



# **NATIONAL UNIVERSITY OF LESOTHO**

**FACULTY OF SCIENCE AND TECHNOLOGY**

**DEPARTMENT OF CHEMISTRY AND CHEMICAL**

**TECHNOLOGY**

**TITLE: Voltammetric Determination of Paracetamol with  
Poly (3, 4-Ethylenedioxythiophene) PEDOT modified  
Glassy Carbon Electrode**

**BY: SETUBATUBA.T.A**

**SURPERVISOR: PROF. H. ALEMU**

## **Acknowledgements**

The most sincere thanks must be given to Almighty Lord (God) for the special combination of talents as well as inspiration and creativity He has given me to make this project to become a reality. I convey my gratitude to Professor H.Alemu who has been my supervisory support in pursuing the success of this project. Not forgetting the support from my colleagues for their words of encouragement during perilous encounters with the project constraints. I highly appreciate the supportive advices from parents and friends.

## ABSTRACT

The voltammetric oxidation of paracetamol on poly (3, 4-Ethylenedioxythiophene) PEDOT modified glassy carbon electrode was explored in 0.1M sodium acetate buffer solution by using cyclic and differential pulse voltammetry. Cyclic and differential pulse voltammetry studies indicated that oxidation of paracetamol at the electrode surface as a two-electron reversible step and fundamentally controlled by diffusion. A quasi-reversible redox process of paracetamol at modified electrode was obtained and the over-potential of paracetamol decreased significantly compared with that at bare electrode. PEDOT modified electrode showed excellent performance for detecting paracetamol in the linear detection range between  $9.99 \times 10^{-6}$  to  $3.38 \times 10^{-4}$  M, with a detection limit of  $4.7 \times 10^{-6}$  M and a sensitivity of 0.043 A/M. The method was then successfully utilised for the determination of paracetamol in a real samples of Panado tablets and Ibupain capsule with recoveries of 99.1% and 80.7% respectively for each sample.

## Table of Contents

Acknowledgements.....	2
ABSTRACT.....	3
1.1 Definition and use.....	6
1.2. Synthesis .....	6
1.3. Adverse effect (Overdose) .....	7
1.4. Quantity reduction of paracetamol .....	7
1.5. Previous methods used in paracetamol determination .....	8
1.6. Conducting polymers .....	9
1.7. PEDOT .....	10
1.8. Voltammetric Techniques.....	11
1.8.1 General Information .....	11
1.8.2. Cyclic Voltametry .....	12
1.8.3. Differential Pulsed Voltammetry (DPV) .....	14
2. EXPERIMENTAL .....	15
2.1 Apparatus.....	15
2.2. Reagents and solutions .....	16
2.3. Preparation of PEDOT modified GC electrode.....	16
2.4. Sample preparation .....	16
2.5. Electrochemical measurements.....	16
3. RESULTS AND DISCUSSION.....	17
3.1. Preparation of PEDOT modified GCE .....	17
3.2. Electrochemical behavior of paracetamol on PEDOT/ GCE .....	17
3.3. Effect of scan rate .....	19
3.4. Effect of pH .....	20
3.5. Analytical Application .....	22
3.5.1. The linear range and detection limit.....	22
3.5.2. Determination of samples .....	22
3.6. Interference Study .....	24
5. REFERENCE.....	26

Figure 1: Synthesis of paracetamol.....	6
Figure 2: The redox mechanism of ACOP. ....	8
Figure 3: PEDOT .....	11
Figure 4: A typical cyclic voltammogram .....	13
Figure 5: A typical differential pulse voltammogram.....	14
Figure 6: A BAS100B Electrochemical Workstation .....	15
Figure 7: Cyclic voltammograms, at scan rate 10 V/s of PEDOT growth from solutions consisting of: a) 10.0 mM EDOT and 0.1 M TBAPC in acetonitrile, during 30 cycles. ....	17
Figure 8: Cyclic voltammograms of $1 \times 10^{-4}$ M paracetamol in 0.1M Sodium Acetate buffer solution pH=3 at a scan rate of 100mV/s on a bare GCE (b), on PEDOT modified GCE (c) and of base electrolyte (a).....	18
Figure 9: (a) Cyclic voltammograms of $1 \times 10^{-4}$ M paracetamol in phosphate buffer pH = 7.0 with different scan rates. (b) The linear relationship of $i_{pa}$ vs $v^{1/2}$ .....	19
Figure 10: (a) Differential pulse voltammograms of $1 \times 10^{-4}$ M paracetamol in 0.1 sodium acetate buffer at different pH (a - i). (b) Plot of $E_{pa}$ versus pH and (c), $i_{pa}$ versus pH. ....	21
Figure 11: (a) DPV of paracetamol on PEDOT modified GCE at different paracetamol concentrations (b) The relationship of current versus concentration .....	22
Figure 12: (a) Recovery study of paracetamol in Ibupain using DPV with modified electrode. (b) Calibration curve of paracetamol in Ibupain using standard addition method.....	23
Figure 13: (a) Recovery study of paracetamol in Panado tablet using DPV with modified electrode.(b) Calibration curve of paracetamol in Panado tablet using standard addition method. ....	24
Table 1: Effect of interferences on DPV response for paracetamol at PEDOT modified GCE.....	25

## 1. INTRODUCTION

### 1.1 Definition and use

Paracetamol, chemically known as N-acetyl-*p*-aminophenol or acetamoniphen (an acylated aromatic amide) is a widely used analgesic (pain reliever) and antipyretic (fever reducer) drug. It is used for therapeutic purposes. For instance, it is applied to reduce fever, relieve coughing, colds and pain including muscular aches, chronic pain, migraine headache, backache and toothache [1]. Its functional mechanism can be generalized as elevating the ache threshold so it can relieve pain via its regulation on thalamencephalon it helps to defervesce. The analgesic-antipyretic effect of paracetamol is similar to aspirin but paracetamol is normally preferred as an alternative to patients who can not tolerate aspirin (sensitive to acetylsalicylic acid) [2].

### 1.2. Synthesis

Industrial preparation of paracetamol usually proceeds from nitrobenzene. In the laboratory, paracetamol is easily prepared by nitrating phenol with sodium nitrate, separating the desired *p*-nitrophenol from the *ortho*- byproduct, and reducing the nitro group with sodium borohydride. The resultant *p*-aminophenol is then acetylated with acetic anhydride. In this reaction, phenol is strongly activating, thus the reaction requires only mild conditions [3].

