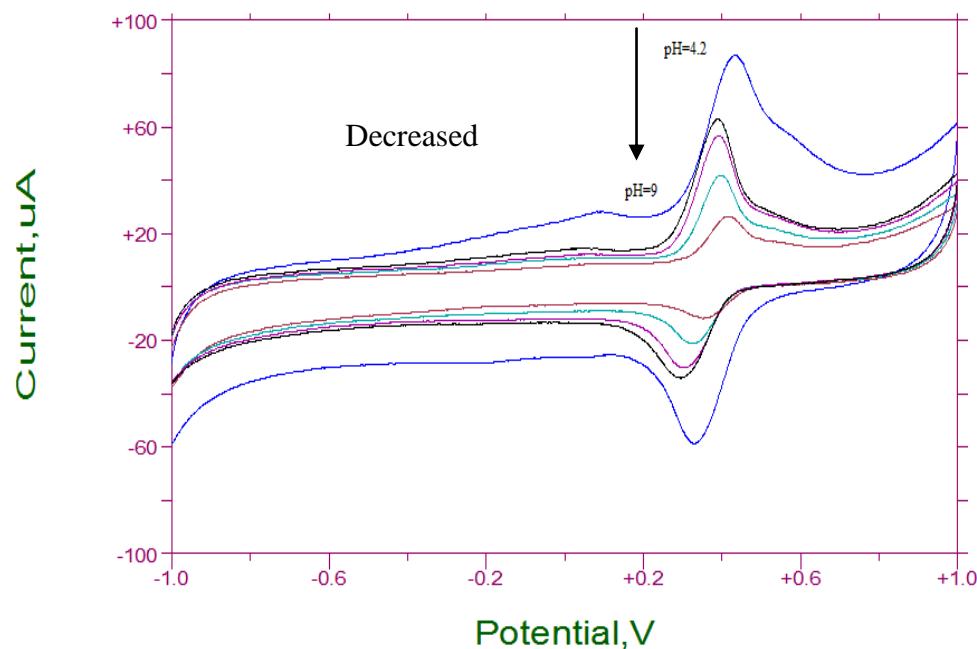


Figure 2. Cyclic voltammograms pH for 0.1 mM paracetamol in 0.1 M KH_2PO_4 with varying pH levels for GC electrode modified with modified GO/GC. Potential scanning in the positive direction from -1000 to +1000 mV vs Ag/AgCl at a scan rate of 100mV/s

3.3. Effect of temperature

Effect of temperature on the oxidation process of paracetamol was studied. The current increased gradually at the temperature of 20 °C to 70 °C. Paracetamol gave a peak response at about 450 mV vs. Ag/AgCl at the bare GC electrode Fig. 3, while the use of (GO) modified GC electrode led to an anodic peak at about 260 mV vs. Ag/ AgCl and the peak current increased greatly. The enhanced peak current response is a clear evidence of the catalytic effect of the (GO) modified GC electrode towards oxidation of paracetamol. In addition, a shift in the oxidation potential of paracetamol by about 190 mV in the cathodic direction was observed at the modified electrode. The plot of log oxidation current of paracetamol versus reciprocal of temperature was found to be fairly linear as described by 0.9899 R². It is also in agreement with thermodynamic expectation of Equations 1 and 2 given below.

