

# Differential Pulse Voltammetric Determination of Paracetamol Using Activated Glassy Carbon Electrode

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**Abstract:** The electrochemical property of paracetamol was investigated at a glassy carbon electrode and activated glassy carbon electrode. Differential pulse voltammetry and cyclic voltammetry were used as diagnostic techniques in the determination of paracetamol. The activated glassy carbon electrode exhibited excellent electro-catalytic behaviour for the oxidation of PAR as evidenced by the enhancement of the oxidation peak current and the shift in the oxidation peak potential to less positive values by (13mv) in comparison with a bare GCE. In the present work the activated glassy carbon electrode was prepared by activating 200 s in a time base technique at a potential of 1750 mV. The electrode process of paracetamol was studied and some the experimental parameters which affect the response paracetamol, such as pH, effect of PAR concentration and scan rate on AGC electrode. The analysis of cyclic voltammogram gave fundamental electrochemical parameters including the electroactive surface coverage, the electron transfer coefficient and the heterogeneous rate constant ( $k_s$ ). The variation of scan rate study shows that the system undergoes adsorption controlled process. The equation of the calibration curve was found to be:  $I_p = 0.429C + 6.43$ ,  $R^2 = 0.993$ . The LOD and LOQ for the developed method were determined to be  $8 \times 10^{-8}$  mol L<sup>-1</sup> and  $2.6 \times 10^{-7}$  mol L<sup>-1</sup> respectively. Phosphate buffer pH 7.0 was selected for analytical purpose.

**Keywords:** Paracetamol, Activated Glassy Carbon Electrode, Differential Pulse Voltammetry

## 1. Introduction

Drug control has been on the global agenda for more a century in the world. So, drug analysis is an important tool for drug formulations which has great impact on public health. Hence, the development of simple, sensitive and rapid method to determine the active ingredients in drugs seems essential [1]. From the environmental point of view, pharmaceuticals including antibiotics are a new group of manmade chemicals of concern entering the environment at concentrations such that their health effects are unknown. So, paracetamol is one of the antibiotic drugs that used to fight infections caused by bacteria or other microbes [2].

Paracetamol, N-(4-hydroxyphenyl) acetamide is a widely used analgesic and antipyretic drug [3]. It is one of the most popular and widely used drugs for the treatment of pain and reduction of fever. It occupies a unique position among

analgesic drugs [4]. Generally, paracetamol does not exhibit any harmful side effects, due to its rapidly and completely metabolized. However, the overdose of paracetamol can lead to the accumulation of toxics metabolites, which may cause liver disorder, kidney damage, skin rashes and inflammatory of the pancreas [5]. Paracetamol described as 4-hydroxyacetanilide or N- acetyl-p-aminophenol is known as acetaminophen [7] and its chemical formula, C<sub>8</sub>H<sub>9</sub>NO<sub>2</sub> and its structure is as shown below,

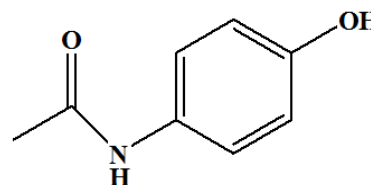


Figure 1. Chemical structure of paracetamol.

The development of simple, sensitive and accurate electroanalytical methods for the determination of paracetamol is very important. The various techniques have been employed for the determination of paracetamol in the body fluids and pharmaceuticals preparations including spectroscopy, chromatography, titrimetry and chemiluminescence [8, 11, 12, 14].

However, most of these techniques suffer from some disadvantages like; high cost, require extraction process, long analysis time, requirement for sample pre-treatment which is time consuming manipulation steps [18], need special training, portable [19], sophisticated instrument and making them unsuitable for routine analysis [15] and also these methods usually involves hydrolysis of paracetamol sample to 4-aminophenol, which the required the formation of a colored complex using an appropriate reagent, which takes a long time to perform [9].

On the other hand electrochemistry offers a number of very attractive advantages such as low cost, easy to manipulate, portable and fast. It has been widely employed in biological matrixes, pharmaceutical and some drugs containing tertiary amine functional group, due to its continuance, sensitivity, reproducibility and selectivity towards many target analytes [19]. Paracetamol is an electroactive compound (contains hydroxyl and NH groups on its aromatic rings) [10] and can be oxidized under suitable conditions, the use of electrochemical detection can be considered appropriate due to its rapid response and high sensitivity.

Many papers have been published about the electrochemical determination of paracetamol based on its oxidation behaviour with different electrodes such as, C<sub>60</sub>-modified glassy carbon electrode [12], Poly (4-vinyl pyridine) multi walled carbon nanotubes modified glassy carbon electrode [8], glassy carbon electrode [13], screen printed graphene electrode [19], gold nanoparticles electrodes [10], Bismuth oxide modified glassy carbon electrode [40] and Ni- modified electrode [39]. These reports showed good detection limits and sensitivity but, the main drawback is the need of extra time through the consuming modification process which usually involves several steps to incorporate the modifier to the substrate and also the costs [19].

