



## Electrochemical Detection of Paracetamol at Multi Wall Carbon Nanotubes/ Titanium Dioxide Composite Modified Electrode

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Electrochemical behaviour of paracetamol at the multi wall carbon nanotubes/titanium dioxide (MWCNT/TiO<sub>2</sub>) composite film modified glassy carbon electrode (GCE) *via* solvent casting method was studied. It is shown that the MWCNT/TiO<sub>2</sub>/GCE exhibits remarkable improvement in analytical response as compared to other electrodes. Comparing the responses of the MWCNT/TiO<sub>2</sub>/GCE with that obtained at the unmodified glassy carbon electrode, the peak currents were enhanced significantly by 8.5 folds (oxidation peak) and 11.0 folds (reduction peak), which showed stable response with enhanced selectivity and sensitivity. A linear calibration plot having a correlation coefficient of 0.991 was obtained in the concentration range of 0.01-0.12 mM paracetamol. The detection limit for the detection of paracetamol was calculated as 11.77 μM based on 3 σ/m. The method was applied in the determination of paracetamol in commercial tablets. The recoveries of the composite modified electrode obtained were 95.2 and 96.2 % for five determinations.

**Key Words:** Multi wall carbon nanotubes, Titanium dioxide nanoparticles, Composite, Paracetamol, Cyclic voltammetry.

### INTRODUCTION

Paracetamol or acetaminophen is a drug commonly used to relieve pains such as aches, headaches, menstrual cramps and fever. It is sold under various brand names like tylenol, panadol and aspirin-free anacin. Paracetamol is also used in combination with narcotic analgesics, which increases its efficacy and reduces the risk of narcotics abuse. It is considered safe for human use when the recommended dose is not exceeded. But because of its wide availability, deliberate or accidental overdose is fairly common. Overdose of acetaminophen may cause nausea, vomiting, sweating and exhaustion. Very large overdose can cause liver damage and death within days. Therefore, there is a clear need to find a selective analytical technique, which has high sensitivity and can be used in the standard analysis for detecting the concentration of paracetamol in the application.

Several methods for analytical determination of paracetamol have been reported in literature; liquid chromatography<sup>1</sup>, spectrometry<sup>2</sup>, spectrophotometry<sup>3</sup>, capillary electrophoresis<sup>4</sup>, amperometric<sup>5</sup> and flow injection analysis<sup>6,7</sup> which are known to produce acceptable results. However, they have some limitations, disadvantages such as high cost and time constraints are known to prevail. Consequently, the development and application of electrochemical sensors and methods

for the determination of paracetamol has received considerable interest in the past few decades<sup>8,9</sup>. Previously, the use of carbon nanotubes modified electrode for detection of paracetamol has been reported<sup>10</sup>, but to the best of our knowledge on the use of MWCNT/TiO<sub>2</sub> composite modified electrodes in the determination of paracetamol has not been reported. In this regard, we have fabricated the MWCNT/TiO<sub>2</sub> composite electrode to detect paracetamol. The result is a new type of modified electrode that has fast response and high sensitivity. Thus, we were able to report a successful implementation of the new sensor in the determination of paracetamol in pharmaceutical tablets.

### EXPERIMENTAL

Multi wall carbon nanotubes (MWCNTs) (purity of 95 %, diameter of 20-49 nm, length of 5-15 μm) and TiO<sub>2</sub> nanoparticles (dispersed in water by 5 % weight, < 100 nm particle size) were purchased from Aldrich, USA and used without any further purification. Paracetamol was purchased from the market. All other reagents used in the experimental were of analytical graded and solutions were prepared with deionized distilled water and deaerated with oxygen-free nitrogen gas before each measurement. Solution containing paracetamol and 0.1 M phosphate buffer solution (PBS) at pH 7.0 were prepared just before running each experiment.

All the electrochemical experiments were performed by Bioanalytical Systems (BAS, West Lafayette, IN, USA) CV-50W voltammetric analyzer, which was connected to an external computer. A conventional three-electrode cell was used: a platinum wire as a counter electrode, an Ag/AgCl (3 M NaCl) as a reference electrode, modified and unmodified (bare) glassy carbon electrode (GCE) as working electrodes.

