REPUBLIC OF TURKEY
HARRAN UNIVERSITY
GRADUATE SCHOOL OF
APPLIED AND NATURAL SCIENCES

MASTER OF SCIENCE (MSc) THESIS

VOLTAMMETRIC DETERMINATION OF PARACETAMOL IN PHARMACEUTICALS USING A NOVEL COMPOSITE ELECTRODE BASED ON NANOPARTICLES OF TUNGSTEN AND ANTIMONY OXIDE

Mohammed Hussein FATTAH

DEPARTMENT OF CHEMISTRY

ŞANLIURFA
2018

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A study entitled "**Voltammetric determination of paracetamol in pharmaceuticals using a novel composite electrode based on nanoparticles of tungsten and antimony oxide**" prepared by Mohammed Hussein Fattah under the supervision of Prof. Dr. Mehmet ASLANOĞLU was approved as a Master of Science thesis on 28/06/2018 by the following committee in Graduate School of Natural and Applied Sciences at the University of Harran.

Signature

Supervisor	: Prof. Dr. Mehmet ASLANOĞLU	.....
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Committee Member	: Assist. Prof. Dr. Zafer UYAR	.....

I certify that this thesis has been carried out in the Department of Chemistry and written in accordance with the regulations of our Institute.

Prof. Dr. Halil Murat ALĞIN
Director of Institute

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CONTENTS

Page No

ÖZET

Yüksek Lisans Tezi

TUNGSTEN VE ANTİMON OKSİT NANOPARÇACIKLAR TEMELLİ YENİ BİR KOMPOZİT ELEKTROT KULLANILARAK İLAÇ ÖRNEKLERİNDE PARASETAMOLUN VOLTAMETRİK TAYİNİ

Mohammed Hussein FATTAH

Harran Üniversitesi
Fen Bilimleri Enstitüsü
Kimya Anabilim Dalı

Danışman: Prof. Dr. Mehmet ASLANOĞLU
Yıl: 2018, Sayfa:35

Parasetamolun saptanması için camsı karbon elektrotlarının çok duvarlı karbon nanotüpler, antimon oksit nanoparçacıklar ve tungsten nanoparçacıklar temelli tekrarlanabilir bir voltametrik yöntem geliştirilmiştir. Modifiye elektrot 0.1 M pH 7.0 PBS içinde parasetamolün saptanması için kullanılmıştır. Pik akımları 6.7×10^{-9} - 2.5×10^{-6} M aralığındaki parasetamolün derişimiyle doğrusal olarak artmaktadır. Saptama sınırı 2.1×10^{-9} M'dır. Önerilen yöntem, parasetamol tabletlerinde parasetamolün saptanmasına başarıyla uygulanmıştır.

ANAHTAR KELİMELER; Parasetamol, karbon nanotüpler, nanoparçacıklar, modifiye elektrot, voltametrik saptama

ABSTRACT

MSc Thesis

VOLTAMMETRIC DETERMINATION OF PARACETAMOL IN PHARMACEUTICALS USING A NOVEL COMPOSITE ELECTRODE BASED ON NANOPARTICLES OF TUNGSTEN AND ANTIMONY OXIDE

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Supervisor: Prof. Dr. Mehmet ASLANOGLU
Year: 2018 , Page:35

A reproducible voltammetric method was developed for the determination of paracetamol based on the modification of a glassy carbon electrodes with multi-walled carbon nanotubes, antimony oxide nanoparticles and tungsten nanoparticles. The modified electrode was used for the determination of paracetamol in 0.1 M PBS at pH 7.0. The peak current increased linearly with the concentration of paracetamol in the range of 6.7×10^{-9}- 2.5×10^{-6} M. The detection limit was 2.1×10^{-9} M. The proposed method was successfully applied for the determination of paracetamol in parol tablets.

KEYWORDS: Paracetamol, carbon nanotubes, nanoparticles, modified electrode, voltammetric detection

ACKNOWLEDGEMENT

I would like to express my special appreciation and thanks to my supervisor Professor Mehmet Aslanoğlu for supporting me in last 2 years. I also wish to thank to following friends for their kind help and assistance in lab work.

- Tuğçe, Fatoş, Şehriban and Esra …

My special thank goes to my family for their encouragement during my studies here at Harran University.

In addition, I would like thank to the examiners for accepting viva invitation and listening to me…

Thank you!

LIST of FIGURES

Page No

LIST of TABLES

Page No

LIST of SCHEMES

Page No

NOMENCLATURE

AA	Ascorbic Acid
UA	Uric Acid
PAR	Paracetamol
DA	Dopamine
GCE	Glassy Carbon Electrode
Pt	Platinum Electrode
Ep	Peak Potential
Epa	Anodic Peak Potential
Epc	Cathodic Peak Potential
Ip	Peak Current
Ipa	Anodic Peak Current
Ipc	Cathodic Peak Current
MWCNT	Multi-Walled Carbon Nanotube
SWCNT	Single-Walled Carbon Nanotube
CNT	Carbon Nanotube
SWV	Square Wave Voltammetry
CV	Cyclic Voltammetry
C	Concentration
ν	Scan rate
R.S.D	Relative Standard Deviation
PBS	Phosphate Buffer Solution
n	Number of electron
r^2	Correlation coefficient
μM	Micromolar
nM	Nanomolar
M	Molar
mV	Milivolt
V	Volt
min	Minute
Eq	Equation
SEM	Scanning Electron Microscopy
EDX	Energy Dispersive X-Ray

1. INTRODUCTION

The quality of human life standards has recently been one of the highest priority purposes on world-wide research efforts. Farther, the standards of life quality are necessary for controlling diseases, drug and food safety, Thus, sensitive, fast and reliable detection of molecules is required to control some important key parameters (Castillo et al., 2004). Recently, researchers have been focusing on monitoring, controlling and preventing or at least minimizing the side effects of chemicals in drugs and foods.

The safety of drugs is closely linked to controlling and reducing their adverse effects. The risk of their contribution to the adverse effects of the drug materials may be controlled and minimized with the determination of purity and degradation products (Görög, 2008). The design of novel sensitive platforms for the simultaneous determination of drugs have been the most popular field in pharmaceutical and clinical interests.

Voltammetric techniques at modified electrodes have a number of advantages when compared to other analytical techniques. They provide outstanding facilities such as; sensitivity, selectivity, low cost, easy automation, miniaturization. Voltammetric methods are based on the control of electrical signal and relation to the concentration of the target analyte in samples (ElKaoutit, 2012).

Electrochemical sensors offer very promising devices for the monitoring of a wide range of analytes due to their sensitivity, specificity and the ease of use, quick responses, low-cost, reliable and reproducible detections with portable devices for the use in the clinical, pharmaceutical applications (Săndulescu et al., 2011).

Furthermore, the modified electrodes as sensors have provided selectivity, sensitivity, chemical and electrochemical stability, large potential window and electrocatalytic activity (Alkire et al., 2009). They also enable low detection limits

and clarify the electrochemical mechanisms.

In last the two decades, scientists have focused on developing novel materials which could serve as electrochemical sensors. Nanomaterials composed of carbon nanotubes have provided several advantages including larger surface area for preventng surface fouling. (Padigi et al., 2007).