In this paper, no study has been reported for determination of paracetamol using activated glassy carbon electrode. Activated glassy carbon-based electrodes usually have a wider potential range than the other solid electrodes because of their broad potential window, low background current; chemical inertness, low cost and suitability for various sensing and detection applications. However, electron transfer rates observed at carbon surfaces are often slower than those observed on noble metal electrodes [6].

## 2. Experimental Part

### 2.1. Apparatus

The electrochemical experiments were carried out in a three electrode systems containing Ag/AgCl as a reference

electrode, platinum wire as a counter electrode, bare glassy carbon electrode and activated glassy carbon electrode as a working electrode. The experiment and processing of data were made using CHI760E electrochemical workstation, CH Instrument (Inc., USA), which was connected to a Dell desktop computer with conventional three electrode configuration. The pH of the all solutions was measured with a JENWAY model 3510 digital pH meter with a combination glass electrode. Digital balance was used for mass measurements. The experiments were conducted in phosphate buffer solution at pH = 7.0 and at room temperature. Cyclic voltammetry and differential pulse voltammetry were used for this study.

### 2.2. Chemicals and Reagents

Pure paracetamol (Addis pharmaceuticals factory, Ethiopia), anhydrous di potassium hydrogen orthophosphate (BDH, England), potassium di hydrogen phosphate (Sigma-Aldrich, Switzerland), sodium hydroxide (BDH, England, India), sulphuric acid and paracetamol tablets (EPHARM) were used in the experiment without any purification. The stock solution of paracetamol was prepared and stored in a refrigerator until used. An aqueous solution was prepared daily of the working days by the dilution of the stock solution with phosphate buffer pH = 7.0. Phosphate buffer solutions (0.1 M KH<sub>2</sub>PO<sub>4</sub> and K<sub>2</sub>HPO<sub>4</sub>) were prepared by using distilled water. Distilled water was used throughout the experiment. All chemicals were of analytical grade.

### 2.3. Preparation of Activated Glassy Carbon Electrode

Before activation, the surfaces of glassy carbon electrode (3mm diameter) was polished to mirror with alumina slurry with a polishing pad and then thoroughly rinses with distilled water. The cleanness of the electrode was checked by a 0.5 M sulfuric acid by running in cyclic voltammetry with a potential window between -800 mV - 800mV at a scan rate of 100 mV/s. Then the GC electrode was activated for 200 s in a time base technique at a potential of 1750 mV in 0.1 M KH<sub>2</sub>PO<sub>4</sub> and K<sub>2</sub>HPO<sub>4</sub> phosphate buffer solution at pH = 7.0 and the GC electrode was activated by running cyclic voltammetry from 0.0 to 700 mV for six cycles. The activated electrode was run in cyclic voltammetry until the voltammogram was stable.

### 2.4. Preparation of Phosphate Buffer and Standard Solutions of the Analytes

For all of the experiments, a mixture of 0.1M K<sub>2</sub>HPO<sub>4</sub> and 0.1M of KH<sub>2</sub>PO<sub>4</sub> buffer solution (pH = 7.0) was used. Concentrated NaOH and HCl solutions were used to adjust the pH of the buffer solutions. Stock solution of paracetamol (1mmol L<sup>-1</sup>) prepared by dissolving 0.075 g of paracetamol in PBS of pH = 7.0. The required amounts of paracetamol working solutions were prepared by diluting the stock solution with phosphate buffer solution supporting electrolyte (pH = 7.0). Standard solutions in tablet were prepared by spiking of the drug in to an aqueous stock solution of

standard paracetamol samples. The stock solution of uric acid was prepared by diluted with phosphate buffer solution.

### 2.5. Sample Preparation from Tablets

Ten tablets were purchased from commercially available pharmaceuticals drug shops (500 mg paracetamol per tablet). Five tablets were accurately weigh using digital balance and finely powder in mortar and pestle. Then an adequate amount of powder which was equivalent to the standard powder was weighed and added into 100 volumetric flasks and diluted with a pH = 7.0 phosphate buffer solution. Then the flask was thoroughly shaken until sample dissolved and the mixture was filled with the buffer solution.

### 2.6. Electrochemical Measurements

Electrochemical determination of paracetamol was carried out in a voltammetric cell 0.1mol L<sup>-1</sup> PBS (pH = 7.0) as a supporting electrolyte solution. The electrochemical behaviour of paracetamol at AGC electrode was investigated using cyclic voltammetry. The determination of paracetamol was carried out by using differential pulse voltammetry (DPV) by scanning the potential in the range from 0.0 to 500 mV at the pulse amplitude of 50mV and pulse repeat time of 0.5 seconds were used. The detection limit was calculated as three times the standard deviation of phosphate buffer solution of paracetamol divided by the slope of the calibration curve and limit of quantification was calculated as ten times of the standard deviation phosphate buffer solution of paracetamol divided by the slope of the calibration curve.