**Preparation of MWCNT/TiO<sub>2</sub>/GCE:** First of all, the surface of the bare glassy carbon electrode (3 mm diameter) was polished carefully with alumina using a microcloth pad followed by ultrasonic grinding for 1 min in distilled water, rinsed with distilled water and dried before use. Then, 1 mg MWCNT was dispersed into 1 mL dimethyl formamide and same volume of distilled water within 0.5 h by ultrasonication. A known amount of the MWCNT/DMF suspension and TiO<sub>2</sub>/water dispersion were deposited onto the cleaned GCE surface using a microsyringe. The two solutions diffused each other homogeneously on the surface of the CGE. The composite was then dried in an oven for 2 min (40 °C) to remove the solvents. Finally, the modified electrode was cooled in room temperature for further measurement.

**General procedure:** To record voltammograms, a stock solution of paracetamol (0.2 mM) was prepared in double distilled water before running the experiments. Required amount of the stock solution was added to 10 mL of 0.1 M phosphate buffer solution at pH 7 containing electrochemical cell. Then, the electrochemical measurements were carried out using cyclic voltammetry.

## RESULTS AND DISCUSSION

**Current enhancement of paracetamol:** Voltammetric behaviour of paracetamol in 0.1 M phosphate buffer solution (pH 7.0) were studied using cyclic voltammetry at various electrodes of the MWCNT/TiO<sub>2</sub>/GCE; MWCNT/GCE and unmodified GCE within the potential range of 0-800 mV using a scan rate of 100 mV/s (Fig. 1). During the electrochemical experiment, the small redox peaks of 0.2 mM paracetamol at bare GCE (Fig. 1c) and greatly increased redox peaks at MWCNT/GCE (Fig. 1b) were observed. An electrochemical response of the MWCNT/TiO<sub>2</sub>/GCE composite (5 μL MWCNT/5 μL TiO<sub>2</sub>) film was characterized in the redox process of paracetamol and remarkable peak currents were found; at +471 mV potential was observed for the oxidation peak current while at +324 mV peak potential *vs.* Ag/AgCl was observed for the reduction peak current as shown in Fig. 1a. The MWCNT/TiO<sub>2</sub> composite film was composed of 5 μL of MWCNT dispersed in DMF and 5 μL TiO<sub>2</sub> dispersed in water were used in this experiment. The process was found to be a quasi-reversible behaviour for paracetamol ( $i_{pa}/i_{pc} \approx 1.34$ ). It can be seen when the MWCNT/TiO<sub>2</sub>/GCE composite was used, a peak current enhancements in the order of 2.3 folds for the oxidative current and 2.0 folds for the reductive current were obtained as compared to when only MWCNT/GCE was used. And when the composite electrode compared with a bare GCE, the higher currents of 8.5 folds for the oxidative current and 11.0 folds for the reductive current were obtained. Besides current improvement, a slight shift of peak potential in the direction of positive value was observed for the MWCNT/

TiO<sub>2</sub> modified GCE as compared to bare electrode potential. The most probable reason of this remarkable peak current enhancement is that, the nano or micro grade size and larger surface area of the nanoparticles led to higher current in the electrochemical reaction.

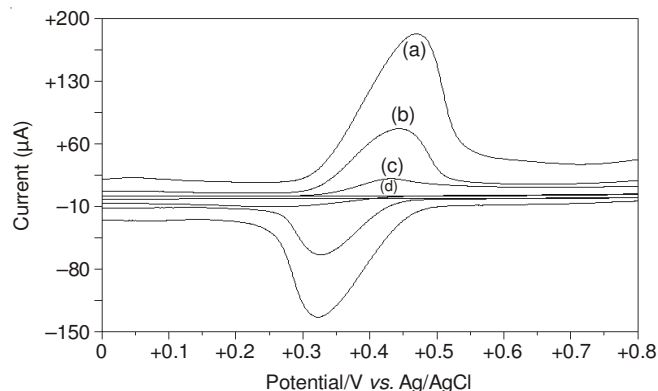


Fig. 1. Cyclic voltammograms of 0.2 mM paracetamol in 0.1 M PBS (pH 7.0) at the MWCNT/TiO<sub>2</sub>/GCE (a); MWCNT/GCE (b); GCE in the presence of analyte (c) and GCE in the absence of analyte (d) with a scan rate of 100 mV/s