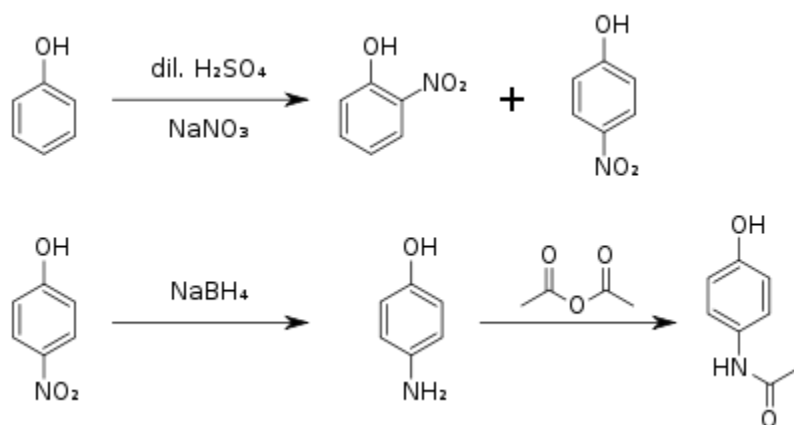


Figure 1: Synthesis of paracetamol

### **1.3. Adverse effect (Overdose)**

Generally, limited or standard use of paracetamol does not exhibit any harmful side effects. However if abused or overdosed, it would be extremely harmful and most common syndromes are liver disorder, skin rashes and inflammation of the pancreases. Also the product of hydrolytic degradation of paracetamol is 4-aminophenol which can be found in pharmaceutical preparations as a degradation product of paracetamol or a synthetic intermediate which can be dangerous and cause teratogenic effect and nephrotoxicity [4]. For instance frequent use of paracetamol in late pregnancy increases the risk of wheezing in the unborn. A case study by MacDonald [5], showed that, in Britain, paracetamol is one of the key factors which may cause the death of the acute liver illness to patient who just had liver transplant operation.

### **1.4. Quantity reduction of paracetamol**

In June 2009, a U.S. Food and Drug Administration (FDA) advisory committee recommended that new restrictions should be placed on paracetamol usage in the United States to help protect people from the potential toxic effects. The maximum dosage to be consumed at any given time would be decreased from 1000 mg to 650 mg, while combinations of paracetamol and narcotic analgesics would be prohibited. Committee members were particularly concerned by the fact that the present maximum dosages of paracetamol had been shown to produce alterations in hepatic function.

On January 13, 2011, the FDA asked manufacturers of prescription combination products containing paracetamol to limit the amount of paracetamol to no more than 325 mg per tablet or capsule and began requiring manufacturers to update the labels of these products to warn of the potential risk for severe liver damage. Manufacturers will have three years to limit the amount of acetaminophen in their prescription drug products to 325 mg per dosage unit. The FDA also is requiring manufacturers to update labels of all prescription combination acetaminophen products to warn of the potential risk for severe liver injury [6].

## 1.5. Previous methods used in paracetamol determination

It is thus, vital to control the amount of paracetamol in a given pharmaceutical formulation in quality control of pharmaceutical industries. It is very important to develop simple, sensitive and accurate methods for detecting active ingredients since drug monitoring plays an important role in drug quality control and this has a great impact on public health. Various analytical methods have been reported for determination of paracetamol in pharmaceutical tablets and biological fluids (urine, blood or plasma) including spectrophotometry [7], chemiluminescence [8], liquid chromatography, capillary electrophoresis [9] and enzyme based assay methods [10]. However, these methods usually involve the hydrolysis of paracetamol, which require the formation of a colored complex using suitable reagent, which takes a long period of time to perform. Besides time-consuming, these methods have some limitations such as high cost, detection limit and low sensitivity.

As a result, electrochemical method, because of its quick response, relatively high sensitivity, selectivity on determination of trace level analyte, as well as its ability to be miniaturized was used as an alternative to the above mentioned methods. This method was considered because paracetamol is an electroactive compound hence it can be oxidized electrochemically. Electroanalytical determination of paracetamol is based on its oxidation to *N*-acetyl-*p*-quinoneimine (shown below), first described and studied by Kissinger et al [11].

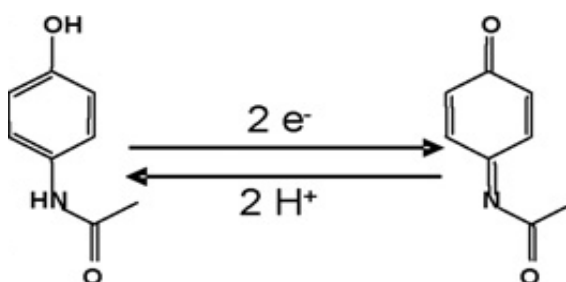


Figure 2: The redox mechanism of ACOP.

The previous electrochemical researches involving paracetamol were primarily performed on bare electrode. However, the oxidation of paracetamol at bare electrode resulted in electrode surface contamination (fouling), due to the adsorption of oxidized product which results in poor selectivity and reproducibility and unstable analytical signals [12]. Also the direct redox



reactions of these species at the bare electrode are irreversible and therefore require high potentials. To overcome these difficulties, bare electrodes are chemically modified.

Various electrodes have been used for the determination of acetaminophen and include modified glassy carbon, boron-doped diamond, carbon ionic liquid, modified electrode surface with zirconium alcoxide porous gels and carbon-coated nickel magnetic nanoparticles, gold nanoparticle modified carbon paste, gold electrodes modified with self assembled monolayer and multi-walled carbon nanotubes modified electrodes. However, electronically conducting polymers (CPs) have been used for surface modification of bare electrodes. The slow electron transfer kinetics on bare electrode is substantially changed by modifying the surface of the electrode which speeds up the electron transfer kinetics [13].

## 1.6. Conducting polymers

Electronically conducting polymers have conjugated  $\pi$ -electron structures that are characterized by a high electrical conductivity and mechanical flexibility. This offers a good electro catalytic behavior, which explains their use as transducers in the preparation of efficient electrochemical sensors. CPs have been extensively studied as electrode modifiers in order to improve the physico-chemical properties of bare electrode. In particular, they are often successfully employed as redox-mediators toward several analytes, significantly enhancing sensitivity and selectivity of the analytical detection, and even lowering the detection limit. They also exhibit anti-fouling properties, which is very important for achieving satisfactory repeatability of the electrochemical response [14].

In many studies, electrodes modified with conducting films of polymers, polythiophene (and its derivatives), polyaniline and polypyrrole have been used. Thin films of CPs can be easily synthesized onto the electrode surface by chemical or electrochemical methods [15]. Preparation of polymer films by oxidation and electropolymerization of aromatic compounds (aniline, phenol, benzene, and their derivatives) and of heteroaromatic compounds (pyrrol, thiophene, and their derivatives) has been widely used in electrode surface modification as a mean to obtain

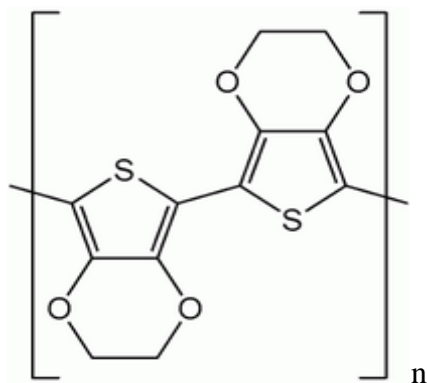
interesting electrode properties. The increasing development of new electrode materials has motivated the electropolymerization study of new organic molecules [16].

Electropolymerization is a good approach to immobilize polymers to prepare polymer modified electrodes (PMEs) as adjusting the electrochemical parameters can control film thickness, permeation and charge transport characteristics. CPs physico-chemical properties strongly depend on the electropolymerization conditions such as solvent type, supporting electrode, electrode material, polymerization potential and electropolymerization method. Polymer-modified electrodes have many advantages in the detection of analytes because of its selectivity, sensitivity and homogeneity in electrochemical deposition, strong adherence to electrode surface and chemical stability of the film. Selectivity of PMEs as a sensor can be attained by different mechanisms such as size exclusion [17], ion exchange [18], hydrophobicity interaction and electrostatic interaction [19].