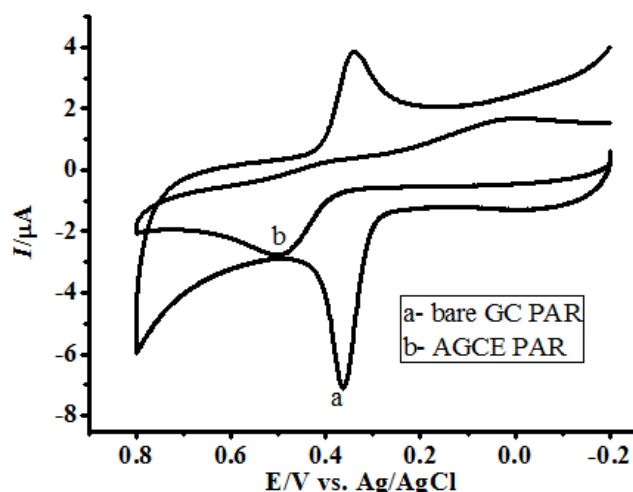
## 3. Results and Discussion

The electrochemical behaviour of paracetamol was examined using cyclic voltammetry at a scan rate of 100 mV/s. Figure 2 shows typical voltammogram of 0.1mmol L<sup>-1</sup> of paracetamol, in phosphate buffer solution pH = 7.0 at a scan rate of 100mV/s recorded at two different working electrodes (i.e. bare glassy carbon and activated glassy carbon electrode. At bare glassy carbon electrode, paracetamol shows quasi-reversible behaviour with relatively weak redox current peaks with high peak potential difference ( $\Delta E_p = 0.476$  V and slow electron transfer behaviour on bare glassy carbon electrode [9].

In comparison to bare glassy carbon electrode, the

response of paracetamol at activated glassy carbon electrode after activated the electrode shows both cathodic and anodic peak current are significantly increased with reducing the over potential by 0.130V. This indicates activation of electrode changes the oxidation of paracetamol from quasi reversible to reversible reaction.

The peak-to-peak separation of activated glassy carbon electrode ( $\Delta E_p = 0.025$ V) is much smaller than that of the bare glassy carbon electrode [10]. The ratio of redox peak current ( $I_{pa}/I_{pc}$ ) was 1.85, which shows the characteristics of irreversible electrode process. However for reversible electrode reaction the ratio of  $I_{pa}$  to that of  $I_{pc}$  is one [7].



**Figure 2.** Cyclic voltammogram of 0.1mmol L<sup>-1</sup> of paracetamol obtained at bare glassy carbon electrode (curve a) and activated glassy carbon electrode (curve b) in 0.1 mol L<sup>-1</sup> PBS at pH = 7.0 with scan rate of 100 mV/s (Background subtracted).

Activated glassy carbon electrode shows a fast electron transfer rate due to good conductivity and a large capacitive current of the electrode. This indicates that the activated glass carbon electrode shows electro-catalytic activity towards paracetamol. To generalized the above discussion the catalytic properties of activated glassy carbon electrode surface caused decrease the over potential of oxidation reaction, increase the sharpness of both cathodic and anodic peak current and the reversibility of electron transfer process [19].

**Table 1.** Peak current and peak potential of Paracetamol on bare and activated glassy carbon electrode taken from the above Figure 2.

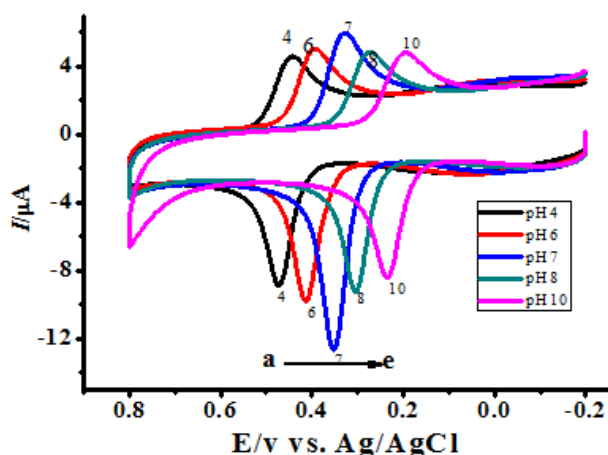
Analytes	Bare glassy carbon electrode			Activated glassy carbon electrode		
	Peak current (μ A)	Peak potential (V)	$\Delta E_p$ (V)	Peak current (μ A)	Peak potential (V)	$\Delta E_p$ (V)
PAR	$I_{pa}$ -2.71	$E_{pa}$ 0.479	0.450	$I_{pa}$ -7.07	$E_{pa}$ 0.36	0.02
	$I_{pc}$ 1.607	$E_{pc}$ 0.29		$I_{pc}$ 3.78	$E_{pc}$ 0.34	