$$\sigma = \sigma^0 \exp(-E_a/RT) \quad (1)$$

$$D = D^0 \exp(-E_a/RT) \quad (2)$$

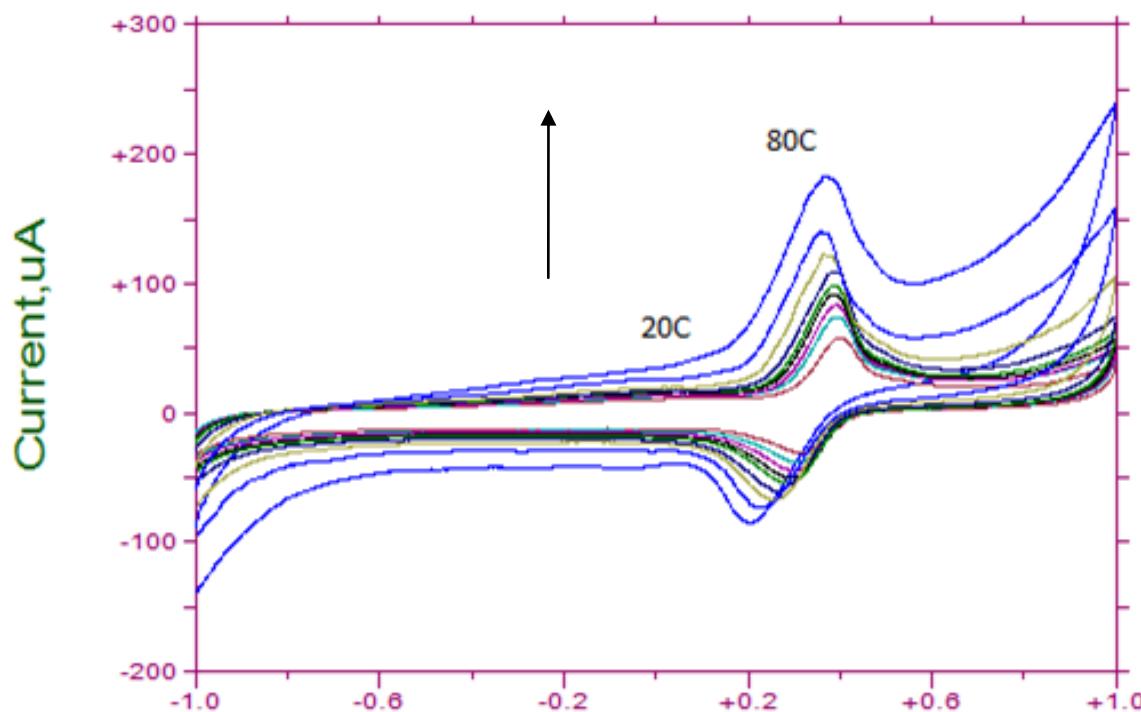


Figure 3. Typical cyclic voltammograms of various temperature 0.1 mM paracetamol at GO modified GC electrode in 0.1 M KH₂PO₄ (pH 4.2), with potential scanning in the positive direction from -1000 to +1000 mV vs Ag/AgCl at a scan rate of 100mV/s.

3.4 Effect of potential cycling

The stability of the Graphene-Oxide/GC modified electrode and its effect on the oxidation current were assessed by continuous potential cycling over the potential range of oxidation current of

paracetamol. Fig 4 shows that the peak remained virtually constant throughout the 10 potential cycles, reflecting the stability of the GO/GC composite modified GCE. This result can be related to the realization of steady condition in solid state cyclic voltammogram and the reaction is in equilibrium condition.