Recently, conducting polymers doped with various anions have been extensively studied due to their improved electrocatalytic, electroreleasing and electrochromic properties. For instance, it is possible to prepare polyaniline films containing ferricyanide, which exhibits potentiometric response to ferricyanide ions [19]. The incorporation of various ions in conducting polymer films, aiming to produce robust and highly conducting coatings capable of fast electron transfer during redox reactions, is based on the electrostatic stabilization and attraction between the positively charged polymer backbone and the negatively charged doping ions.

### **1.7.PEDOT**

Among different CPs, great attention has been recently devoted to poly (3, 4-ethylenedioxythiophene), PEDOT. PEDOT is a conducting polymer based on 3, 4-ethylenedioxythiophene, EDOT monomer and has the backbone structure shown below;



**Figure 3: PEDOT**

Advantages of this polymer are optical transparency in its conducting state, high stability and moderate band gap and low redox potential [20]. Moreover, the presence of dioxyalkyl residues on the  $\beta$ -thiophene positions strongly reduces the potential at which  $\pi$ -doping occurs (-0.05V), with respect to many other polythiophene derivatives.

## 1.8.Voltammetric Techniques

### 1.8.1General Information

Voltammetric methods are the most effective and versatile electrochemical techniques used for the mechanistic study of redox system. In this method, information about the analyte is obtained by measuring current as the potential is varied. The heart of this electrochemical technique is the potentiostat. A potentiostat is a device which will apply a potential across a pair of electrodes and simultaneously measures the current which flows through a solution of the analyte [21]. A potentiostat controls the potential between working electrode and reference electrode while current flows between working electrode and auxiliary electrode.

The three-electrode method is the most widely used because the electrical potential of reference does not change easily during the measurement. This method uses a reference electrode, an electrode which has a stable and well-known electrode potential, working electrode (the electrode at which the analyte is oxidized or reduced), and counter electrode (also called the

secondary or auxiliary electrode). The auxiliary electrode passes all the current needed to balance the current observed at the working electrode. Electrolyte is usually added to the test solution to ensure sufficient conductivity. The combination of the solvent, electrolyte and specific working electrode material determines the range of the potential [22].

The different voltammetric techniques that are used are distinguished from each other primarily by the potential function that is applied to the working electrode to drive the reaction, and by the material used as the working electrode. Cyclic voltammetry and differential pulse voltammetry are important types of voltammetric techniques used for the determination of pharmaceutical interest.

### 1.8.2. Cyclic Voltammetry

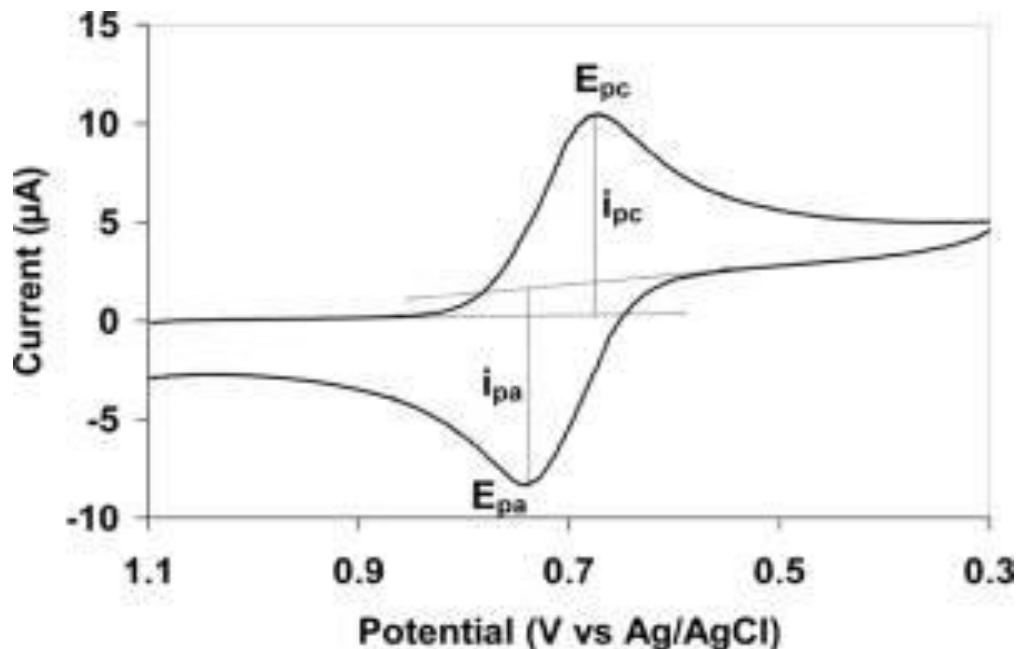
Cyclic voltammetry is one of the commonly used electrochemical techniques and is based on linear potential waveform, that is, the potential is changed as a linear function of time. The rate of change of potential with time is referred to as scan rate. The potential range is scanned starting at the initial potential and ending at the final potential. It offers a rapid location of redox potentials of the electroactive species and convenient evaluation of the effect of media upon the redox process. It also provides qualitative information about electrochemical processes under various conditions. The important parameters for a cyclic voltammogram are the peak potentials  $E_p$  and peak currents  $i_p$ , which are measured using the peak parameters operation [23].

The peak current,  $i_p$ , for a reversible couple is described by the Randles-Sevcik equation:

$$i_p = (2.69 \times 10^5) n^{3/2} A C D^{1/2} v^{1/2} \quad (1)$$

where  $n$  is the number of moles of electrons transferred in the reaction,  $A$  is the area of the electrode ( $\text{cm}^2$ ),  $C$  is the analyte concentration (in  $\text{moles}/\text{cm}^3$ ),  $D$  is the diffusion coefficient ( $\text{cm}^2 \text{ s}^{-1}$ ), and  $v$  is the scan rate of the applied potential ( $\text{V s}^{-1}$ ) [22,23]. From this equation, the current is directly proportional to the concentration and increases with square root of scan rate.

A typical cyclic voltammogram recorded for a reversible single electrode transfer reaction is shown in below.



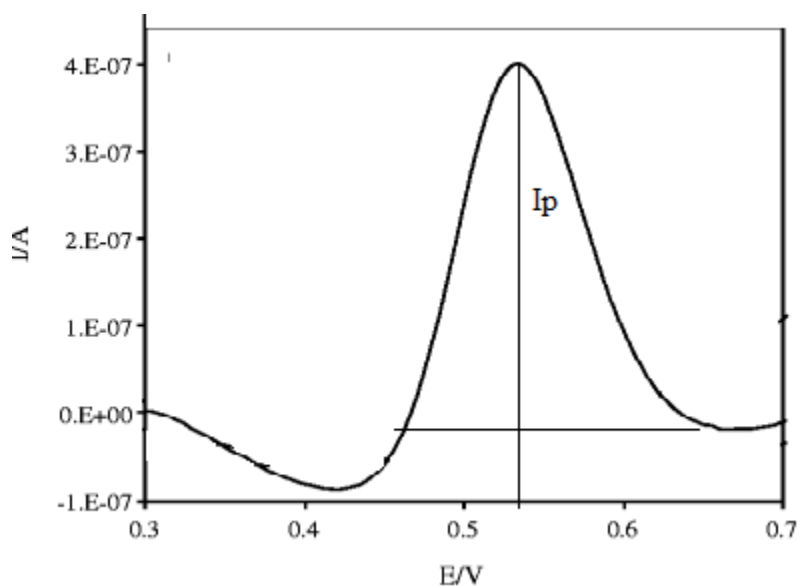
**Figure 4: A typical cyclic voltammogram**

As the waveform shows, the forward scan produces a current peak for any analytes that can be reduced through the range of the potential scan. The current will increase as the potential reaches the reduction potential of the analyte, but then falls off as the concentration of the analyte is depleted close to the electrode surface. As the applied potential is reversed, it will reach a potential that will reoxidize the product formed in the first reduction reaction, and produce a current of reverse polarity from the forward scan. This oxidation peak will usually have a similar shape to the reduction peak. As a result, information about the redox potential and electrochemical reaction rate of the compound is obtained.