Nanomaterials including carbon nanotubes and metal nanoparticles have been used for the modification of electrodes to study the electrochemistry of several drug molecules. Carbon nanotubes (CNTs) show excellent physical and chemical properties. Carbon nanotubes (Lijima, 1991) have been the subject of many reports owing to their remarkable, mechanical, structural, electronic properties (Ajayan, 1999; Odom et al., 1998). It was reported that CNTs exhibit electrical conductivity and chemical stability (Ajayan, 1999; Sinnott et al., 2002).

The purpose of the study in this thesis was to develop a novel method based on MWCNTs and nanoparticles of metals to obtain a sensitive electrochemical procedure for the study of paracetamol in pharmaceuticals.

2. LITERATURE REVIEW

Carbon nanotubes based electrodes represent a novel and interesting alternative for the determination of several drug molecules (Gooding, 2005; Wildgoose et al., 2006 and Kachoosangi et al., 2008). Several studies were carried out using carbon nanotubes based electrodes. In this review of the literature, MWCNTs and nanoparticles were utilized for the preparation of a novel procedure to study the electrochemistry of paracetamol.

The literarure reveals that carbon nanotubes were first used for the modification of an electrode to study the voltammetry of dopamine by Britto et al. (1996), In that study, MWCNTs-based electrodes were prepared and applied to the oxidative behaviour of dopamine (DA). The results showed that DA showed an oxidation peak at Epa = 0.22 V and a corresponding reduction peak at 0.19 V on the surface of MWCNTs-based electrodes. Data clearly revealed that the separation in peak potential was 0.030 V. This was significantly superior to that observed at other carbon electrodes. They reported that the current *(ip)* was proportional to $v^{1/2}$ over the range of 20–200 mV/s. The consistency of the current function suggested that dopamine was processing a diffusion-controlled process on MWCNTs-based electrodes.

Luo et al. (2001) also reported the voltammetric properties of carboxylic acid functionalized single walled CNTs (SWCNTs) on a glassy carbon electrode (GCE). They threated SWCNTs with nitric acid for the production of carboxylic acid groups on the surface of nanotubes. Data revealed that single-walled carbon nanotube film showed stable electrochemical behavior. Afterwards, SWCNTs were utilized as a surface modifier for the investigation of several molecules including epinephrine, ascorbic acid and DA. Data revealed that the electrodes SWCNTs/GCE exhibited excellent electro-catalytic activities for several molecules. For instance DA showed an anodic peak at 0.182 V and a cathodic peak at 0.129 V BR buffer solution at pH

6.9 on SWCNT film-modified GC electrode. Epinephrine and ascorbic acid were also showed a similar catalytic behavior on SWCNT film electrode.

Wang et al. (2001) also showed that SWCNT-modified electrodes provided great catalytic activity towards the electrochemical oxidation of 3,4-dihydroxy phenylacetic acid (DOPAC). A well-defined redox couple with ΔEp=49 mV was obtained at pH 4.4 using the SWCNT-modified electrodes. The peak current increased has also increased significantly when compared to bare electrodes. The current was linear with DOPAC concentration with a detection limit of 4.0×10^{-7} M.

Ye et al. (2003), developed a procedure for the quantification of uric acid (UA) in the presence of ascorbic acid (AA) at CNTs modified electrode. The proposed carbon nanotube modified electrode exhibited catalytic oxidation of uric acid (UA) and L-AA.

Wu et al. (2004) studied the electrochemistry of tryptophan (TRP) at a GCE modified with MWCNTs. The electrode was applied to the oxidation of tryptophan Trp by voltammetric methods. Data exhibited a great catalytic activity for Trp. The electrode enabled a linear range of 2.5×10^{-7} - 1.0×10^{-4} mol/L with a detection limit of 2.7×10^{-8} mol/ L.

Qu et al. (2004), described a procedure for the voltammetric quantification of pyridoxine (Vitamin B6) on carbon nanotubes/GCE. The CNT/GCE exhibited an obvious catalytic activity for pyridoxine. The peak appeared at 0.80 V in 0.1 M PBS at pH 6.0. A linear response for pyridoxine was obtained in the range of 5.0×10^{-7} - 1.0×10^{-4} mol/Lwith a detection limit 2.0×10^{-7} mol/L by using DPV.

Salimi et al. (2005) reported the quantification of morphine at GCE modified MWCNT. The electrode exhibited a single oxidation peak at 0.3 V. The plot was linear over the concentration between 0.5 - 150 μM with a detection limit of 0.2 μM.

Wu and Hu (2005), investigated the quantification of cytochrome-*c* by a composite film on a Au electrode. The composite electrode was applied to detect cytochrome-*c* in 0.06 M PBS at pH 7.0. A linear regression equation was obtained over a cytochrome-*c* range of 1.5-45 μM.

Xu and Wang (2005), reported a GCE modified ewith MWCNTs for the study of oxidation of L-tyrosine by voltammetric methods. Cyclic voltammetry was used to investigate L-tyrosine. It showed that L-tyrosine exhibited only one oxidation peak, suggesting that the electrochemical process of L-tyrosine was irreversible. Data showed that the peak was linear correlated to the L-tyrosine over the range 2.0×10^{-6} - 1.0×10^{-4} M. The detection limit was 4.0×10^{-7} M.

Duan et al. (2007), investigated voltammetric behavior of paracetamol. In this work, voltammetry was performed to investigate the electrochemistry of paracetamol on MWNTs/GCE. A couple of quasi-reversible process was obtained with separation in peak potential of $\Delta Ep=80$ mV. Data indicated that the responses were linear for PAR concentrations between 4.0×10^{-7}- 1.5×10^{-4} M with a detection limit of 1.2×10^{-7} M.

Li and Jing (2007), investigated the voltammetry of paracetamol using a composite electrode based on PANI–MWCNTs. The electrode exhibited a great catalytic effect for the oxidation of paracetamol. The electrode well-defined anodic and cathodic peaks were observed for paracetamol at 58 and 41mV in 0.2 M acetate buffer solutions (ABS) at pH 5.5. The peak repsonse was linear from 1.0×10^{-6} - 1.0×10^{-4} M. The detection limit was 2.5×10^{-7} M for PAR.

Shahrokhian and Mehrjardi (2007), reported quantification of UA and AA on a carbon-paste electrode modified with MWCNTs/nafion and cobalt(II)- 5-nitro-salophen. The linear range was ranged from 1.0×10^{-7} - 1.0×10^{-4} M for UA. In addition, a detection limit of 6.0×10^{-8} M was calculated for UA. The voltammetric

response of AA was linear for the AA concentration between 5.0×10^{-7} - 1.0×10^{-4} M with a detection limit of 1.0×10^{-7} M.

Fei et al. (2008), demonstrated determination of diethylstilbestrol using a composite electrode based on CNTa-PtNPs. The electrode was used for detemine diethylstilbestrol (DES) using by linear sweep voltammetry and cyclic voltammetry in optimized 0.1 M PBS at pH 7.0. A linear response of DES was obtained in the range from 1.0×10^{-7} - 2.0×10^{-5} M and with a limit of detection (LOD) was 1.5×10^{-8} M.