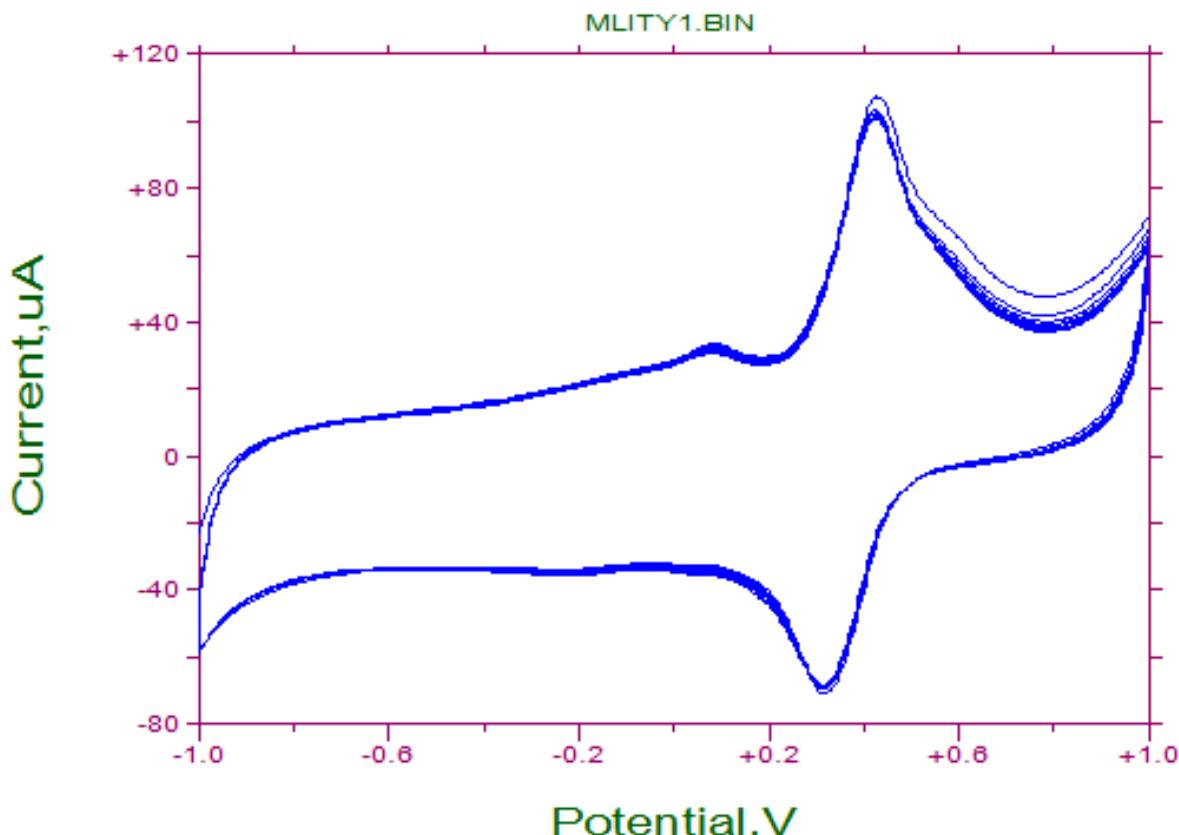


Figure 4. Multiple Cyclic voltammogram of in at pH 4.2, for the GC modified electrode with Graphene-Oxide modified electrode.

3.5 Effect of varying scan rate

The effect of varying scan rates on the cyclic voltammograms of 0.1 mM paracetamol using Graphene-Oxide modified working electrode in 0.1 M KH_2PO_4 supporting electrolyte was studied over scan rate range of 5 – 1000 mV/s. Oxidation currents were observed to increase with scan rate due to heterogeneous kinetics. In the present experiment a linear relationship between $\log i_p$ and $\log v^{1/2}$ is obtained suggesting the diffusion of paracetamol at surface of GO/GCE (Fig 5), which can be expressed by the following equation :

$$\text{Log } i_p = 0.47 \text{ log } v - 0.4339 ; R^2 = 0.9963$$

A slope of 0.4681, which agrees with the theoretical slope of 0.5 for diffusion controlled process, was obtained. [13-14]

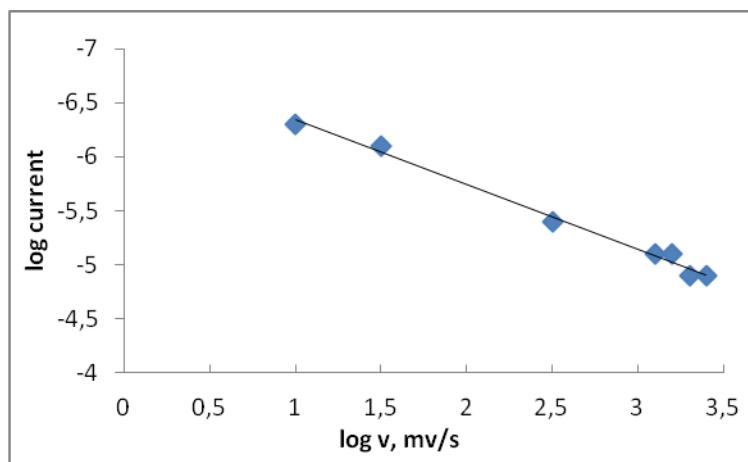


Figure 5. Graph of log peak current versus log scan rate for 0.1 mM paracetamol in 0.1 M KH_2PO_4 (pH 4.2), in different scan rate, for the GC modified electrode with Graphene-Oxide modified electrode.