**Effect of pH:** The effect of pH on voltammetric response of paracetamol was investigated in the range of pH 2.0-12.0 using pH buffer solutions. The voltammetric peak currents of paracetamol redox obtained in different pH conditions were shown as well-defined at the MWCNT/TiO<sub>2</sub> composite (10 μL MWCNT/5 μL TiO<sub>2</sub>) modified GCE. Fig. 2 shows the cyclic voltammograms recorded at various pH values (pH 6.0-10.0) for 0.2 mM paracetamol. The height of the peaks in this region is almost same, means the pH working range is wider when the use of the MWCNT/TiO<sub>2</sub>/GCE for the detection of paracetamol. As can be seen in the Fig. 3, the redox current increase with increasing pH value (2.0 to 5.0), then between the pH value of 6.0 and 10.0, the value of the redox current is found to be optimized, after which it begins to decrease.

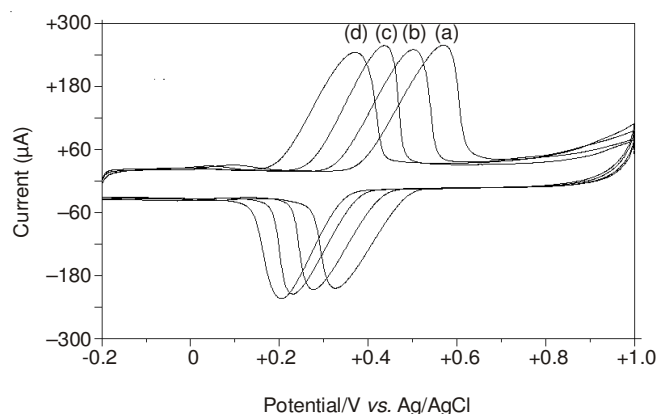


Fig. 2. Cyclic voltammograms of 0.2 mM paracetamol at the MWCNT/TiO<sub>2</sub>/GCE film using pH buffer solutions of pH 6.0 (a); pH 7.0 (b); pH 8.0 (c); 10.0 (d) with a scan rate of 100 mV/s

The peak potentials shift toward the origin and Fig. 4 presents a linear dependence of peak potentials on pH at the modified electrode which is expressed by the following equations:  $E_{pa} = -52.2 \text{ pH} + 844.1$  with  $R^2 = 0.942$  for the oxidation

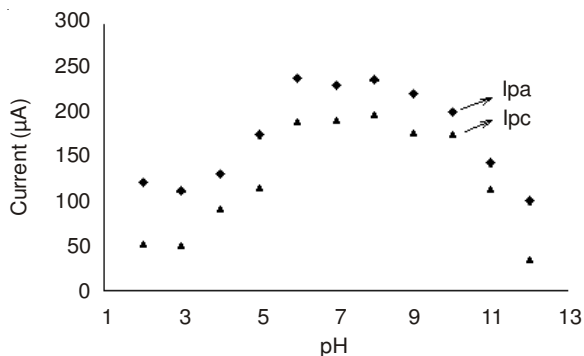


Fig. 3. A plot of the redox peak currents of 0.2 mM paracetamol on different pH solutions of pH 2.0-12.0

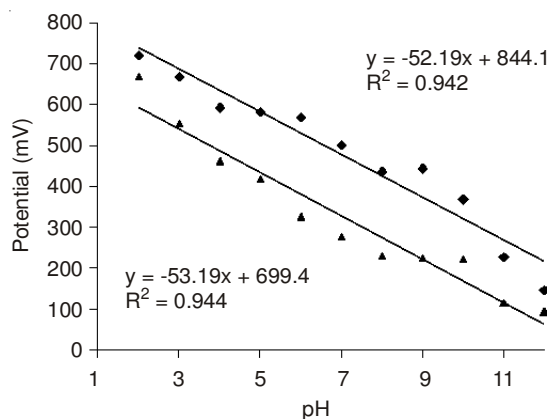


Fig. 4. Dependence of the peak potentials on the different pH of electrolyte solutions ranging from pH 2.0-12.0

and  $E_{pc} = 53.2 \text{ pH} + 699.4$ ,  $R^2 = 0.944$  for the reduction process of paracetamol. From the foregoing observations, it can be inferred that the peak potentials and peak currents of paracetamol for both the oxidation and the reduction process are dependent on pH value.