Liu et al. (2008), reveaşed the quantification of adenine and guanine in DNA using a modified electrode based on polythionine/NPAu/MWNTs. Detection limits was calculated as 1.0×10^{-8} M for guanine and 8.0×10^{-9} M adenine. This procedure was also applied for measuring guanine and adenine in DNA.

Shahrokhian et al. (2009), investigated that sensitive electrochemical determination of thioridazine (TR) using a composite of SWCNTs and cobalt nanoparticle modified GCE. Voltammetry was applied for the quantification of low levels of TR. A linear working range was obtained for TR at concentrations from 5.0×10^{-7}- 1.0×10^{-4} M with a detection limit of 5.0×10^{-8} M was obtained for TR.

Manjunatha et al. (2011), studied the direct electrochemical determination of cholesterol oxidase on MWCNTs. Cyclic voltammetry procudes well defined redox peaks which were corresponding to the direct electron transfer of FAD/$FADH_2$ of ChOx and carboxylic groups of MWCNTs. The response of oxygen was linear with the cholesterol concentration in the range of 0.2-1 mM using cyclic voltammetry. The detection limit was 3.0×10^{-6} M.

Wang et al. (2012), suggested a new voltammetric sensor based on Fe_3O_4/MWCNTs/β-CD modified electrode. The procedure was used for investigation of the oxidation behaviour of hypoxanthine. The current is proportional to the

hypoxanthine in the range from 5.0×10^{-8} - 1.0×10^{-5} M. A detection limit of 3.0×10^{-9} M was calculated for the drug.

3. MATERIAL and METHOD

3.1. Instrumentation

For the current study, there are several instruments have been used. Some of them are listed below;

- Voltammetry was performed on an Autolab PGSTAT 12 potentiostat/galvanostat (Eco-Chemie, The Netherlands).
- A GCE was utilized as working electrode, a Pt wire served as auxiliary electrode and a Metrohm Ag/AgCl was used as reference electrode .
- A Metrohm 744 pH Meter was used for the pH measurements (Metrohm, Switzerland).
- Scanning electron microscopy and energy dispersive X-ray analysis (EDX) was performed on a ZEIS EVO 50 brand instru was used for the characterization of multi walled carbon nanotubes, polymer film layers, metal nanoparticules and composite materials on the electrode surfaces.
- KUDOS (SK3301OHP) model ultrasonic bath was used for dispersing carbon nanotubes and synthesis of carbon nanotubes-metal nanoparticules composites.
- NUVE (MK-418) model magnetic stirrer was used to mix the solutions.
- SHIMADZU (AY-220) model balances was used for analytical weighing.

3.2. Reagents

The reagents used in this study were of analytical reagent grade or equivalent. All chemicals were purchased from Sigma–Aldrich, Fluka or Merck and used without further purification.

- Acetone (≥ 99.8 %, Merck, Germany),
- Acetonitrile (99.9 % , Merck, Germany),
- Alumina powder, (0.05; 0.3; 1.0 micron, Buehler, USA),
- Ascorbic acid (99.7 %, Sigma Aldrich, Germany),
- Chloroform (99.0 %,Merck, Germany),
- Disodium monohydrogen phosphate dihydrate (99.5 %, Merck, Germany),
- Dopamine hydrochloride (99.0 %, Merck, Germany),
- Ethanol (≥99.5%, Merck, Germany),
- Hydrochloric acid, (37-38 %, Merck, Germany),
- Lactic acid (≥98.0 %, Sigma Aldrich, USA),
- Multiwalled carbon nanotubes (MWCNTs) (95.0 %, NanoLab, USA),
- Nitric acid (65.0 %, Merck, Germany),
- Paracetamol (98.0%, Alfa Aesar, Germany),
- Perchloric acid (70-72 %, Merck, Germany),
- Potassium chloride (99.5 %, Merck, Germany),
- Potassium dihydrogen phosphate (99.5 %, Merck, Germany),
- Sodium hydroxide (≥99.0 %, Merck, Germany),
- Sodium nitrate (≥99.0 %, Sigma Aldrich, USA),
- Uric acid (≥98.0 Fluka, Germany),

3.3. The Samples Used for Analytical Applications

- PAROL® Tablet, 500 mg paracetamol/tablet (Atabay Pharm. Co., Turkey,).

3.4. Preparation of Used Standard Stock Solutions

- Phosphate buffer saline solutions (PBS) were prepared from potassium dihydrogen phosphate, KH_2PO_4 (6.8 g/L), disodium monohydrogen phosphate

dihydrate, $Na_2HPO_4.2H_2O$ (8.8 g/L) and potassium chloride, KCl (0.75 g/L) as a saline and then the pH adjusted from 4 to 10 bt the addition of 0.1 M HCl or 0.1 M NaOH solutions. Ionic strength was kept nearly constant for each buffer solution as 0.1 M.

All of the standard stock solutions were prepared freshly before each use and the all stock solutions were kept in amber bottles in order to protect from light. The standard stock solutions were also diluted before use when it was needed.

3.5. Preparations of Electrodes

3.5.1. Activation of glassy carbon electrodes

Prior to the modification, GCEs were polished with 1 micron, and then with 0.3 micron alumina on a pad. The electrode throughly washed with water and sonicated in ethanol for 5 min. Afterwards, the CV was performed fort he activation of GCEs.

3.5.2. Preparation of W-Sb_2O_3NPs/MWCNT/GCE

The MWCNTs were first sonicated in a concentrated solution of perchloric acid and nitric acid. CNTs were then filtered and washed washed with water. Then tunsgten and antimony oxide nanopowders were mixed with the functionalized multi-walled carbon nanotubes and then sonicated for 45 min in an ultrasonic bath. Then, a known volume of the mixture was cast on the GCE using a micropipet.

4. RESULTS and DISCUSSIONS

4.1. Determination of Paracetamol (PAR)

In this study, a GCE coated with MWCNTs, antimony oxide nanoparticles (Sb_2O_3) and tungsten nanoparticles (WNPs) for quantifying paracetamol.

Voltammetry provided a sensitive approach to the electroanalysis of drugs (Kachoosangi and Compton, 2007; Wildgoose et al., 2006; Ensafi et al., 2009). However, the approach might be restricted in the presence of interfering molecules such as AA (Streeter et al., 2008; Kachoosangi et al., 2008). For example, the quantification of paracetamol (PAR) can be restricted by the presence of AA. The conventional electrodes can be modified with nanopouros materilas to overcome such a problem (Walcarius, 2008; Jones and Compton, 2008; Griese et al., 2008; Gooding, 2008; Chow and Gooding, 2006).

CNTs represented a good alternative for the quantification of drugs for providing sensitivity and selectivity in electroanalys (Jain and Sharma, 2012; Geto et al., 2013; Gupta et al., 2013; Li et al., 2012).

PAR is an effective and widely used effective pain killer (Carvalho et al., 2004). The overdose of PAR may cause several diseases (Martin and MacLean, 1998). Therefore, the amount of PAR should always be controlled in pharmaceuticals.