### 3.1. Effect of Operational Parameters

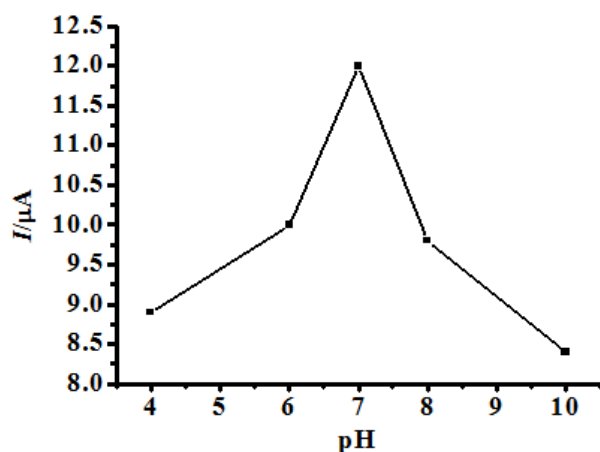
#### 3.1.1. Effect of Solution pH

To optimize the response of activated glassy carbon electrode for paracetamol oxidation, the effect of pH on the electrochemical oxidation was investigated by cyclic

voltammetry technique at different pH using phosphate buffer solution with a pH range of 4 - 10 at a scan rate of 100 mV/s to determine its effect on the catalytic oxidation of 0.1mmol L<sup>-1</sup> paracetamol at activated glassy carbon electrode [20]. As shown Figure 3, the pH of the solution influenced the potential and the currents of both cathodic and anodic peaks of paracetamol.



**Figure 3.** Cyclic voltammogram of 0.1 mmol L<sup>-1</sup> of Paracetamol in 0.1 mol L<sup>-1</sup> PBS at different pH values (4, 6, 7, 8 and 10) with a scan rate of 100 mV/s using activated glassy carbon electrode (Background subtracted).

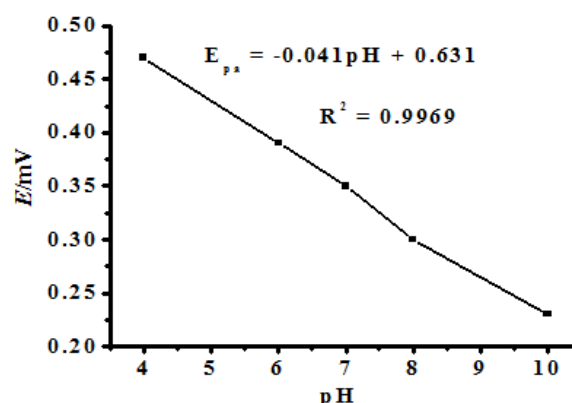


**Figure 4.** The relation between peak current ( $I_{pa}$ ) and pH at a scan rate of 100 mV/s.

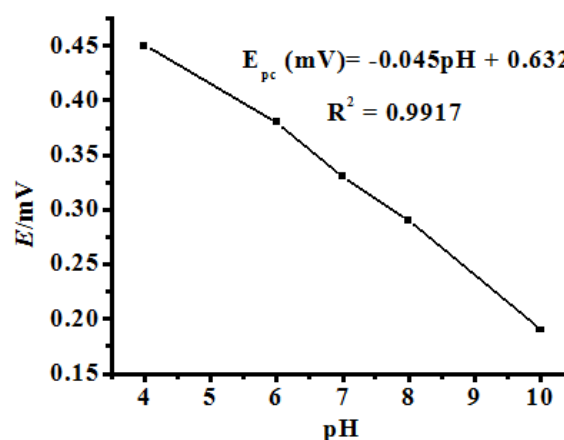
From the above figure, it can be seen that the peak currents increase with increasing pH up to 7.0 and the peak currents slowly decreased from 7-10 (i.e. higher pH values). In addition, Figure 9 also shows the relationship between the peak potential of paracetamol and the pH value. As can be seen that, both oxidation potential ( $E_{pa}$ ) and reduction potential ( $E_{pc}$ ) shift to negatively direction with the increase of pH from 7.0 to 10. This observation is reflects the involvement of protons in the electrode process [39]. Furthermore, the potential was shifted to the direction of more negative potentials with increasing pH values, i.e. to the lower potential, suggesting that the ease of oxidation the protonated molecules [40]. The better sensitivity and shapes of voltammogram (maximum peak current) was observed at pH = 7.0 suggested it as optimal pH value.

Generally, the electrochemical oxidation of paracetamol at activated glassy carbon electrode is pH dependent. At a pH near to 7.0 N-acetyl-p-Quinoneimine exists in its stable and unprotonated form [7]. If the pH was higher than 7, the drugs inclined to decompose, resulting in the decrease of the response. As can be seen, the peak potential for paracetamol oxidation varies linearly with. Therefore, pH = 7.0 was better

for further analysis.