**Effect of varying percentages in composite:** The effect of varying dosage/percentage of MWCNT (dispersed in DMF) and TiO<sub>2</sub> (dispersed in water) in the composite of MWCNT/TiO<sub>2</sub> was studied for the redox process of 0.2 mM paracetamol. Percentage for MWCNT (5-30  $\mu\text{L}$ ) and TiO<sub>2</sub> (5-10  $\mu\text{L}$ ) were coated on surface of the 3 mm diameter GCE by composite film of the MWCNT/TiO<sub>2</sub>. Fig. 5 shows the peak currents of paracetamol increased considerably with increase in the dosage of MWCNT 5-30  $\mu\text{L}$ . But an increase in the dosage of TiO<sub>2</sub> until 10  $\mu\text{L}$  (with 5  $\mu\text{L}$  MWCNT) resulted in the decrease of peak current. Obtained peak current changes of 0.2 mM paracetamol for the both oxidation and reduction process at the MWCNT/TiO<sub>2</sub> composite film with different dosages of components can be seen in the result presented in Table-1.

The reason of dropping the peak current with increase of TiO<sub>2</sub> in the composite was TiO<sub>2</sub> nanoparticles has a poor electrochemical activity, so when the particles were increased and surrounded MWCNT, they caused to decrease the electron transfer process of paracetamol at the modified electrode. Despite, higher dosage of MWCNT gave excellent result, it was better to use less amount of substance on limited electrode surface (only 3 mm diameter) to avoid certain errors. For rest of the studies, the MWCNT/TiO<sub>2</sub> composite film was created

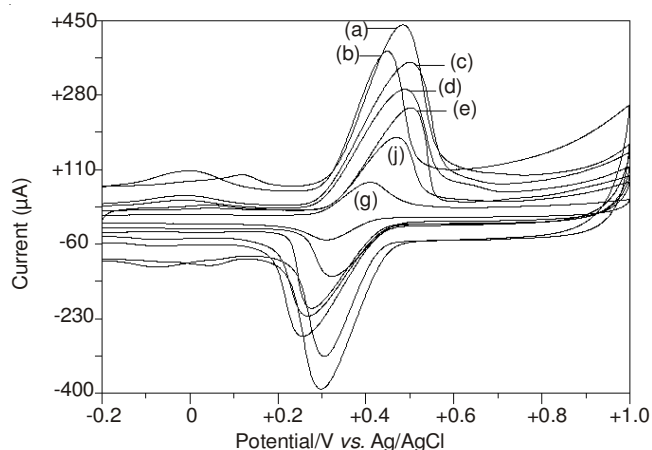


Fig. 5. Cyclic voltammograms of 0.2 mM paracetamol at the MWCNT/TiO<sub>2</sub>/GCE with different dosages/percentages of components in the composite: (a) 30  $\mu\text{L}$  MWCNT/5  $\mu\text{L}$  TiO<sub>2</sub>; (b) 25  $\mu\text{L}$  MWCNT/5  $\mu\text{L}$  TiO<sub>2</sub>; (c) 20  $\mu\text{L}$  MWCNT/5  $\mu\text{L}$  TiO<sub>2</sub>; (d) 15  $\mu\text{L}$  MWCNT/5  $\mu\text{L}$  TiO<sub>2</sub>; (e) 10  $\mu\text{L}$  MWCNT/5  $\mu\text{L}$  TiO<sub>2</sub>; (f) 5  $\mu\text{L}$  MWCNT/5  $\mu\text{L}$  TiO<sub>2</sub>; (g) 5  $\mu\text{L}$  MWCNT/10  $\mu\text{L}$  TiO<sub>2</sub>

Volume of components in the composite ( $\mu\text{L}$ )		Peak current of 0.2 mM paracetamol	
TiO <sub>2</sub>	MWCNT	Oxidation peak current/ $\mu\text{A}$	Reduction peak current/ $\mu\text{A}$
10	5	75.07	50.02
5	5	166.40	123.30
5	10	270.50	207.90
5	15	232.50	191.80
5	20	326.50	247.80
5	25	318.90	259.60
5	30	367.70	340.70

by the dosage of 5  $\mu\text{L}$  MWCNT/DMF with 5  $\mu\text{L}$  TiO<sub>2</sub>/water because of some reasons described above. However, TiO<sub>2</sub> nanoparticles in the composite could enhance the electrochemical activity (or edge effect) of the MWCNT homogeneously coated onto GCE surface for the redox of paracetamol, the dosage/percentage of components in the composite should be in the notice of the further study.

