

## Effective Determination of Acetaminophen Present in Pharmaceutical Drug Using Functionalized Multi-Walled Carbon Nanotube Film

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Carboxylic acid functionalized multi-walled carbon nanotube (f-MWCNTs) was synthesized by simple acid treatment of pristine multi-walled carbon nanotube. The surface morphology of f-MWCNTs showed the existence of functional groups on the outer sidewalls of f-MWCNTs. These functional groups, -OH and C=O species of carboxylic acid on f-MWCNTs were confirmed by Fourier transform infrared spectroscopy. The f-MWCNT was applied to modify the glassy carbon electrode (GCE) to study the electrocatalysis of acetaminophen. The electrochemical studies showed better diffusion coefficient with stable signal, enhanced effective area and reduced charge transfer resistance results in presence of f-MWCNTs film on GCE. The f-MWCNTs film modified GCE also showed enhanced electrocatalysis towards acetaminophen. The sensitivity of f-MWCNTs film towards acetaminophen ( $9.6 \mu\text{A } \mu\text{M}^{-1} \text{cm}^{-2}$ ) was higher than the value obtained for bare GCE ( $0.33 \mu\text{A } \mu\text{M}^{-1} \text{cm}^{-2}$ ). Similarly, the limit of detection of acetaminophen at f-MWCNTs film (39.8 nM) was lower than other electrodes. The DPV and selectivity studies revealed that f-MWCNTs modified GCE can be efficiently applied for acetaminophen determination in real samples.

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**Keywords:** Multiwall carbon nanotubes; modified electrodes; electrocatalysis; acetaminophen; p-acetaminophenol.

### 1. INTRODUCTION

Acetaminophen is a well known drug which has extensive applications in pharmaceutical industries. It is an antipyretic and analgesic compound that has high therapeutic value. It is also used as precursor in penicillin synthesis, stabilizer for hydrogen peroxide, photographic chemical, etc. Various studies reported the determination of acetaminophen in drug formulations by different techniques such

as spectrophotometry [1,2], sequential injection system [3], spectrofluorimetry [4], etc [5-8]. In all the above mentioned studies the estimation was done by the oxidation of acetaminophen by various oxidants. However, electrochemical methods are more advantageous than the conventional methods because of their quick response, high accuracy and wide range of detection. But the electrochemical analysis by unmodified electrodes has limitations, for example glassy carbon electrode (GCE) has pronounced fouling effect, poor selectivity and reproducibility. To overcome these limitations and enhance electrocatalysis reaction of acetaminophen, electrodes were modified by catalysts such as C<sub>60</sub> [9], Nafion-ruthenium oxide pyrochlore [10], Cu(II)-terthiophene carboxylic acid [11], etc [12-16].

Among the catalysts used for electrode modification, matrices made of carbon nanotubes (CNTs) received considerable attraction in the past two decades. CNT matrices were of great interest because of their properties such as high surface area, electrical conductivity and good chemical stability. The structure of CNTs enables the electron transport along the tube axis, but their electrochemical behavior is highly sensitive to local environments [17]. These properties made CNTs ideal for usage in electrochemical sensors to determine chemical and biochemical compounds [18-21]. Even though the electrocatalytic activity of pristine CNT matrices show good results, some properties like mechanical stability, sensitivity for different techniques, detection limit were not excellent. Further, the pristine CNTs generally insoluble in common solvents and usually form stabilized bundles due to van der Waals force. So, it is extremely difficult to disperse them in a solution and cast as a uniform matrix. To overcome these limitations, new studies were developed for the preparation of functionalized CNTs [22-24]. The chemical functionalization of CNT is one of the few methods which enhanced the interfacial adhesion between the nanotubes and electrode surface [25]. Also, the interaction between the electrode surface and CNT enhances the electron shuttling between the analyte in solution and electrode surface.

In the past years various chemical methods were devised for functionalizing CNTs [26]. One such method uses strong acids such as nitric and sulfuric acid to generate carboxylic acid moieties on the side walls of CNTs [27,28]. A few studies reported the successful usage of these functionalized CNTs for electrochemical determination of compounds such as hydrogen peroxide [29], choline [30], theophylline [31], etc [32,33]. In this article we report carboxylic acid group functionalized multi-walled carbon nanotubes (f-MWCNTs) for the determination of acetaminophen. Literature survey shows that there were no attempts made for the acetaminophen determination using carboxylic acid group f-MWCNTs. The objective of our study was to prepare an efficient f-MWCNTs matrix modified electrode without any heterogeneous catalyst by simple CNT functionalization method. The characterization and the efficiency of the f-MWCNTs are also reported in this article. The f-MWCNT film modified electrode preparation process involves the modification of electrode with uniformly well dispersed f-MWCNTs.