Several quantitative procedures were proposed for the analysis of PAR such as chromatography (Ravinsankar et al.,1998), spectrophotometry (Hanaee, 1997), chemiluminescence (Easwaramoorty et al., 2001), capillary electrophoresis (Zhao et al., 2006), FTIR and Raman spectrometry (Zhoubi et al., 2002), and flow injection analysis (Knochen et al., 2003; Silva et al., 2006). However, the sensitivity of the some of above mentioned techniques is poor.

Voltammetric procedures have many advantageous such as simplicity, high sensitivity and rapidness (Walcarius, 2008; Li et al., 2012). A number of authors have focused on the development of novel voltammetric procedures for quantifying PAR including a voltammetric methos based on the modification of electrodes with MWCNT (Kachoosangi et al., 2008), carbon nanoparticles (Ghorbani-Bidkorbeh et al., 2010), SWCNT-graphene (Chen et al., 2012), CNTs (Fanjul-Bolado, 2009), SWCNTs (Habibi et al., 2011), and D50wx2-GNP (Sanghavi and Srivastava et al., 2011).

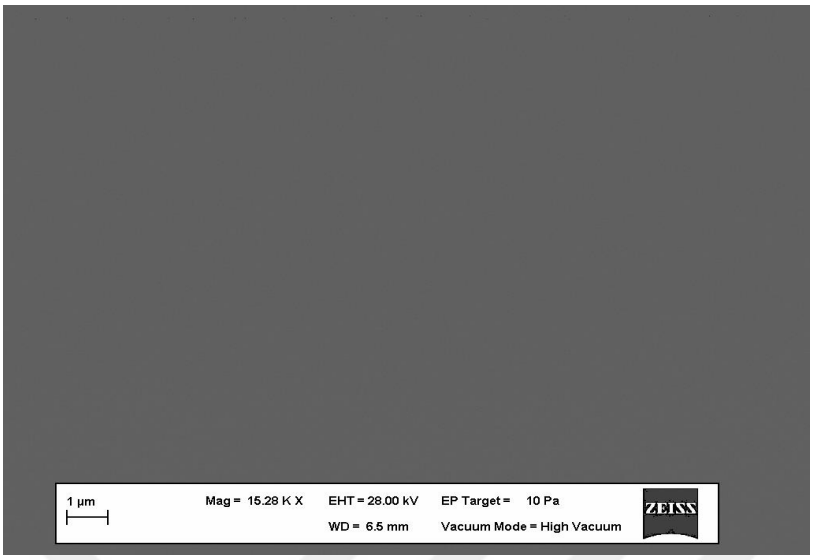
4.1.1. Surface characterizations of bare GCE and MWCNT modified GCE

Surface characterizations of bare GCE and MWCNT modified GCE were performed with a scanning electron microscope (SEM) at Harran University Central Laboratory. SEM images of bare GCE (a) and MWCNT/GCE (b) are given in Figure 4.1. It can be seen that MWCNT modified GCE have a rough surface and this can provide larger specific surface area than bare GCE for electrochemical oxidation.

4.2. Voltammetric properties of paracetamol

Cyclic voltammetry was applied to the oxidation of PAR at a GCE for 0.1 M PBS at pH 7.0. PAR exbibite a quasi-reversible response on GCE. Figure 4.2. shows CVs of PAR at various scan rates. The current was proportional to $v^{1/2}$ in the range from 50-250 mV/s as shown in Figure 4.3. This suggests that the process of PAR is diffusional in nature.

(a)



(b)

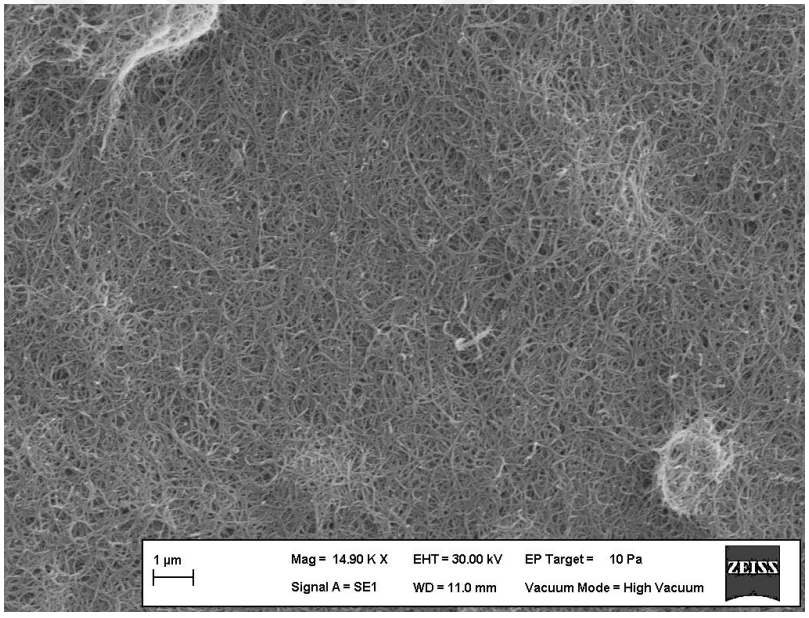


Figure 4.1. SEM images of bare GCE (a) and MWCNT modified GCE (b)

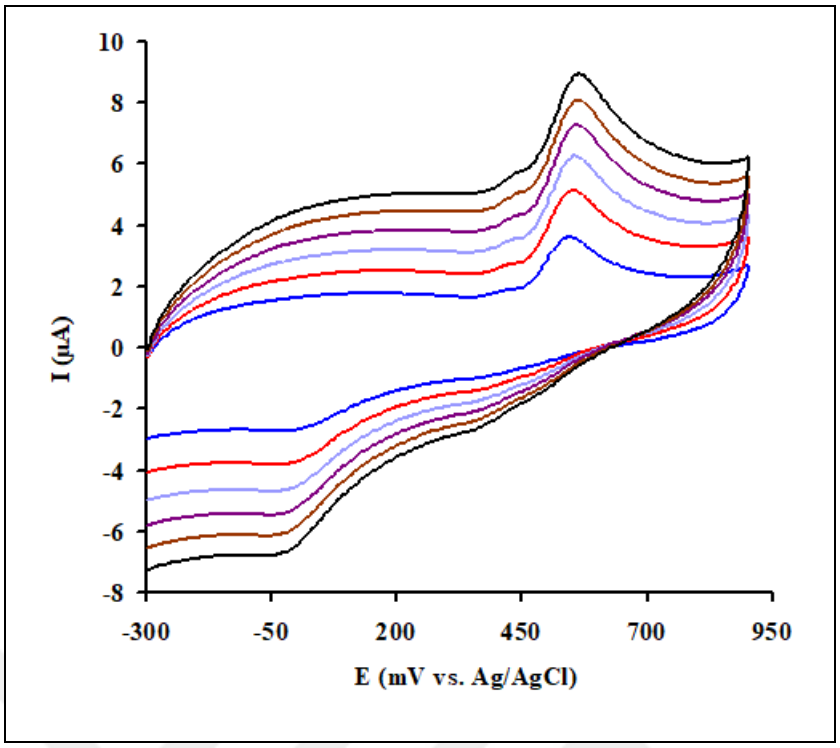


Figure 4.2. CVs of 3.8×10-6 ^{M} PAR at GCE. Supporting electrolyte 0.1 M PBS at pH 7.