**Effect of scan rate:** The effect of scan rate on the oxidation and reduction of 0.2 mM paracetamol in 0.1 M phosphate buffer solution was investigated at the MWCNT/TiO<sub>2</sub>/GCE composite film by cyclic voltammetry in the range of 5-600 mV/s and voltammograms were shown in Fig. 6. The oxidation and reduction peak currents increased with increase in scan rates. The relationship between the oxidation peak currents and square root of the scan rates was 0.998, expressed by the equation  $y = 0.73x + 0.53$  were shown in Fig. 7.

This linearity indicated that the electrochemical reaction was certainly and diffusion controlled mechanism. When the scan rate increased, the peak current increased significantly, following the peak current separation increased as shown in Fig. 8. Also peak potential shift was observed, while the oxidation peak potential shifts positively the reduction peak

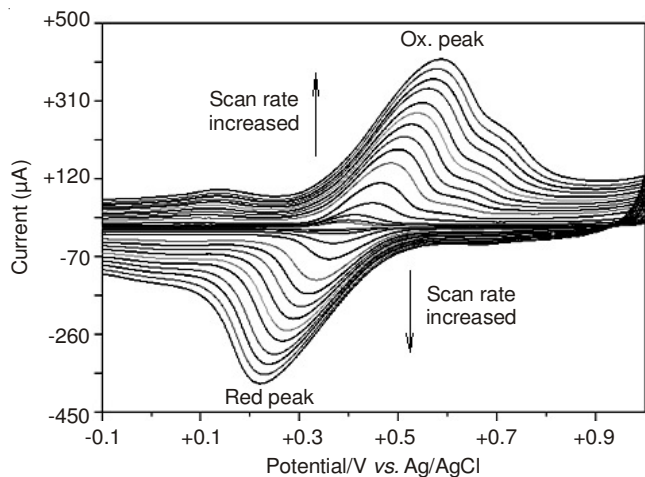


Fig. 6. Cyclic voltammograms of 0.2 mM paracetamol at the MWCNT/TiO<sub>2</sub>/GCE composite film in PBS (pH 7.0) using different scan rates of 5-600 mV/s

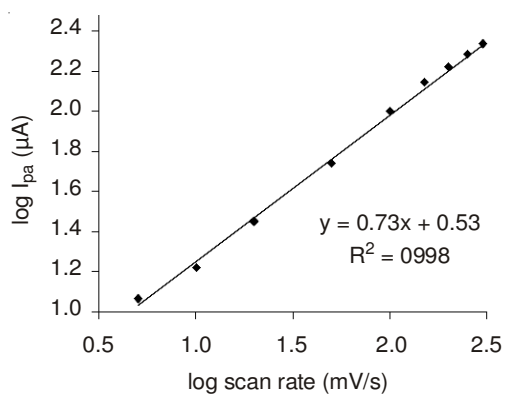


Fig. 7. Dependence of the log oxidation peak current of paracetamol on the log scan rates at the MWCNT/TiO<sub>2</sub>/GCE with different scan rates of 5-600 mV/s

potential was negatively shifted. From a plot of the peak current against peak potential (Fig. 8), the 'zero-current' was found for the oxidation potential at 400 mV ( $y = -1.77x + 709.7$ ;  $R^2 = 0.990$ ) and for the reduction potential at 417 mV ( $y = 1.952x - 813.1$ ;  $R^2 = 0.997$ ) versus Ag/AgCl at the MWCNT/TiO<sub>2</sub> composite film modified GCE in aqueous solution.