## 2. EXPERIMENTAL

### 2.1. Materials

Multi-walled carbon nanotubes (MWCNTs) (outer diameter = 7-15 nm, inner diameter = 3-6 nm and length = 0.5-200  $\mu$ m) and acetaminophen obtained from Aldrich and Sigma-Aldrich were used

as received. All other chemicals used were of analytical grade. The preparation of aqueous solution was done with twice distilled deionized water. Solutions were deoxygenated by purging with pre-purified nitrogen gas. Phosphate buffer solution (PBS) pH 7.0 was prepared from 0.1 M  $\text{Na}_2\text{HPO}_4$  and 0.1 M  $\text{NaH}_2\text{PO}_4$  aqueous solutions.

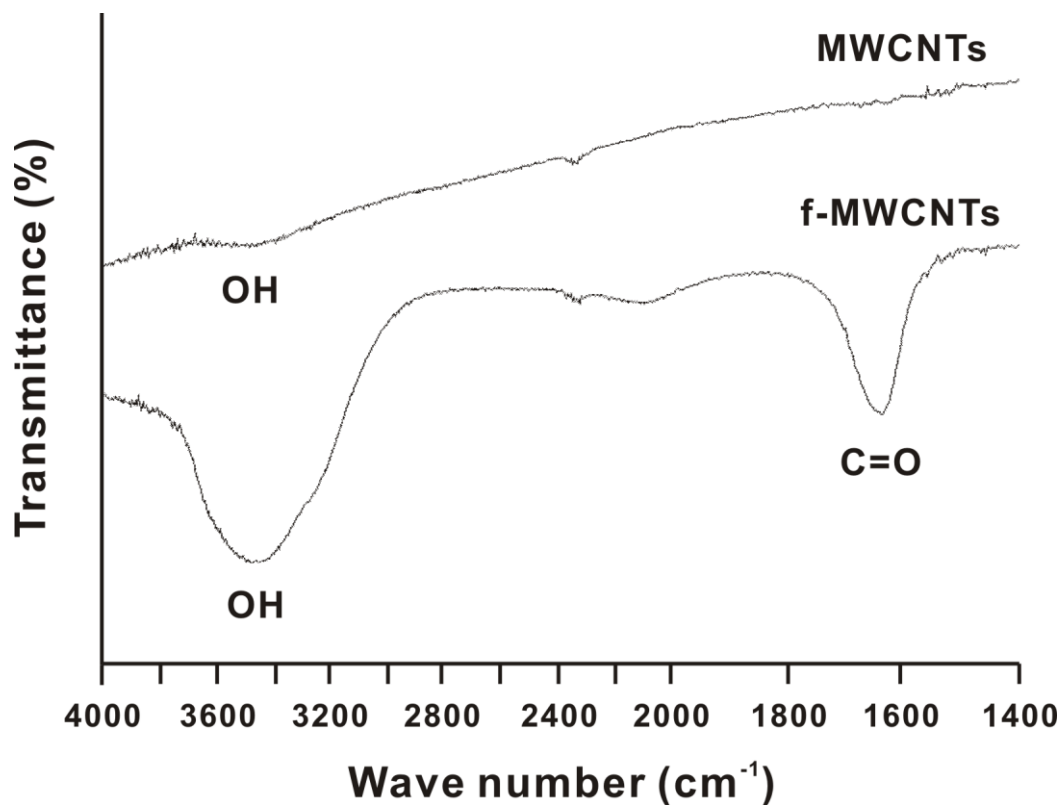
## 2.2. Apparatus

Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) were performed using analytical system models CHI-1205 and CHI-750 potentiostats respectively. A conventional three-electrode cell assembly consisting of an Ag/AgCl reference electrode and a Pt wire counter electrode were used for electrochemical measurements. The working electrode was either unmodified GCE or GCE modified with f-MWCNTs film. In all the experimental results, potential reported was with reference to Ag/AgCl electrode. The Fourier transform infrared (FT-IR) spectroscopy measurements were carried out using Perkin Elemer spectrum GX-49935 model instrument. The morphological characterization of various films was examined by means of transmission electron microscopy (TEM) (JEOL JEM-2100F). The electrochemical impedance spectroscopy (EIS) measurements were performed using IM6ex ZAHNER (Kroanch, Germany). Rotating disk electrode (RDE) experiments were performed using CHI-750 potentiostat with analytical rotator AFMSRX (PINE instruments, USA). All the measurements were carried out at  $25\text{ }^\circ\text{C} \pm 2$ .