### 1.8.3. Differential Pulsed Voltammetry (DPV)

DPV is an extremely useful technique for measuring trace levels of organic and inorganic species. In (DPV), a direct current potential, which is increased linearly with time, is applied to an electrochemical cell. One advantage of the derivative-type voltammogram is that individual peak maxima can be observed for substances with half-wave potentials differing by as little as 0.04 to 0.05 V. More important, however, differential pulse voltammetry increases the sensitivity of the voltammetric method by about three orders of magnitude. The great sensitivity of DPV can be attributed to two sources. The first is an enhancement of the faradaic current, and the second is a decrease in the nonfaradaic charging current [24].

The differential pulse voltammogram consist of current peaks, the height of which is directly proportional to the concentration of the corresponding analyte.



**Figure 5: A typical differential pulse voltammogram**

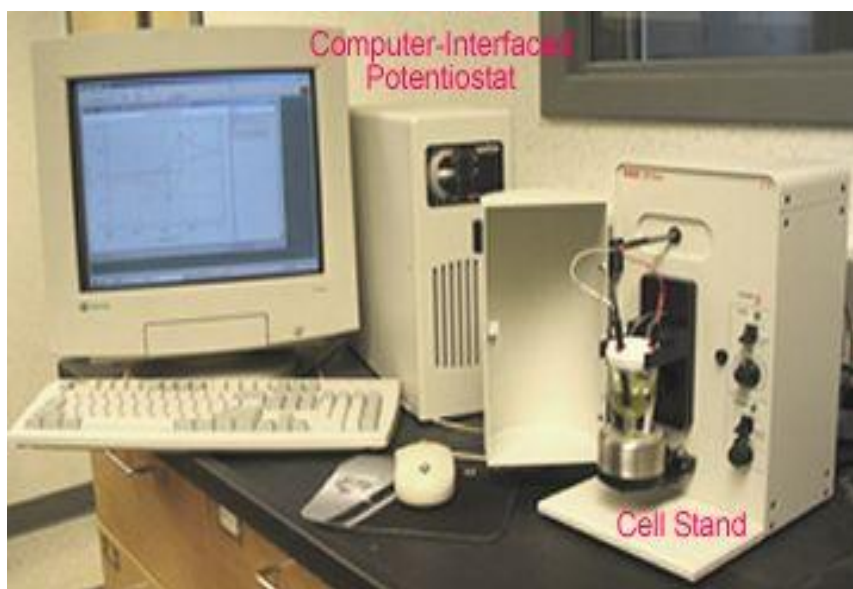
Simple, precise and sensitive, cyclic voltammetric and differential pulse voltammetric methods utilizing a modified glassy carbon electrode vs. saturated calomel (Hg/ Hg<sub>2</sub>Cl<sub>2</sub>) electrode for the assay of acetaminophen is reported. This report shows the preparation and electrocatalytic

application of PEDOT modified GC electrode. This method is based on modifying a GC electrode with PEDOT using electropolymerisation of EDOT and then studies its electrocatalytic activity towards the electrochemical oxidation of paracetamol. The method developed was applied for the determination of paracetamol in commercial samples.

## 2. EXPERIMENTAL

### 2.1 Apparatus

All the voltammetric measurements were done using a Bioanalytical Systems (BAS 100B) voltammetric analyzer controlled by a computer. The three-electrode system was used for measurements, with PEDOT modified glassy carbon electrode as the working electrode, a platinum wire served as the counter electrode and saturated calomel being the reference electrode. The pH of the buffer solution was measured with a pH meter. The schematic diagram of BAS 100B analyzer connected to a computer system together with the three electrode cell is shown below:



**Figure 6: A BAS100B Electrochemical Workstation**

A small magnetic stirrer was used to provide the convective transport during the electrochemical cleaning of the electrode also it was employed to stir the solution to ensure the reproducibility of the experiments by ensuring that there is unevenly distribution of ions within the solution hence the oxidation process is enhanced.

## **2.2. Reagents and solutions**

Paracetamol, EDOT, tetrabutylammonium perchlorate ( TBAPC), acetonitrile, phosphate buffer solution was comprised of 0.1M disodium hydrogen phosphate and 0.1M sodium dihydrogen phosphate and pH was adjusted with NaOH and HCl, stock solutions of 0.1M sodium acetate were prepared using deionised water and pH was adjusted by adding acetic acid and NaOH. Deionised water was used throughout the experiment.

## **2.3. Preparation of PEDOT modified GC electrode**

Before modification, the bare GC electrode was polished with 0.05 $\mu$ m alumina slurry and then cleaned with deionised water. 10mM EDOT was added to 0.1M TBAPC in acetonitrile. Then PEDOT was electrodeposited on the bare GC electrode by potential cycling between -0.9 to 1.5V for thirty cycles. After electropolymerization, the PEDOT modified electrode was washed with deionised water.

## **2.4. Sample preparation**

A table (500mg paracetamol) was accurately weighed and finely powdered in a mortar. An adequate amount of the powder was weighed and dissolved in 0.1M sodium acetate (pH 3.0).

## **2.5. Electrochemical measurements**

The electrochemical behavior of paracetamol and its determination at bare and PEDOT modified GC electrode was investigated using cyclic voltammetry and differential pulse voltammetry.



### 3. RESULTS AND DISCUSSION

#### 3.1. Preparation of PEDOT modified GCE

PEDOT films were potentiodynamically prepared on GCE from 10 mM EDOT and 0.1 M TBAPC in acetonitrile, being representative cyclic voltammograms shown in Figure 5. The continuous increase of the current with the number of cycles reveals the formation and expansion of a conducting phase at the electrode surface.