**Figure 5.** The relation between peak potential ( $E_{pa}$ ) and pH at a scan rate of 100 mV/s.

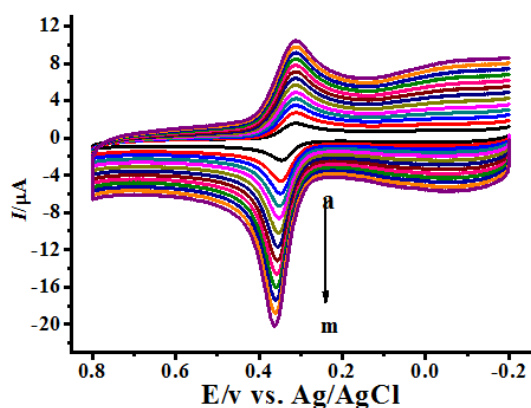


**Figure 6.** The relation between cathodic peak potential ( $E_{pc}$ ) and pH at a scan rate of 100 mV/s using activated glassy carbon electrode.

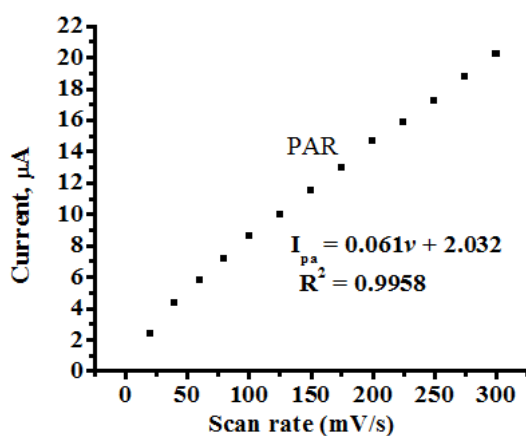
The linear dependence of the peak potential on pH was represented by the equation:  $E_{pa}(V) = -0.041pH + 0.631$  ( $R^2 = 0.9969$ ) and  $E_{pc} (mV) = -0.045pH + 0.632$  ( $R^2 = 0.9917$ ). The slopes of  $-0.045$  V/pH and  $-0.041$  V/pH and according to the equation of  $dE_{pa}/dpH = 2.303mRT/nF$  [17], the ratio of the number of protons and the number of electrons in the oxidation process was calculated to be 0.7, which is close to 1. This indicates that equal number of electrons and protons were involved in the electrochemical oxidation of paracetamol at activated glassy carbon electrode within the studied pH range (scheme 4), which is in agreement with the reported literature [8, 10].

### 3.1.2. Effect of Scan Rate on Peak Current and Peak Potential

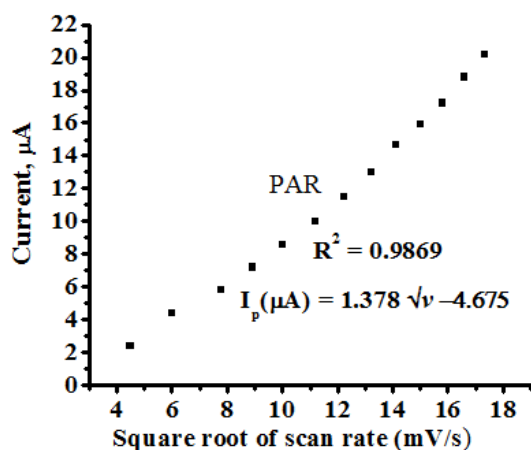
The influence of varying scan rates on the response of paracetamol at activated glassy carbon electrode was investigated by cyclic voltammetry. The effect of scan rate on the oxidation peak current of 0.1 mmol L<sup>-1</sup> paracetamol using activated glassy carbon electrode as working electrode in 0.1 mol L<sup>-1</sup> PBS (pH = 7.0) was studied by varying the scan rate from 20 - 300 mV/s. The resulting voltammogram as shown below in Figure 7.



**Figure 7.** Cyclic voltammogram of 0.1 mmol L<sup>-1</sup> Paracetamol at different scan rates in the range (20, 40, 60, 80, 100, 125, 150, 175, 200, 225, 250, 275 and 300 mV/s) in 0.1mol L<sup>-1</sup> PBS (pH = 7.0) at activated glassy carbon electrode (Background subtracted).



**Figure 8.** Effect of variation of scan rate on the anodic peak current of 0.1 mmol L<sup>-1</sup> of Paracetamol in 0.1mol L<sup>-1</sup> of PBS at pH = 7.0.



**Figure 9.** The dependence of peak current of 0.1 mmol L<sup>-1</sup> of Paracetamol on the square root of scan rate at activated glassy carbon electrode in 0.1mol L<sup>-1</sup> PBS at pH = 7.0.

From the above voltammogram observed that, the oxidation peak current of paracetamol increased linearly as the scan rate increased gradually and the oxidation potential shifted towards more positive potential (i.e. increase over potential) and due to excellent peak response. This indicated that the oxidation of paracetamol is reversible at activated

glassy carbon electrode. The relation between peak current versus scan rate and square root of scan rate were drawn in Figures 8 and 9 respectively.