## 2.3. Preparation of f-MWCNTs film modified electrode

The important challenge in the preparation of MWCNT solution for electrode modification was the difficulty in preparing a homogeneous solution. Generally, the dispersion of CNTs was carried out by physical (milling) and chemical methods (covalent and noncovalent functionalization). In this work the functionalization and dispersion of MWCNTs were carried out by following the literature [34,35], where, 50 mg of pristine MWCNTs was heated at  $350\text{ }^\circ\text{C}$  for 2 h to remove the amorphous carbon and catalyst impurities, and cooled to room temperature. The heat treated MWCNTs were ultrasonicated for 4 h in 20 mL concentrated HCl to remove other impurities, and washed several times with water and then dried at  $100\text{ }^\circ\text{C}$  in air oven. These purified MWCNTs were acid treated using sulfuric acid and nitric acid mixture (3:1) for 6 h by ultrasonication at room temperature, and then washed several times with water until the pH of the supernatant was neutral. The acid treatment process adds carboxylic acid groups on the side walls of MWCNTs [27,28]. The carboxylic acid group functionalized MWCNTs were dried overnight at  $60\text{ }^\circ\text{C}$ . Finally the uniform dispersion of f-MWCNTs was obtained by 6 h ultrasonication of f-MWCNTs in water.

Before starting each experiment, GCEs were polished by BAS polishing kit with  $0.05\text{ }\mu\text{m}$  alumina slurry and it was rinsed and then ultrasonicated in double distilled deionized water. The GCEs studied were uniformly coated with  $50\text{ }\mu\text{g cm}^{-2}$  of f-MWCNTs from f-MWCNTs dispersion and dried at room temperature. Then the f-MWCNTs modified electrode was carefully washed with double distilled deionized water before using it for electrochemical experiments.



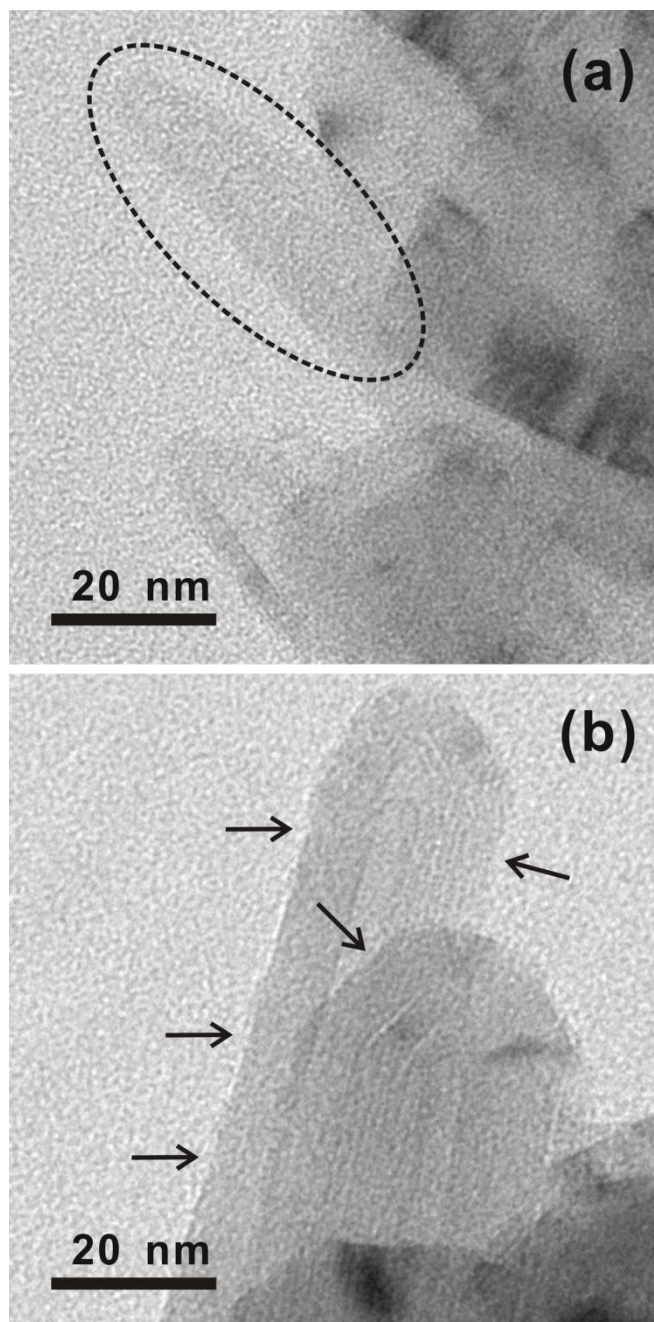
**Figure 1.** FT-IR spectra of pristine MWCNTs and f-MWCNTs.