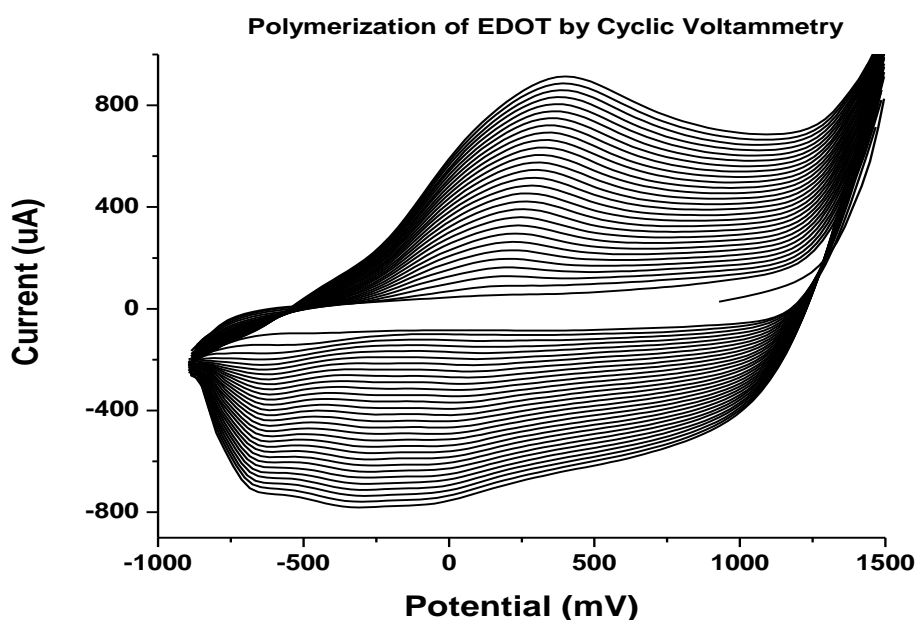


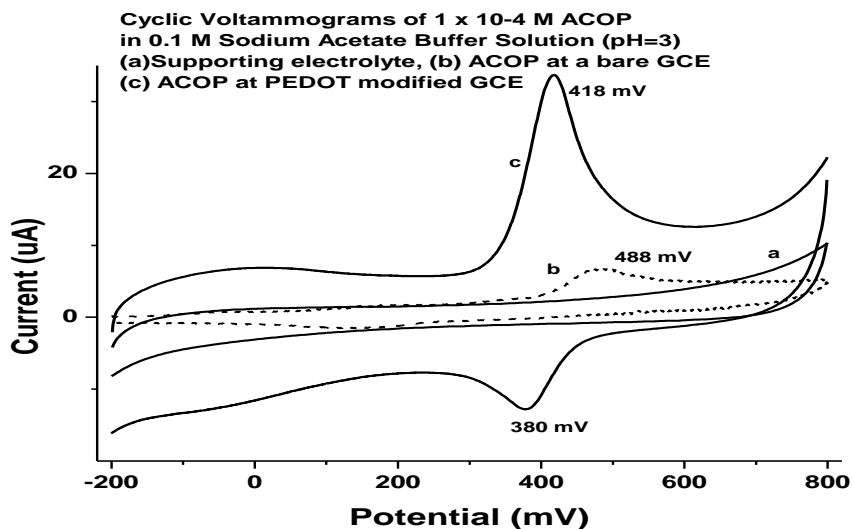
Figure 7: Cyclic voltammograms, at scan rate 10 V/s of PEDOT growth from solutions consisting of: a) 10.0 mM EDOT and 0.1 M TBAPC in acetonitrile, during 30 cycles.

#### 3.2. Electrochemical behavior of paracetamol on PEDOT/ GCE

A CV was used to investigate the electrochemical behavior of  $1 \times 10^{-4}$  M paracetamol on a bare GCE and on PEDOT modified GCE in 0.1M Sodium Acetate buffer solution pH= 3.0 at a scan rate of 100mV/s. At bare GCE, figure 5(b)-dotted line, paracetamol showed an irreversible

behavior with relatively weak redox current peaks at anodic peak potential,  $E_{pa} = 488\text{mV}$ . However, as could be seen from figure 5(c) (solid line), paracetamol exhibited a pair of well-defined quasi-reversible reduction-oxidation peaks with  $E_{pa} = 418\text{mV}$  and  $E_{pc} = 380\text{mV}$  with  $E(E_{pa} - E_{pc}) = 38\text{mV}$ . The over-potential of paracetamol on PEDOT modified GCE became lower than that on bare GCE. This indicated that PEDOT can greatly enhance electron transfer rate and reduce the over-potential. Hence the PEDOT modified GCE displayed very good electrocatalytic property for the redox reaction of paracetamol.

Moreover, it could be seen from Fig. 5c that there is a large background current at the PEDOT modified GCE, which is caused by a larger surface area of the PEDOT film on the GCE. That is, PEDOT enlarged the effective surface area of the electrode and also proved that PEDOT had been successfully modified onto the bare electrode surface



**Figure 8: Cyclic voltammograms of  $1 \times 10^{-4}$  M paracetamol in 0.1M Sodium Acetate buffer solution pH=3 at a scan rate of 100mV/s on a bare GCE (b), on PEDOT modified GCE (c) and of base electrolyte (a).**

### 3.3. Effect of scan rate

The effect of scan rate on the oxidative and reductive peak currents of  $1 \times 10^{-4}$  M paracetamol at the surface of PEDOT modified GCE in a 0.1 M phosphate buffer solution pH 7.0 was studied. Figure 6(a) shows the cyclic voltammograms of paracetamol obtained in the range of 10–300 mV/s in order to investigate whether or not the redox behaviour of paracetamol was due to paracetamol diffusing in solution or adsorbing on the PEDOT. The linear relationship between the oxidative and reductive peak currents of paracetamol and the square root of scan rate,  $v^{1/2}$  (scan rates from 10 mV/s to 300 mV/s), in figure. 6 (b) confirms that redox process is a diffusion controlled process.

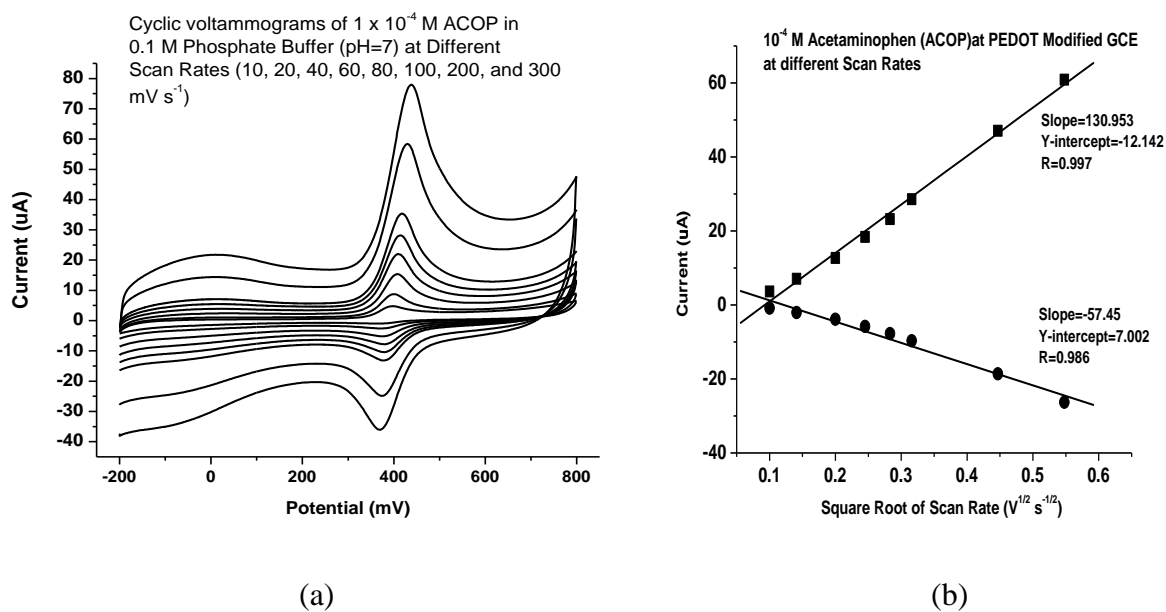
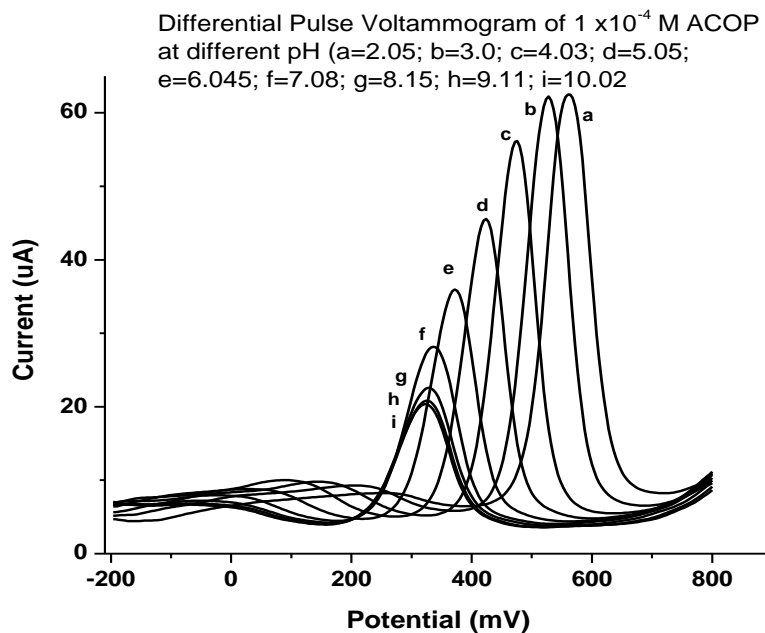