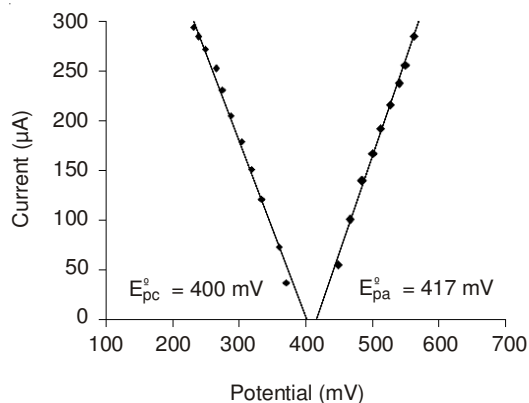


Fig. 8. A plot of the peak current against peak potential of paracetamol at the MWCNT/TiO<sub>2</sub>/GC composite film electrode in phosphate buffer solution using different scan rates of 5-600 mV/s

**Calibration curve:** Fig. 9 shows the cyclic voltammograms of different concentrations of paracetamol at the MWCNT/TiO<sub>2</sub> composite film modified GCE in 0.1 M phosphate buffer solution. A curve was observed from the dependence of the peak current on the concentration ranging between 0.01 and 2.00 mM of paracetamol. Cyclic voltammograms of paracetamol with different concentrations are shown in Fig. 10.

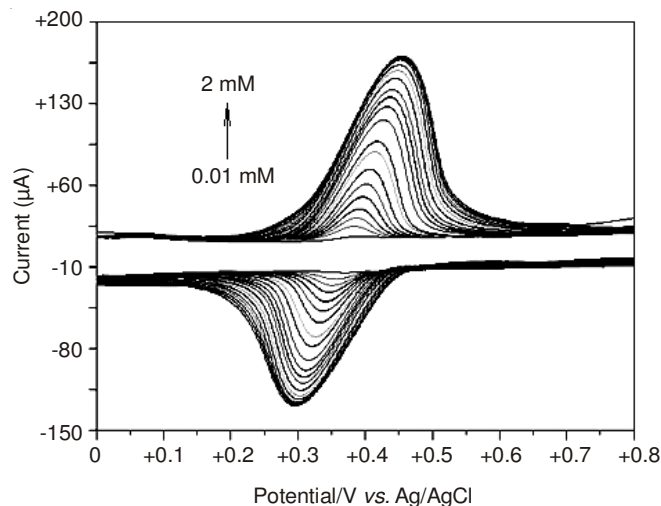


Fig. 9. Cyclic voltammograms were recorded at the MWCNT/TiO<sub>2</sub>/GC composite film electrode of different paracetamol concentration ranging from 0.01 to 2.00 mM in PBS (pH 7.0) with a scan rate of 100 mV/s

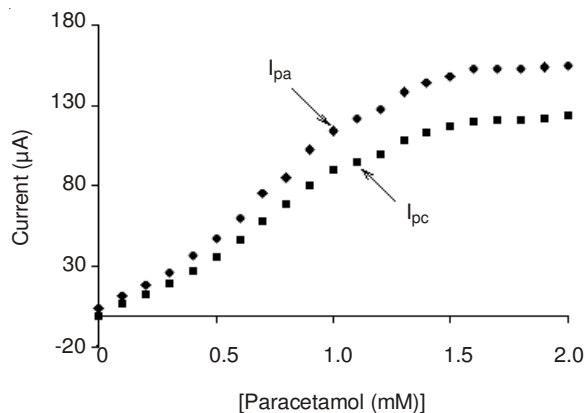


Fig. 10. Calibration curve for the determination of paracetamol with various concentration ranging from 0.01 mM to 2 mM at the MWCNT/TiO<sub>2</sub>/GCE

The linear relationship was found from the dependence of peak current on concentration of paracetamol for both the oxidation and reduction within the range of 0.01 and 1.2 mM concentration as shown in Fig. 11. The linear equations were found with correlation coefficient as  $i_{pa} = 89.94c - 4.22$ ;  $R^2 = 0.991$  and  $i_{pc} = 113.3c - 2.27$ ;  $R^2 = 0.990$ . From the Fig. 12, the relationship between peak potential and concentration can be seen clearly. A good linearity described by the equation:  $y = 40.09x + 386.1$ ;  $R^2 = 0.942$  for the oxidation and  $y = -35.42x + 356$ ;  $R^2 = 0.909$  reduction process of paracetamol. Detection limit was calculated as 11.77  $\mu\text{M}$  based on three times the standard deviation for the blank solution divided by the slope of the analytical curve.