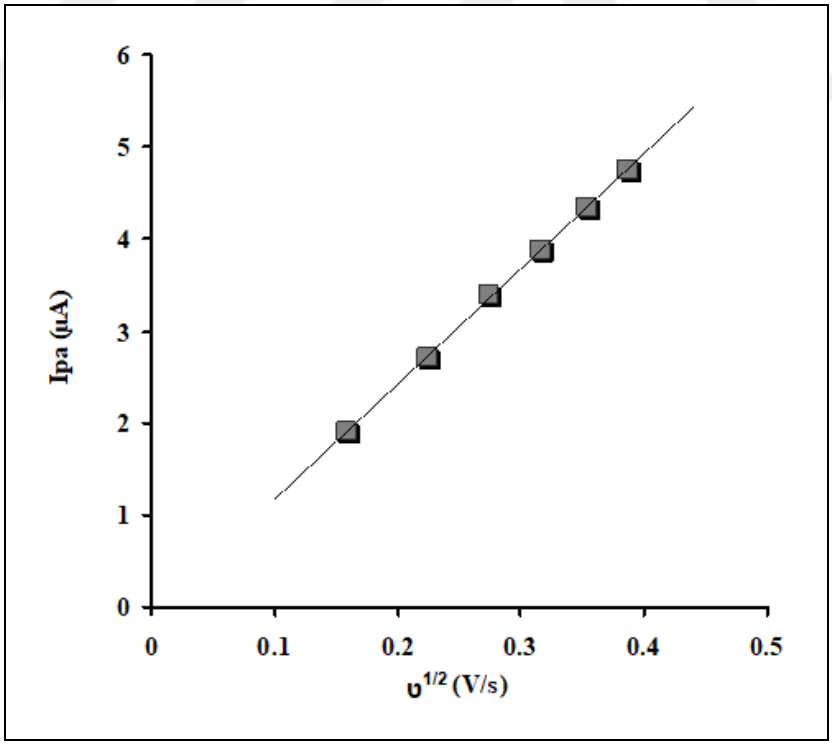


Figure 4.3. plot of anodic peak currents of PAR versus scan rates at the bare GCE.

Figure 4.4. shows CVs of PAR at various electrodes. At MWCNTs/GCE, PAR exhibits an oxidation peak at 405 V and a reduction peak at 393 V. It is clear that a GCE modified with MWCNTs shifted the oxidation potential of PAR in the negative direction. This is a great evidence of catalytic effect of the electrode towards the process of PAR. The oxidation of PAR and a GCE modified with Sb_2O_3 and CNTs is also shown in Figure 4.4. As shown, a large increase is observed for the process of PAR. In addition, the response of the electrode process of PAR is high improved at a GCE modified with W-Sb_2O_3 and MWCNTs. The electrode has increased the current response of PAR process when compared with several electrodes including Sb_2O_3-MWCNT/GCE and MWCNTs/GCE. The increase in response has probably occurred by the increase in the real area of the film.

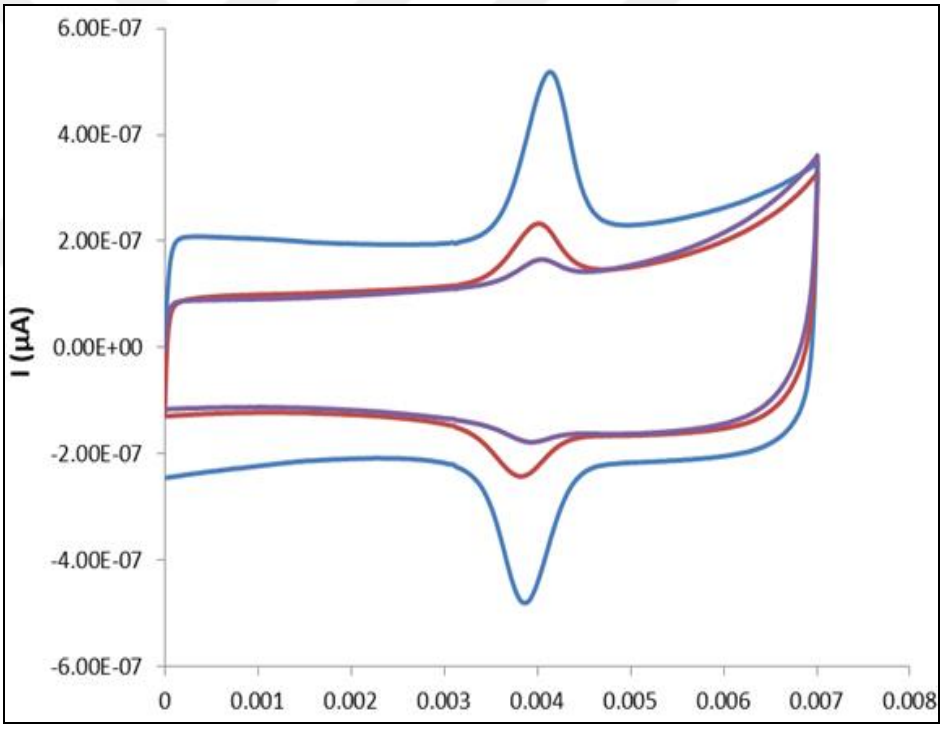


Figure 4.4. Cyclic voltammograms of $3.8x10^{-7}$ ul PAR CNT (a),Sb (b), W- Sb/CNT (c)in 0.1 M PBS at pH 7. Scan rate 50 mV/s.

The CVs of 7.5×10^{-7} M PAR at various sweep rates on W-Sb_2O_3NPS-MWCNTs/GCE are shown in Figure 4.5. The current was linear with scan rate. This

indicated that the mechanism of PAR has changed from diffusional dependence to adsorptional behaviour (Streeter et al., 2008; Henstridge et al., 2010).

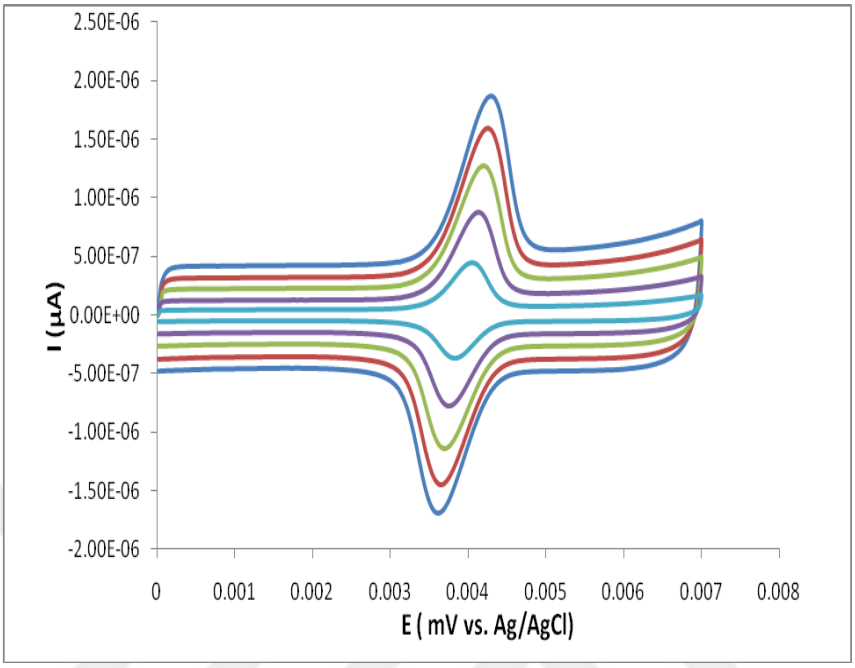


Figure 4.5. CVs of 7.5×10^{-7} M PAR at proposed electrode. Scan rates: 50 mV/s to 250 mV/s.