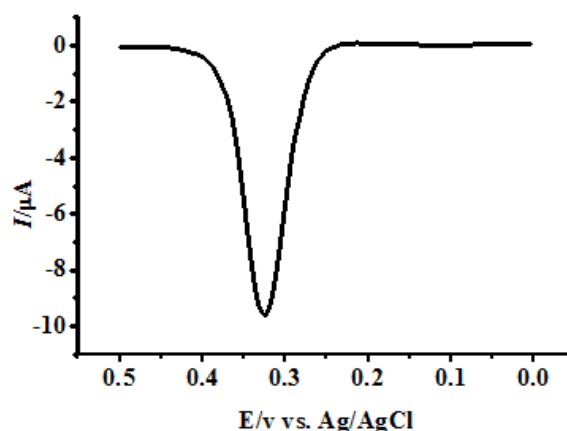
The linear equation of oxidation peak current on both scan rate and square root of scan rate as follows,  $I_{pa} = 0.061v + 2.032$  ( $R^2 = 0.998$ ); and the oxidation peak current increased linearly as the square root of the scan rate,  $\sqrt{v}$ ,  $I_{pa} = 1.37\sqrt{v} - 4.675$  ( $R^2 = 0.9869$ ).

Further evidence for non-diffusion behaviour of paracetamol was obtained, when the working electrode was switched to a medium containing only phosphate buffer solution after being in voltammetric measurements of paracetamol solution, voltammetric signal was observed [7]. This indicates paracetamol shows adsorption controlled process. From these results, a scan rate of 100 mV s<sup>-1</sup> was chosen for further analysis.

### 3.2. Differential Pulse Voltammetric Investigation of Paracetamol Using Activated Glassy Carbon Electrode

To further increase the sensitivity and lower detection limit, a more sensitive technique compared to cyclic voltammetry is differential pulse technique used to detect paracetamol at activated glassy carbon electrode to evaluate calibration characteristics, validation (such as linearity, accuracy of real sample, limit of detection and limit of quantification).

The above voltammogram shows the peak current response in cyclic voltammetry and differential pulse voltammogram was -7.10 and -9.66  $\mu A$  respectively. This shows the peak current enhancement of paracetamol response was better in differential pulse voltammetric than cyclic voltammetry. So, differential pulse voltammetric was better peak current enhancement and good sensitive for the determination of paracetamol at activated glassy carbon electrode. Only one sharp peak was observed at 325mV, which indicates that paracetamol undergoes only one step electrochemical reaction at glassy carbon electrode when the potential was run in the positive direction, i.e., oxidation reaction at 325mV.

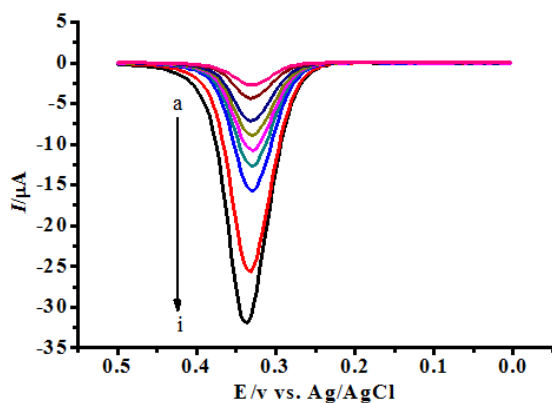


**Figure 10.** Differential pulse voltammogram of 0.1mmol L<sup>-1</sup> Paracetamol in 0.1mol L<sup>-1</sup> PBS (pH = 7.0) at activated glassy carbon electrode with a scan rate of 100mV/s (Background subtracted).



### 3.3. Effect of Concentration and Detection Limit

The effects of varying paracetamol concentration on the differential pulse voltammetric peak current response of paracetamol was studied at activated glassy carbon electrode. The Figure 11 below shows differential pulse voltammogram of Paracetamol from  $1 \mu\text{mol L}^{-1}$  -  $60 \mu\text{mol L}^{-1}$ .



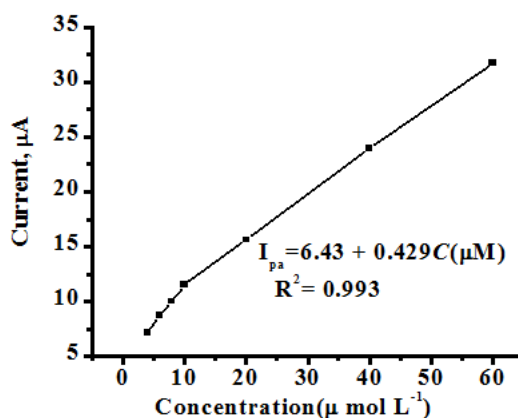
**Figure 11.** Differential pulse voltammogram of Paracetamol at different concentrations range ( $1, 2, 4, 6, 8, 10, 20, 40$  and  $60 \mu\text{mol L}^{-1}$ ) in  $0.1\text{mol L}^{-1}$  PBS pH = 7.0 at the scan rate of  $100 \text{ mV/s}$  (Background subtracted).