### 3. RESULTS AND DISCUSSION

#### 3.1. FT-IR and TEM studies of pristine MWCNTs and f-MWCNTs

The pristine MWCNTs and the f-MWCNTs were characterized using FT-IR spectroscopy and TEM. The carboxylic acid functionalization of MWCNTs was confirmed using FT-IR spectroscopy. The FT-IR spectroscopy measurements were carried out with potassium bromide pellets containing very low concentration of pristine MWCNTs or f-MWCNTs. Fig. 1 shows the FT-IR spectra of pristine MWCNTs and f-MWCNTs. In both spectra, the band around  $3400\text{ cm}^{-1}$  attributed to the presence of hydroxyl groups ( $-\text{OH}$ ) on the surface of MWCNTs [25,36]. However, in the case of f-MWCNTs the  $-\text{OH}$  characteristic band appeared significantly broad and with higher intensity. This increase in intensity is attributed to the increase in number of hydroxyl groups on MWCNTs surface after the acid treatment. Similarly, the presence of carboxylic acid groups on f-MWCNTs was confirmed with the  $\text{C}=\text{O}$  band stretching of  $-\text{COOH}$  appearing at  $1650\text{ cm}^{-1}$  [37-39]. But there was no  $\text{C}=\text{O}$  band stretching of  $-\text{COOH}$  observed in pristine MWCNTs spectrum. These observations clearly indicate the existence of  $-\text{OH}$  and  $-\text{COOH}$  groups on the surface of f-MWCNTs.

The morphological difference between pristine MWCNTs (Fig. 2 (a)) and f-MWCNTs (Fig. 2 (b)) was studied using TEM. The darkened areas in Fig. 2 (a) are the amorphous carbon and catalyst impurities present on untreated MWCNTs, whereas only few darkened areas are seen in Fig. 2 (b). This shows the increase in purity of f-MWCNTs after acid treatment.



**Figure 2.** TEM images of (a) pristine MWCNTs and (b) f-MWCNTs.

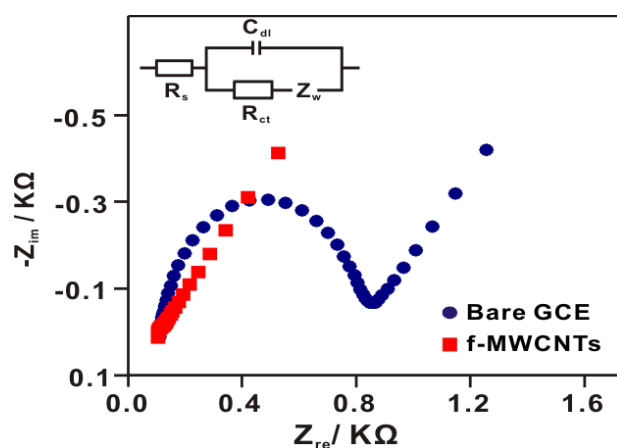
The arrow markings in Fig. 2 (b) indicate that the functional groups generated on the outer sidewalls created “bumpy” morphology, whereas there were no “bumpy” structures observed on the sidewalls of untreated MWCNTs (marked ellipse in Fig. 2(a)). It is obvious that the outer sidewalls of untreated MWCNTs have uniform morphology without any damage. The bends and stretches along the sidewalls of f-MWCNTs are due to the attached moieties [40,41]. Even though the morphology of outer walls of f-MWCNTs was affected by acid treatment, the morphology of inner walls was still intact. The above discussed morphology of f-MWCNTs proved the existence of functional groups such as  $-OH$  and  $-COOH$  on its surface.

### 3.2. Electrochemical studies of bare and f-MWCNT modified GCEs

For various electrochemical characterizations, f-MWCNTs dispersion was casted on GCEs as mentioned in section 2.3. The prepared f-MWCNT film modified GCEs were washed carefully with deionized water before transferring them in to aqueous solution for electrochemical characterizations. In all the following experiments, pristine MWCNTs were excluded because of difficulty in dispersion and electrode modification, whereas bare GCE and f-MWCNTs have been compared in each study. The effective area of GCE electrode before and after modification with f-MWCNTs was calculated using Randles-Sevcik equation (1).