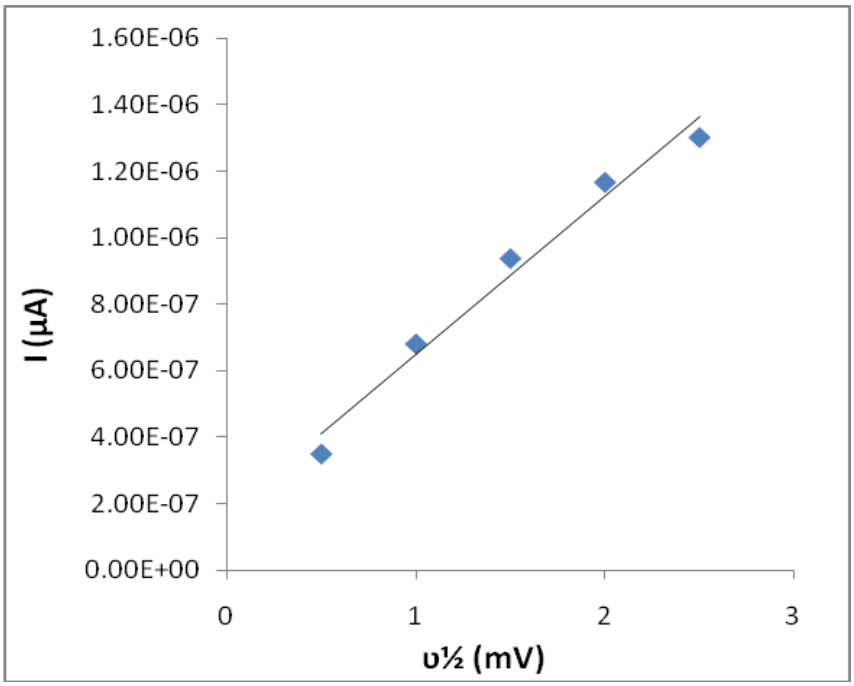


Figure 4.6. Plot of anodic peak currents of PAR versus scan rates at the bare GCE

4.3. Voltammetric behaviour of PAR at various pH values

Fig 4.7. shows the CVs of PAR at various pH values. Data indicated that shifts in potential in the negative direction was observed with increasing pH which suggested that the process included the proton transfer. The slope of E_{pa} 0.057 vs. pH was 7.0 mV/pH (Figure 4.7.). This revealed that the process contained equal numbers of protons and electrons. Therefore, the number of protons is 2. The electrodes reaction of is given in Scheme 4.1.

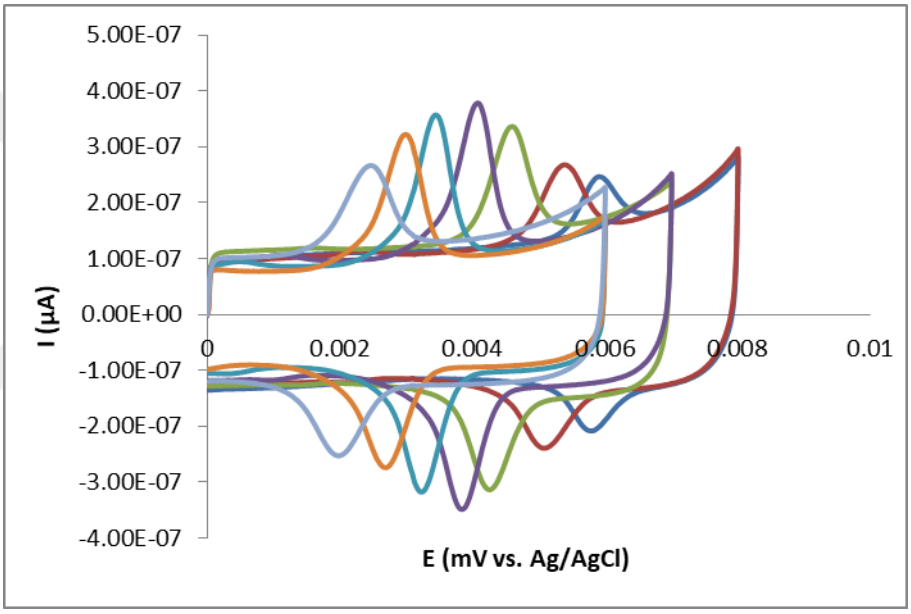
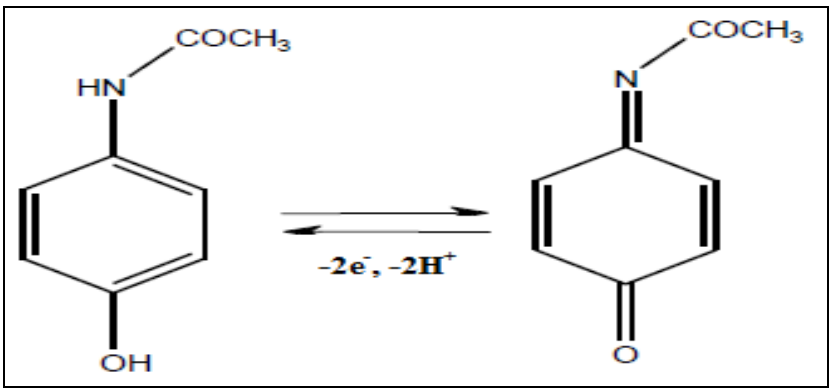


Figure 4.7. CVs of 3.9×10^{-7} M PAR at different pH values. pH:; 4.0; 5.0; 6.0; 7.0; 8.0;9.0; 10. Scan rate: 50 mV/s.