TABLE-2  
RECOVERY RATES OF PARACETAMOL (0.2 mM) EXTRACTED FROM COMMERCIAL PARACETAMOL TABLET SAMPLES IN 0.1 M PHOSPHATE BUFFER SOLUTION USING MWCNT/TiO<sub>2</sub> COMPOSITE MODIFIED GLASSY CARBON ELECTRODE

Chemical formulation	Mentioned concentration of paracetamol (mg/per table)	Obtained concentration of paracetamol (mg/per table)	Recovery rate (%)	Mean recovery (%)	Relative standard deviation (%)
Paracetamol	125	120	96	95	2
		119	95		
		115	92		
		122	97		
		118	94		
Panadol	500	494	99	96	2
		477	95		
		485	97		
		475	95		
		470	94		

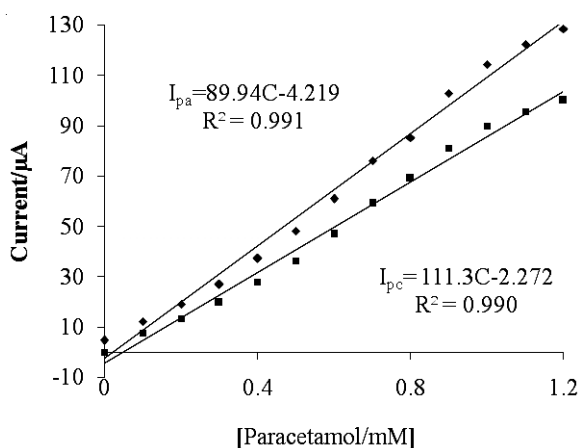


Fig. 11. Plot of the redox peak currents on the different concentrations of paracetamol ranges of 0.01-1.20 mM at the MWCNT/TiO<sub>2</sub>/GCE

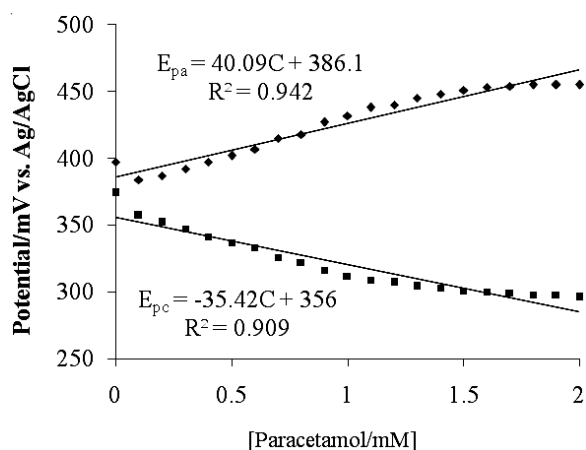


Fig. 12. Plot of peak potential on the concentration (0.01-2.00 mM) of paracetamol at the MWCNT/TiO<sub>2</sub>/GCE

**Paracetamol determination:** The applicability of the MWCNT/TiO<sub>2</sub>/GCE in detection of paracetamol was confirmed by its ability to detect in the presence of paracetamol in commercially available paracetamol tablets. Cyclic voltammetric technique was used for the determination of the extracted paracetamol since it is a very sensitive and rapid method with low detection limit to detect the trace amounts of paracetamol. 0.2 mM concentration of paracetamol extracted from commercial

tablets such as paracetamol and panadol, which contain 125 and 500 mg paracetamol per tablet. The recoveries were obtained for the paracetamol determination in commercial table using the MWCNT/TiO<sub>2</sub>/GCE in 0.1 M phosphate buffer solution (pH 7.0). The voltammetric detection for paracetamol extracted from commercial tablet sample using composite electrode was successfully applied and the recovery rates were 95 ± 2 % for the paracetamol tablet and 96 ± 2 % for the panadol tablet for five replicates (Table-2).

### Conclusion

The MWCNT/TiO<sub>2</sub> composite film modified glassy carbon electrode has been fabricated and successfully applied in the determination of synthetic and real pharmaceutical sample by cyclic voltammetric technique. In both oxidation and reduction, the peak currents of paracetamol were remarkably enhanced at the MWCNT/TiO<sub>2</sub> composite film modified glassy carbon electrode as compared to those at MWCNT modified and unmodified electrodes. Linear relationship of 0.998 and a good detection limit of 1 μM were obtained. Furthermore, some common analytical interfering substances such as ascorbic acid and methionine introduced did not affect the peak current of paracetamol in pharmaceutical sample.

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