3.6 Effect of varying paracetamol concentrations

Figure 6 shows the electrochemical oxidation of paracetamol determined over a concentration range of 5×10^{-8} mol L⁻¹ to 1×10^{-6} mol L⁻¹. The calibration plot shows a linear relationship with a correlation coefficient of 0.9950 ($n = 7$), obeying the equation:

$$i_p = 0.010443 \mu\text{A L mol}^{-1} \times [\text{PA}] + 7.3197$$

The formula $3\sigma/\text{slope}$ was employed to calculate detection limit, where σ is the standard deviation of the blank. Under the optimized conditions, the detection limit of this method is 4.869×10^{-8} M. The detection limit was found to be in good agreement with those reported in literature [2, 17, 18].

The DL of paracetamol obtained by GO/GCE appears to be comparable and in some cases more superior to that obtained by the reported chemically modified electrode as shown in Table 1.

Table 1. Comparison of electroanalytical data for paracetamol determination

Electrode	Analytical range	Limits of detection	reference
glassy carbon electrode	$6.6 \times 10^{-6} \sim 1.3 \times 10^{-4}$ mol L ⁻¹		¹¹
C-60-modified electrode	$0.05 \sim 1.5$ mmol L ⁻¹	0.05 mmol L ⁻¹	¹²
nanogold modified indiumtin oxide electrode	$2.0 \times 10^{-7} \sim 1.5 \times 10^{-3}$ mol L ⁻¹	1.8×10^{-7} mol L ⁻¹	¹³
Carbon Nano-tube Composite Film Electrode	$5.0 \times 10^{-7} \sim 1.0 \times 10^{-4}$ mol L ⁻¹	5.0×10^{-8} mol L ⁻¹	¹⁴
Graphene Oxide electrode	5×10^{-8} mol L ⁻¹ to 1×10^{-6} mol L ⁻¹	4.9×10^{-8} M	this work

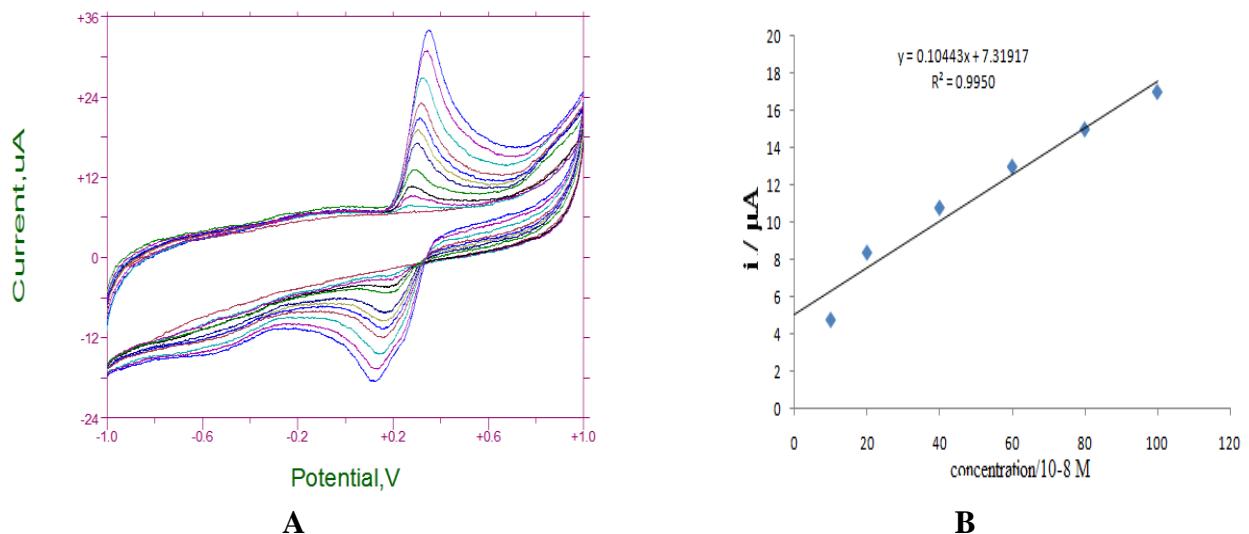


Figure 6. (a) Typical cyclic voltammograms of various paracetamol concentrations at Graphene-Oxide modified electrode, immersed in 0.1 M KH_2PO_4 , pH 4.2, at scan rate of 100 mV/s (b) Calibration graph of paracetamol (Similar conditions as above).