Figure 9: (a) Cyclic voltammograms of  $1 \times 10^{-4}$  M paracetamol in phosphate buffer pH = 7.0 with different scan rates; 10, 20, 40, 60, 80, 100, 200 and 300 mV/s. (b) The linear relationship of  $i_{pa}$  vs  $v^{1/2}$  (Regression coefficient = 0.997) and of  $i_{pc}$  vs  $v^{1/2}$

### 3.4. Effect of pH

The pH of the supporting electrolyte has a significant effect on the oxidation peak of paracetamol at PEDOT modified GCE. Effect of pH was studied in the range of 2.05–10.02 at a scan rate of 50mV/s using DPV, figure 7(a) . The response of the modified electrode was highest at pH 3.0 and lower for high pH values. At lower pH, it is attributed to hydrogen ion which is one of the products formed in the oxidation of paracetamol. A significant decrease in the oxidation current peak was found with increasing pH and the peak current reached its summit at pH 3.0 (figure 7(c)). Therefore, 0.1 M sodium Acetate buffer of pH 3.0 was chosen as the best pH condition for further experiments.

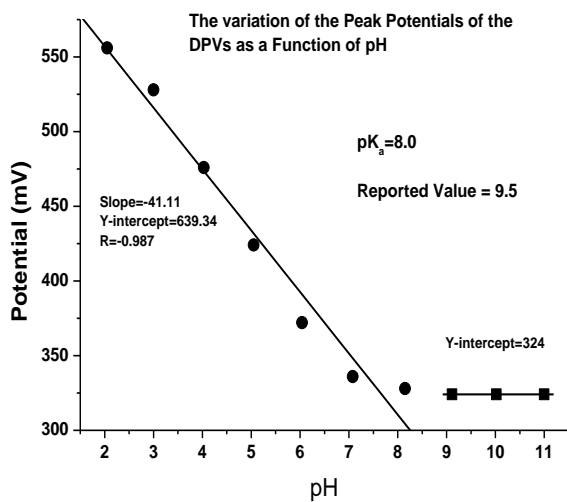


(a)

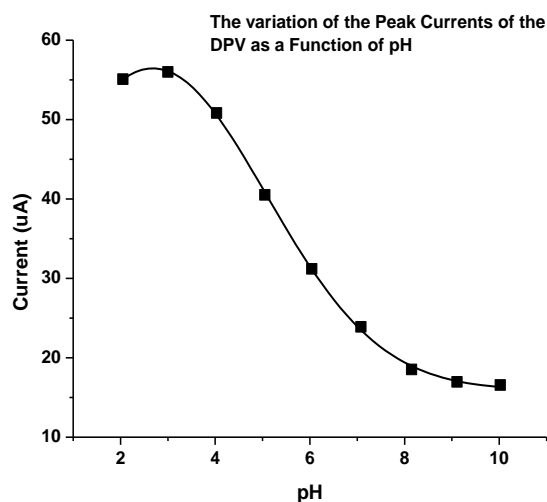
The peak current and peak potential were plotted versus pH in the range 2.05-10.02 as shown in figures 7 (b) and (c). In the range of pH 2.05-10.02, with the increase of pH, both the reduction and oxidative peak shift negatively, indicating the reaction is accompanied with the proton

transfer. According to the slope in Figure 7(b), it could be concluded that the  $E_{pa}$  was pH dependent with a slope of 41.11 mV per pH, which is close to the anticipated Nernstian Value of 59 mV for electrochemical process involving the same number of protons and electrons. While on the grounds of  $(E_p - E_{p/2}) = 56/n$  (Wang et al. 2007) [25], the number of electron transferred was found to be 2. Thus, the proton numbers intervening in the redox process could also be calculated approximately to be 2 from the slope.

The electrochemical mechanism of ACOP can be described as follows (Miner et al. 1981) [26] (Figure 4). It is an electrochemical redox involving two electrons and two protons to generate N-acetyl-p-quinoneimine.



(b)



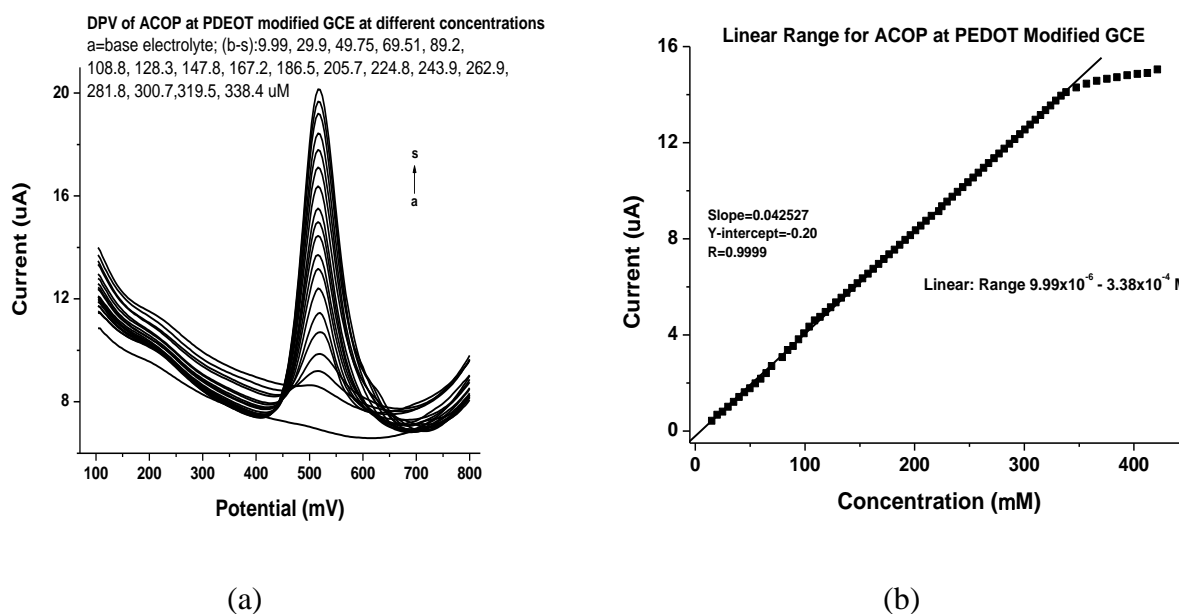
(c)