The above voltammogram shows the oxidative peak current of paracetamol increases rapidly and linearly with increasing concentration from ( $1$ -  $60 \mu\text{mol L}^{-1}$ ). The resulting differential voltammogram consists of current peaks and the height of these current peaks is directly proportional to the paracetamol concentration [1]. The enhancement of peak current on increasing paracetamol concentration in the above voltammogram is due to the presence of more ions in the solution which makes the flow of electrons easy [7, 22]. The plot of differential pulse voltammetric peak current versus concentrations of paracetamol was found to be in the linear range of  $8$  -  $60 \mu\text{mol L}^{-1}$  with correlation coefficient  $r^2 = 0.996$  with the equation  $I_{pa} (\mu\text{A}) = 6.43 + 0.429 C (\mu\text{mol L}^{-1})$ .

The detection limit of Paracetamol can be calculated by measuring the differential pulse voltammetry of activated glassy carbon electrode without paracetamol 8 times and calculate the standard deviations of 8 repeat measurements. The standard deviation of 8 measurements was  $0.0115$ . The magnitude of detection limit calculated by using the formula;  $\text{LOD} = 3 \delta / m$ , where  $\delta$  represent the standard deviation of blank solution of 8 measurements and  $m$  represents the slope of the calibration curve. The detection limit was found to be  $8 \times 10^{-8} \text{mol L}^{-1}$ .

The limit of quantification was calculated by the equation:  $\text{LOQ} = 10 \delta / m$ . The limit of quantification was found to be  $2.6 \times 10^{-7} \text{mol L}^{-1}$ . The relative standard deviation (RSD) was calculated by standard deviation divided by the mean of 8 repeated measurement times 100. The relative standard

deviation was calculated to be  $1.02\%$ .



**Figure 12.** Plot of peak current versus concentration.

As can be seen from the above figure, the peak currents of paracetamol concentration from  $1$  to  $6 \mu\text{mol L}^{-1}$  was lie outside the straight line. Therefore, the linear range extends only from  $8$  to  $60 \mu\text{mol L}^{-1}$  paracetamol concentration.

### 3.4. Determination of Degree of Recovery of Paracetamol

To determine whether excipients in the tablets interfered or not, the accuracy of the proposed method was evaluated by recovery tests without spiking these samples and also on spiking known standard concentration of paracetamol in these tablets sample. The recovery results of paracetamol obtained by using DPV technique with activated glassy carbon electrode, for all spiked and non-spiked tablet sample have been calculated by using the concentration of spiked sample obtained from the calibration curve minus the concentration of non-spiked sample divided by the concentration of the analytes added to the spiked portion ( $10 \mu\text{mol L}^{-1}$ ) times 100.

$$\% \text{ Recovery} = \frac{S - U}{A} \times 100$$

Where  $S$  represents the spiked sample paracetamol in  $\mu\text{mol L}^{-1}$ ,  $U$  represents un-spiked sample in  $\mu\text{mol L}^{-1}$  and  $A$  represents the concentration of analyte added to the spiked portion ( $10 \mu\text{mol L}^{-1}$ ).

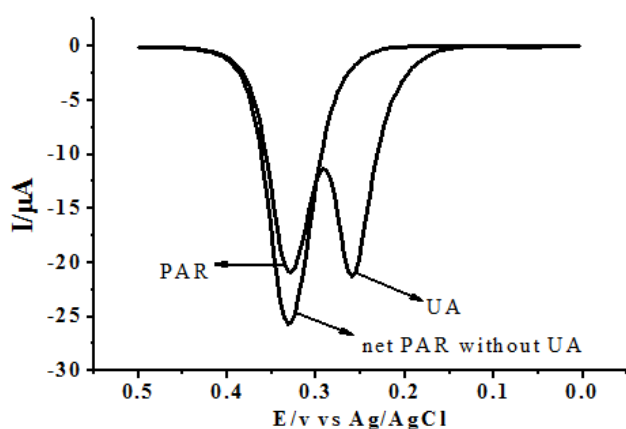
The %recovery of Paracetamol in EPHARM tablets was calculated to be  $105\%$ , indicating that the AGCE could be successfully applied for paracetamol determination in tablets with a good recovery. The analysis of the obtained responses allowed concluding that the drug excipients do not significantly interfere with the proposed method. The amount of paracetamol on pharmaceuticals formulations of EPHARM was good agreement with the tablet manufacturer.