3.7. Scanning Electron Microscopy (SEM)

Before electrolysis (Fig 7a), it was observed that the GO sheets are thin and loosely attached. After electrolysis, the GO sheets seem to come close contact with each other and combined to produce thicker sheets. There also seems to be some root like structure present. It is also apparent that the GO sheets are well uniformly dispersed onto the GCE surface and form a coating on the surface which is also very obvious when seen with the physical eye

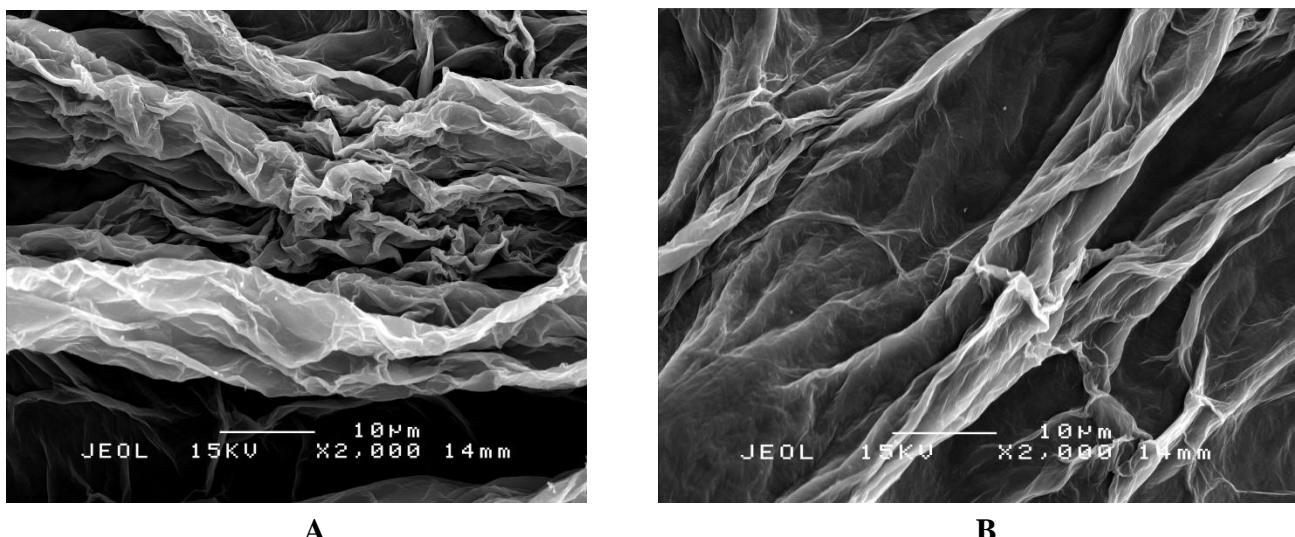


Figure 7. Scanning electron micrographs of GO mechanically attached to a basal graphite electrode (5 mm diameter) and immersed in 0.1 KH_2PO_4 electrolyte (a) before electrolysis (b) after electrolysis with an enlargement of 2000 times

4. CONCLUSION

A sensitive and reliable electrochemical method for detection of paracetamol in real samples using graphene as electrode modifier is proposed. The electrocatalytic behavior of GO/GC was studied by CV. Conclusively, graphene can be used as an advanced carbon –based electrode matrix for the selective determination of paracetamol. Upon modification with graphene, the oxidation peak current of paracetamol was significantly improved due to high catalytic activity and conductivity of graphene. Under the optimized conditions, the detection limit was found to be 4.869×10^{-8} M which is comparable to other electrodes and is of economic significance. Owing to the high sensitivity of graphene-modified GCE, this method may be used for the detection of other compounds in food or biological fluids.

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