Figure 10: (a) Differential pulse voltammograms of  $1 \times 10^{-4}$  M paracetamol in 0.1 sodium acetate buffer at different pH (a - i): 2.05, 3.0, 4.03, 5.05, 6.04, 7.08, 8.15, 9.11 and 10.02. (b) Plot of  $E_{pa}$  versus pH and (c),  $I_{pa}$  versus pH.

### 3.5. Analytical Application

#### 3.5.1. The linear range and detection limit

The determination of paracetamol was carried out through DPV (Fig. 8a). The oxidative peak current increased linearly with the concentration of paracetamol in the range  $9.99 \times 10^{-6}$  to  $3.38 \times 10^{-4}$  M, figure 8b. The regression analysis of the plot yielded the sensitivity (slope) of 0.043 A/M. The PEDOT modified GCE had a detection limit of  $4.7 \times 10^{-6}$  M at a signal ratio (S/N) of 3.



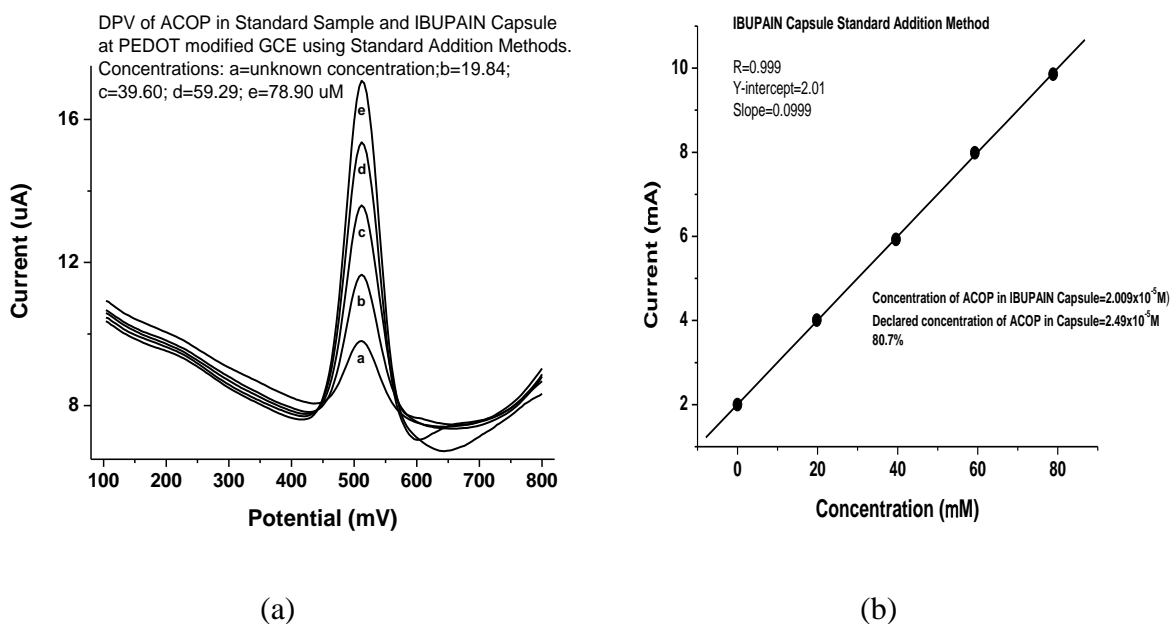
**Figure 11: (a) DPV of paracetamol on PEDOT modified GCE at different paracetamol concentrations (a–s): base electrolyte, 9.99, 29.9, 49.75, 69.51, 89.2, 108.8, 128.3, 167.2, 186.5, 205.7, 224.8, 243.9, 262.9, 281.8, 300.7, 319.5 and 338.4  $\mu$ M. (b) The relationship of current versus concentration.**

#### 3.5.2. Determination of samples

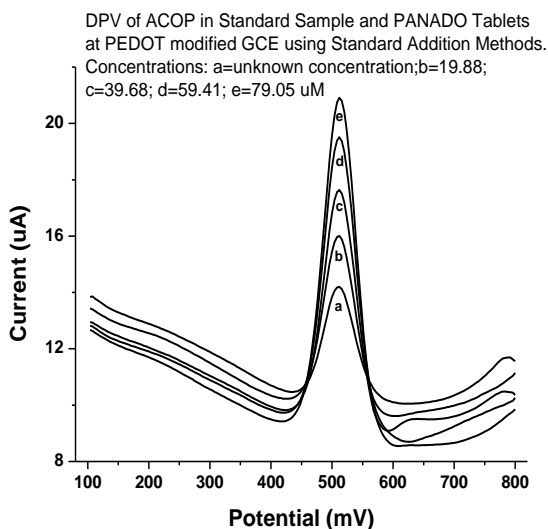
Commercial pharmaceutical samples i.e Ibupain capsule and Panado tablet containing paracetamol were analysed to evaluate the validity of the PEDOT modified GCE. 0.1 M solutions were obtained by dissolving adequate amount of those samples in 0.1 M sodium

acetate. Differential pulse voltammograms were then recorded for each sample as shown in figures 9 and 10, together with the calibration curves obtained using standard addition method.

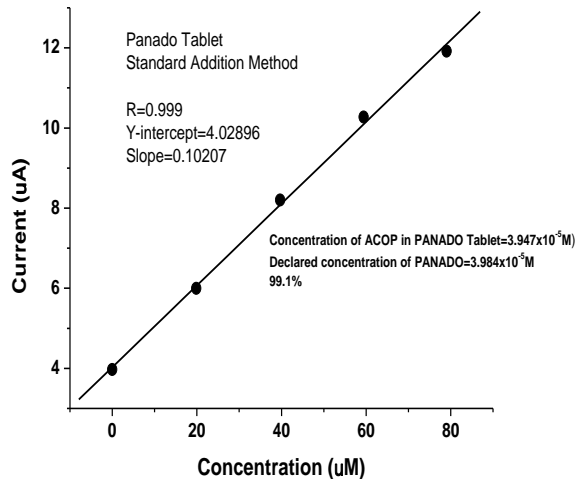
Standard addition method was used to calculate the content four times for each sample and the results were calculated as 161.4 mg and 495.5 mg of Ibupain capsule and Panado tablet respectively. The reported masses of paracetamol in each capsule and in each tablet are 200 mg and 500 mg for Ibupain and Panado respectively. The results were consistent with the standard content. Recovery test shows 80.7% paracetamol in Ibupain and 99.1% in Panado. The recovery study indicates that the PEDOT modified GCE can be effectively used for the selective determination of paracetamol in pharmaceutical samples.