Scheme 4.1. The electrode reaction of PAR

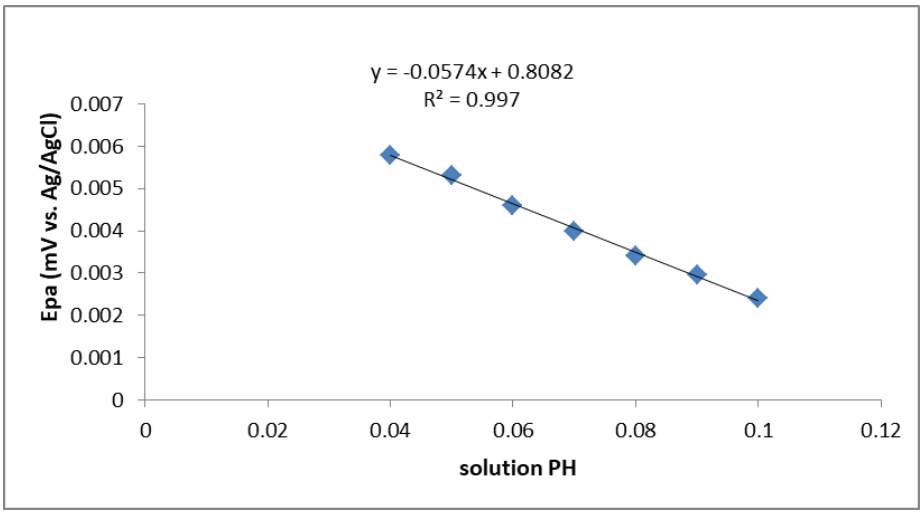


Figure 4.8. Plot of potentials of PAR versus solution pH

4.4. Determination of paracetamol

Cyclic voltammetry was applied for determining PAR at W-Sb_2O_3NPs/MWCNTs/GCE in 0.1 M PBS at pH 7.0 (Fig 4.9.). The response was plotted vs the PAR concentration (Fig. 4.10). The peak current was linear in the range of 6.7×10^{-9} - 2.5×10^{-6} M. The detection limit was 2.1×10^{-9} M. Also, the results obtained at the proposed electrode are compared with other methods are given in Table 4.1.

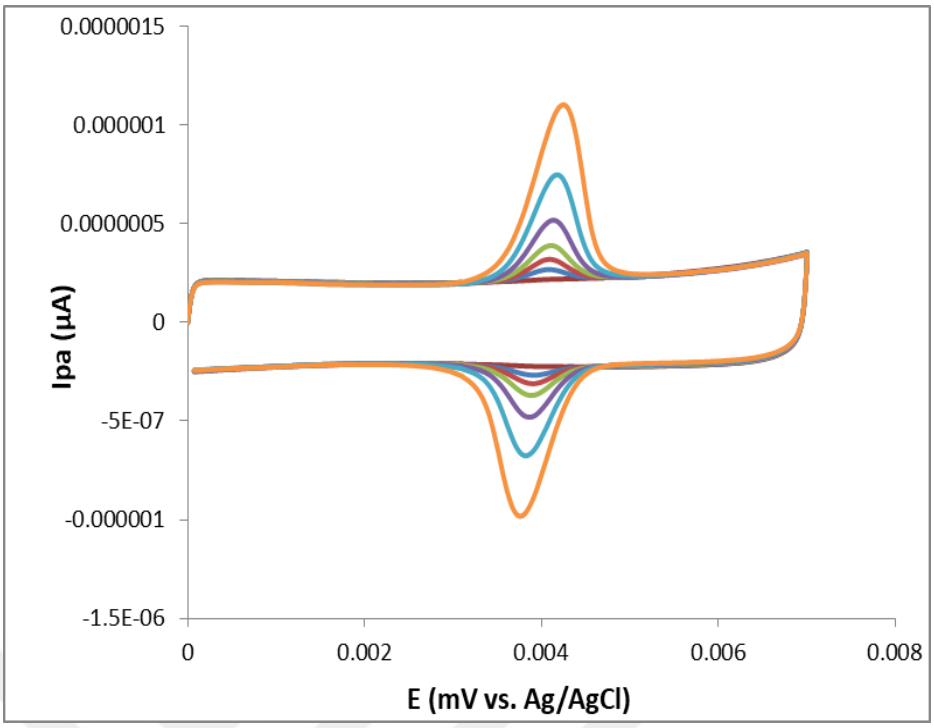


Figure 4.9. CVs of various concentrations of PAR at W-Sb2O3NPS-MWCNT/GCE: PAR Concentrations:6.7×109M;1.3×108M;2.7×108M;4.7×109M;8.1×108M; 1.35×107M;2.35×10M;4.0×10-7M;6.6×10-7M;1.3×10-9M;2.5×10-6M Scna rate: 50 mV/s.

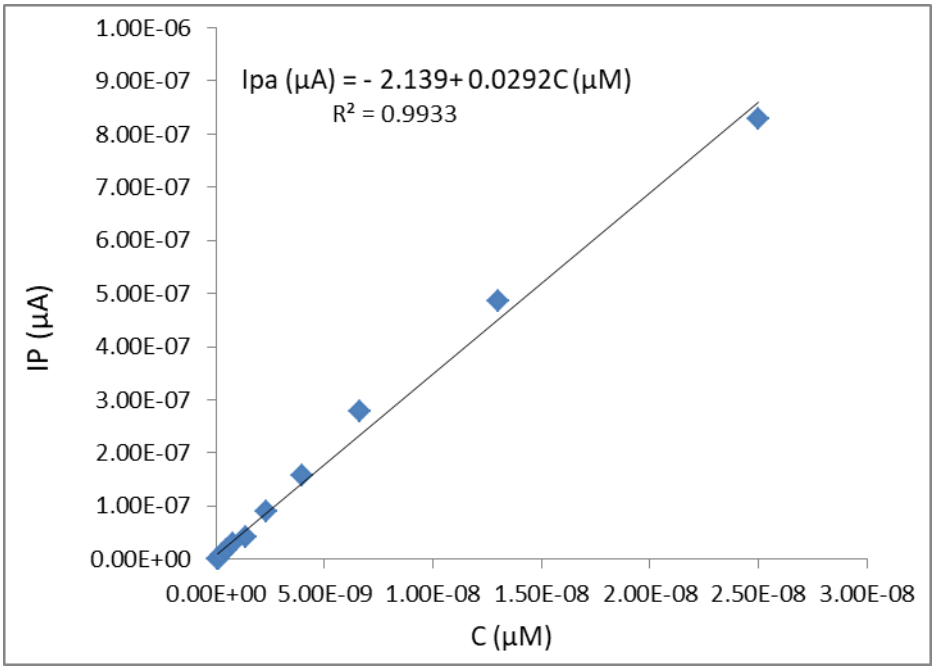


Figure 4.10. Plot of peak currents vs. increasing concentrations of PAR.