**Table 2.** Determination of paracetamol in formulation EPHARM tablets with activated glassy carbon electrode.

Analyte	Concentration expected ( $\mu\text{mol L}^{-1}$ )	Concentration found ( $\mu\text{mol L}^{-1}$ )	% Recovery
EPHARM	40	40.6	105
	50	51.1	

### 3.5. Interference Study on the Behaviour of Paracetamol.

Paracetamol generally suffers from the interferences such as p-aminophenol, caffeine, ascorbic acid, uric acid and glucose [23, 24]. Hence, in this study a systematic study of interference due to the presence of uric acid only [12, 32, 36]. The interference uric acid was examined on activated glassy carbon electrode on the determination of paracetamol. The oxidation potential of Paracetamol is the same as that of uric acid, 0.3V and that of uric acid is very close at, 0.2 V. The voltammetric current response of successive addition PAR were recorded in Figure 13, using activated glassy carbon electrode in PBS (pH = 7.0), containing equal amount of 0.1mmol L<sup>-1</sup> paracetamol and 0.1mmol L<sup>-1</sup> uric acid to check the selectivity of the method in the presence of interference.



**Figure 13.** Differential pulse voltammogram of 0.1 mol L<sup>-1</sup> of PBS (pH = 7.0) containing 0.1 mmol L<sup>-1</sup> Paracetamol and 0.1mmol L<sup>-1</sup> uric acid using activated glassy carbon electrode at a scan rate of 100 mV/s (Background subtracted).

As shown the above figure, two completely resolved peaks are observed at activated glassy carbon electrode and the E<sub>p</sub> of uric acid was observed at positive potential (~25 mV) with activated glassy carbon electrode also the potential peak to separation of the two analytes were 90 mV. The well-defined peak of paracetamol was obtained at activated glassy carbon electrode with good peak separation from Uric acid [12, 28, 35]. Generally, the above voltammogram was observed that Uric acid affect peak current for paracetamol compared with paracetamol without Uric acid under the potential range used (i.e decrease the peak current and causes to the broadness of the peak of paracetamol), but do not affect the peak potential of paracetamol.

The percent changes in the peak current response of Uric acid was 2.02%, suggested that Uric acid do not significantly interfere in the determination of paracetamol.

### 3.6. Comparison of the Proposed Method with Other Methods

The determination of paracetamol in this study is compared to other methods as summarised in table 3. As can be seen that the determination of PAR in different electrode such as, nano-gold modified carbon paste electrode [21, 32], C<sub>60</sub>-modified glassy carbon electrode [12, 33], Poly (4-vinylpyridine/multi-walled carbon nanotubes modified glassy carbon electrode [8], glassy carbon electrode [13, 37] and Poly (3, 4-ethylenedioxythiophene modified glassy carbon electrode [9]. This electrode were provides a reasonable analytical performance and good detection limit. But the activated glassy carbon electrode offers easy to activate with a potential and rapid electrode preparation compared to other electrodes.

**Table 3.** Comparison between the results of the present study and the studies recently reported in literature.

Electrodes	Techniques	Linear dynamic Range	Detection limit	References
NiHCFMCPE	CV	5×10 <sup>-4</sup> -7.5×10 <sup>-3</sup> M	8.89×10 <sup>-5</sup> M	[7]
PEDOT/GCE	DPV	1.5 – 150 μM	1.3 μM	[9]
PolyAniBMCPE	DPV	0.1 – 0.8 μM	1.179 μM	[10]
C <sub>60</sub> -modified GCE	DPV	0.05 -1.5 mM	0.05mM	[12]
GCE	DPV	4×10 <sup>-6</sup> - 1×10 <sup>-4</sup> M	3.69×10 <sup>-7</sup> M	[13]
GNMCPE	DPV	5×10 <sup>-8</sup> -2.7×10 <sup>-4</sup> M	1.46×10 <sup>-8</sup> M	[17]
SPGrE	CV	0.1-50 μM	20nM	[19]
AGCE	DPV	8 - 60 μM	8 × 10 <sup>-8</sup> M	The present study

## 4. Conclusions

In the present study, an easily activated glassy carbon electrode was used to investigate the behaviour of paracetamol. The reported activated electrode significantly improved the response of Paracetamol and clearly demonstrates the excellent electro-catalytic properties of the activated glassy carbon electrode toward the oxidation of paracetamol. Compared to other modified electrode, the potential activated glass carbon electrode was easily activated by applied potential and no need steps to activate. But the chemically modified glassy carbon electrode is the

need of extra time through the consuming modification process which usually involves several steps to incorporate modifier to the substrate and also the costs.

The proposed method is clean, easy to set up (no need of special training) and furthermore, it does not require any expensive reagents apart from a simple buffer solution, and more time efficient. The activated glassy carbon electrode showed a linear response range between 8 – 60 μmol L<sup>-1</sup>, with a detection limit of 8.0 × 10<sup>-8</sup> mol L<sup>-1</sup>. The proposed method was applied for paracetamol determination in EPHARM commercial tablets with a recovery of 105%.

## Conflicts of Interest

The authors declare no conflict of interest.

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