**Figure 12: (a) Recovery study of paracetamol in Ibupain using DPV with modified electrode. (b) Calibration curve of paracetamol in Ibupain using standard addition method.**



(a)



(b)

**Figure 13: (a) Recovery study of paracetamol in Panado tablet using DPV with modified electrode.(b) Calibration curve of paracetamol in Panado tablet using standard addition method.**

### 3.6. Interference Study

The selectivity of the PEDOT modified GCE was studied in the presence of interfering species. Voltammetric responses of paracetamol at the modified electrode were examined in the presence of possible interfering substances such as ascorbic acid, creatinin, glucose, dopamine, tartaric acid, tri-sodium-citrate, epinephrine and uric acid. Differential pulse voltammograms were recorded for the oxidation of paracetamol in the presence two folds of interferences and results obtained are given in table 1.



**Table 1: Effect of interferents on DPV response for paracetamol at PEDOT modified GCE**

Interferents (two folds concentration addition)	Percentage increase or decrease in peak height of paracetamol
1) Ascorbic acid	0
2) Creatinin	0
3) Glucose	0
4) Dopamine	+20
5) Tartaric acid	-5
6) Tri-Sodium-Citrate	-5
7) Epinephrine	+14
8) Uric acid	+40

From table 1, it could be seen that uric acid interferes strongly, followed by dopamine and epinephrine, while the rest did not interfere with the determination of paracetamol.

#### 4. CONCLUSION

The results found in this experiment confirmed that PEDOT modified GCE prepared by electropolymerisation of EDOT on GCE is a very good electrochemical sensor for the determination of paracetamol. The modified electrode showed excellent electrocatalytic behavior, thus PEDOT accelerated the rate of electron transfer of paracetamol in the dynamic linear range between  $9.99 \times 10^{-6}$  to  $3.38 \times 10^{-4}$  M, with a detection limit of  $4.7 \times 10^{-6}$  M and a sensitivity of 0.043 A/M. The redox mechanism of paracetamol on PEDOT modified GCE was found to be a diffusion controlled quasi-reversible process involving two electron and two protons. The real sample analysis revealed that the modified electrode was suitable for determination of paracetamol in pharmaceutical samples. The method was then successfully utilised for the determination of paracetamol in a real samples of Panado tablets and Ibupain capsule with recoveries of 99.1% and 80.7% respectively for each sample

## 5. REFERENCE

1. R.M.D. Carvalho, R.S. Freire, S. Rath, L.T. Kubota, *J. Pharm. Biomed. Anal.* 34 (2004) 871.
2. S.J.R. Prabakar, S.S. Narayanan, *Talanta* 72 (2007) 1818
3. Navarro, I., Gonzalez-Arjona, D., Roldan, E. and Rueda, M. **1988** Determination of Paracetamol in Tablets and Blood Plasma by Differential Pulse Voltammetry, *J. Pharm. Biomed. Anal.*, 6, 969-976
4. A. Yesilada, H. Erdogan, M. Ertan, *Anal. Lett.* 24 (1991) 129
5. MacDonald, T.M. 2006. Acetaminophen: Risk-management urgently required *Pharmacoepidemiol and drug safety.* 15: 406–409.
6. Ozkan, S.A., Uslu, B. and Aboul-Enein, H.Y. **2003** Analysis of Pharmaceuticals and Biological Fluids Using Modern Electroanalytical Techniques, *Crit. Rev. Analyt. Chem.*, 33, 155-181.
7. Erk, N. 1999. Application of derivative-differential UV spectrophotometry and ratio derivative spectrophotometric determination of mephenoxalone and acetaminophen in combined tablet preparation. *J. Pharm. Biomed. Anal.*, 21: 429–437.
8. Easwaramoorthy, D., Yu, Y.C., and Huang, H.J. 2001. Chemiluminescence detection of paracetamol by a luminol-permanganate based reaction. *Anal. Chim. Acta*, 439: 95–100.
9. . Ravisankar, S., Vasudevan, M., Gandhimathi, M., and Suresh, B. 1998. Reversedphase HPLC method for the estimation of acetaminophen, ibuprofen, and chlorzoxazone in formulations. *Talanta.*, 46: 1577–1581.
10. He, F.Y., Liu, A.L., and Xia, X.H. 2004. Poly(dimethylsiloxane) microchip capillary electrophoresis with electrochemical detection for rapid measurement of acetaminophen and its hydrolysate. *Anal. Bioanal. Chem.*, 379: 1062–1067.
11. P.T. Kissinger, D.A. Roston, J.J. Van Benschoten, J.Y. Lewis, W.R. Heineman, J. *Chem. Educ.* 60 (1983) 772–776.
12. Bi, S.Y., Wang, G.F., and Piao, Y.Z. 2000. Voltammetric determination of paracetamol on the glassy carbon electrode. *Journal of Yanbian University (Natural Science)*, 26
13. Felix,F.S; Brett, C.M.A; Angnes,L.J.*Pharma.Biomed.Anal.*2007,123,495
14. Li,M; Jing,L.*Electrochim.Acta.*2007,52,3250
15. G. Natta, G. Mazzanti, P. Corradini, *Atti. Acad. Naz. Lincei, Cl. Sci. Fis. Mat. Rend.*, **25**, 8, 3, 1958
16. M. Hatano, S. Kambara, S. Okamoto, *J. Polym. Sci.*, **51**, S26, 1961
17. H. Shirakawa, E.J. Louis, A.G. MacDiarmid, C.K. Chiang, A.J. Heeger, *J. Chem. Soc., Chem. Commun.* 578, 1977
18. J. Margolis, *Conductive Polymers and Plastics*, Chapman and Hall, 2-11, 1989

19. I.M. Cambell, *Introduction to Synthetic Polymers*, Oxford Science Publications, 196, 1994
20. Kumar, S. Senthil; Mathiyarasu, J.; Phani, K. L. N.; Yegnaraman, V. (2005). "Simultaneous determination of dopamine and ascorbic acid on poly (3,4-ethylenedioxythiophene) modified glassy carbon electrode". *Journal of Solid State Electrochemistry* **10**
21. Bello, A; Giannetto, M; Mori, G; Seeber, R; Terzi, F; Zanardi, C (2007). "Optimization of the DPV potential waveform for determination of ascorbic acid on PEDOT-modified electrodes". *Sensors and Actuators B: Chemical* **121**: 430.
22. J. Zhou, E.Wang, *Anal. Chim. Acta* 236 (2) (1990) 293–298.
23. M. Musameh, J.Wang, A. Merkoci, Y. Lin, *Electrochem. Commun.* 4 (2002) 743.
24. I. G. Casella, *Electroanalysis* 1996, 8, 128.
25. Miner, D.J., Rice, J.R., Riggin, R.M., and Kissinger, P.T. 1981. Voltammetry of acetaminophen and its metabolites. *Anal. Chem.*, 53: 2258–2263
26. Wang, S.F., Xie, F., and Hu, R.F. 2007. Electrochemical study of brucine on an electrode modified with magnetic carbon-coated nickel nanoparticles. *Anal. Bioanal. Chem.*, 387: 933–939.