Table 4.1. A comparison of various electrodes

Electrode	***pH used***	***Linear range (μM)***	***Detection limit (nM)***	***Reference***
C_{60}/GCE	7.2	50-1500	50000	(Goyal and Singh, 2006)
N-DHPB-MWCNT/CPE	7.0	15-270	10000	(Ensafi et al., 2011)
PANI-MWCNT/GCE	5.5	1-100	2500	(Li and Jing, 2007)
PAY/nano-TiO_2/GCE	7.0	12-120	2000	(Kumar et al., 2008)
PEDOT/SPE	5.0	4-400	1390	(Su and Cheng, 2010)
ZrO_2/CPE	7.0	1- 2500	912	(Mazloum-Ardakani et al., 2010)
C-Ni/GCE	3.0	2-230	600	(Wang et al., 2007)
f-MWCNT/GCE	8.0	3-300	600	(Alothman et al., 2010)
PR/MCPE	5.0	0.7-100	530	(Thomas et al., 2013)
IL/CNTPE	7.0	1-600	500	(Tavana et al., 2012)
PSS-PDDA/GE	7.0	25-400	500	(Manjunatha et al., 2011)
Poly(taurin)-MWCNT/GCE	7.3	1-100	500	(Wan et al., 2009)
CoOx/CCE	13	5-35	370	(Razmi and Habibi, 2010)
Carbon ionic liquid electrode	4.6	1-2000	300	(Shang-Guan et al., 2008)
Nafion/TiO_2-graphene	7.0	1-100	210	(Fan et al.,2011)
Chitosan-MWCNT/GCE	7.0	1-145	100	(Babaei et al., 2010)
Ppyox/AZ/Au	2.8	0.2-100	80	(Gholivand and Amiri, 2012)
MWCNT-ACS/GCE	9.0	0.05-2	50	(Lu and Tsai, 2011)
MWCNT/CPE	4.0	0.1 – 100	50	(Shahrokhian and Asadian, 2010)
Carbon NP/GCE	7.0	0.1-100	50	(Ghorbani-Bidkorbeh et al., 2010)
Graphite oxide/GCE	2.0	0.165-26.5	40	(Song et al., 2011)
SWCNT-DPF/GCE	6.5	0.1-20	40	(Sun and Zhang, 2007)
SWCNT-Graphene/GCE	7.0	0.05-64.5	38	(Chen et al., 2012)
Graphene/GCE	9.3	0.1-20	32	(Kang et al., 2010)
ISSM-CNT/PE	7.0	0.112– 69.4	25.8	(Sanghavi et al., 2010)
MWCNT/BPPGE	7.5	0.01-20	10	(Kachoosangi et al., 2008)
Poly(CCA)/GCE	6.0	0.1-10	10	(Liu et al., 2012)
D50wx2-GNP/GCPE	6.0	0.0334-45.5	4.71	(Sanghavi and Srivastava, 2011)
W-Sb2O3MWCNT/GCE	7.0	0.00067- 25	2.1	This work

4.5. Reproducibility and stability

Repitative voltammograms of PAR were recorded to calculate the relative standard deviation (RSD). The results showed that the RSD for 10 successive scans was 5.4% suggesting that the reproducibility was excellent. However, 20 scans of the electrode in 0.1 M PBS in buffer solution may regenerate a clean background CV. Also, the decrease in the current over a period of week is only by 5-6% indicating stable currents are observed.

4.6. Determination of paracetamol in the presence of AA

Voltammetry provides sensitive approaches to the quantification of molecules (Kachoosangi et al., 2007; Wildgoose et al., 2006; Ensafi et al., 2009). However, this approach may be restricted in the presence of AA since PAR and AA both exhibits at similar potentials. CVS of various concentrations of PAR in the presence of AA is shown in Figure 4.11.

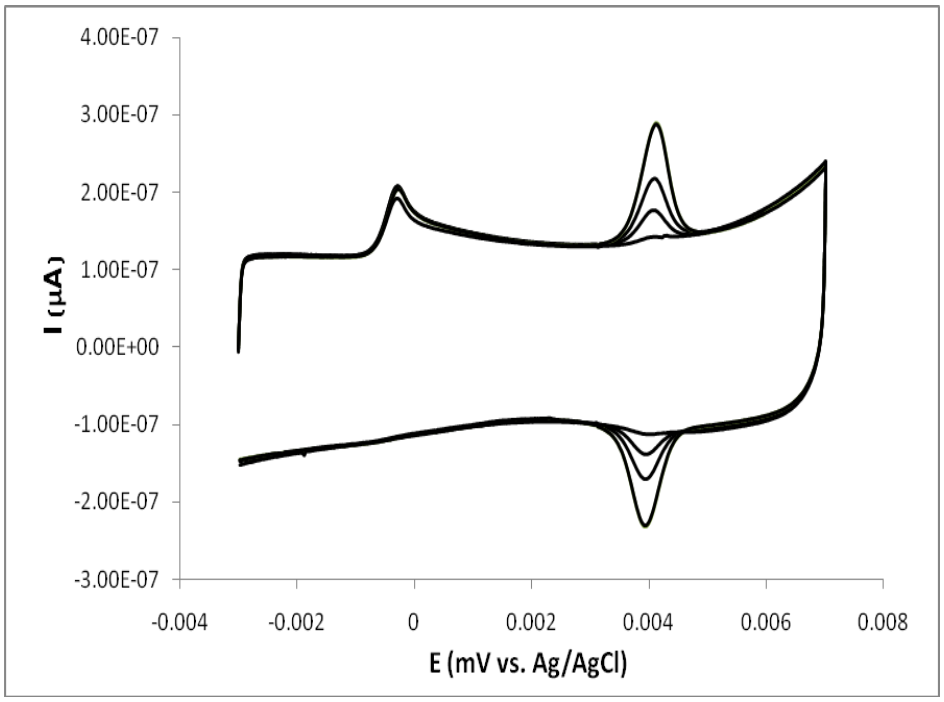


Figure 4.11. Cyclic voltammograms of 2500 ul AA PAR at 0.5 µg W- Sb_2o_3/CNT/GCE in 0.1M PBS at pH 7.0. Scan rate: 50 mV/s. PAR concentrations: 5 ul;, 10ul; 15 ul.

However, tow sharp peaks were obtained for AA and PAR at W-Sb_2O_3-MWCNTs/GCE (Figure 4.11.). As shown, the voltammetry of PAR was not influenced in the presence of AA indicating that AA has no influence on the quantification of PAR.

4.7. Quantification of paracetamol in tablets

PAR containing PAROL tablets were used as the real samples. The electroanalysis of tablets is summarised in Table 4.2. The proposed procedure enabled an avearge recovery of 99.0% with RSD of 1.6% analysis of tablets. As given in Table 4.2, the value obtained was in agreement with the label value. This indicated proposed voltammetric approach can be easily utilized for quantifying PAR in pharmaceuticals.

Table 4.2. Determination of PAR in pharmaceuticals

Content (mg)	Found (mg)	Recovery %	R.S.D %
500.0	495±7.2	99.0	1.6

Mean ± standard deviation (n = 5)

5. CONCLUSION and SUGGESTIONS

A novel electroanalytical approach for the detection of PAR was developed using a GCE modified with MWCNT and antimony oxide nanoparticles and tungsten nanoparticles. The proposed electrode a great electrocatalytic effect for the process of PAR. The W-SB_2O_3-MWCNT/GCE also exhibited a great increase in the current response. The procedure was used for the determination of PAR. It wa shown that the peak current increased linearly with of PAR concentration. A linear range 6.7×10^{-9} M - 2.5×10^{-6} M was obtained for the quantification of PAR. The procedure enabled a detection limit of 2.1×10^{-9} M. The proposed electrode was also used for the determintaion of PAR in the presence of AA. The results showed that AA did not interfere with the detection of PAR.

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