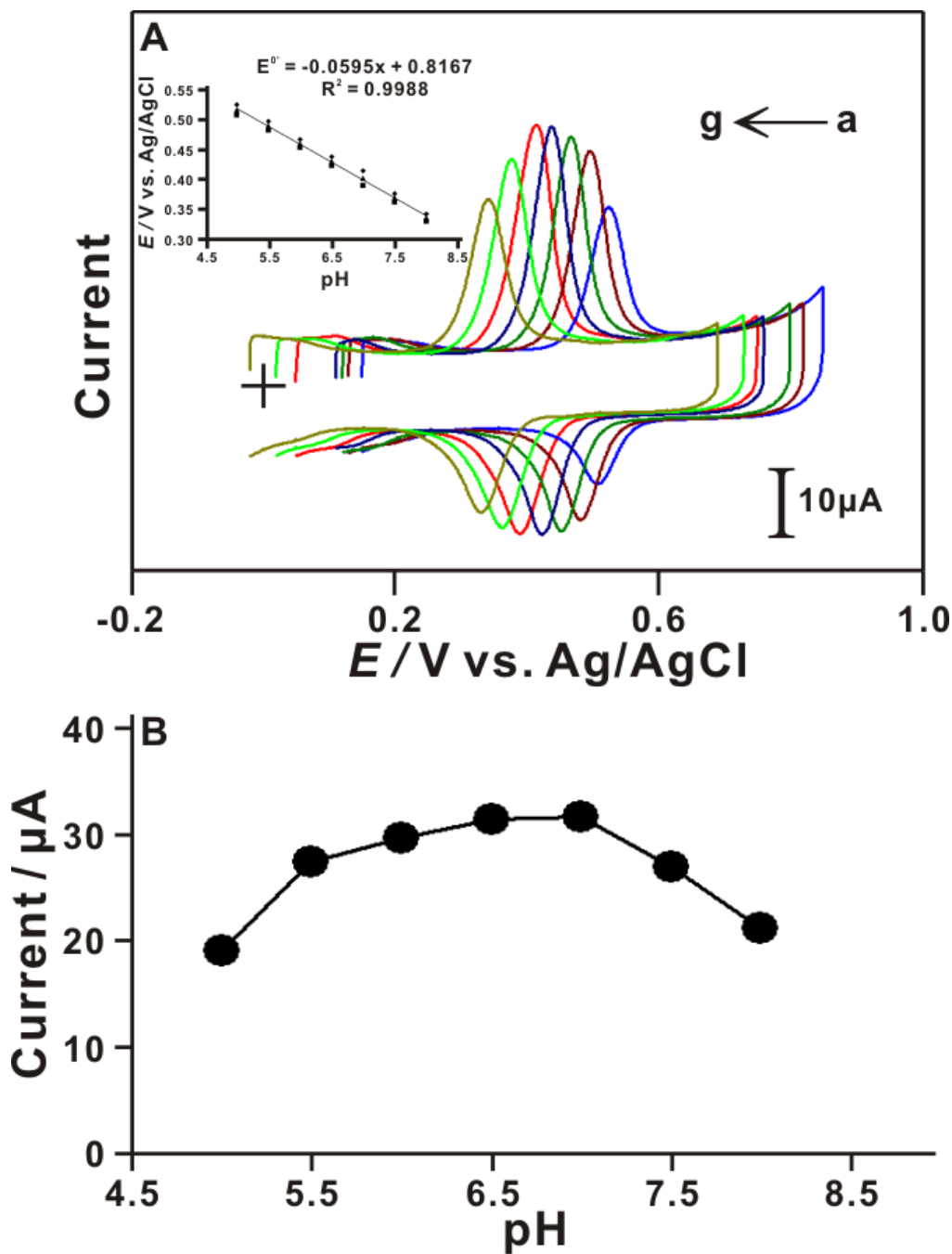
$$I_p = 0.4463nFAC(nFvD/RT)^{1/2} \quad (1)$$

where,  $I_p$  is the peak current,  $n$  is the number of electrons appeared in the half-reaction for the redox couple,  $F$  is Faraday's constant,  $v$  is the scan rate,  $D$  is the analyte's diffusion coefficient,  $A$  is the electrode area,  $R$  is the universal gas constant,  $T$  is the absolute temperature and  $C$  is the concentration of analyte. From the above equation and cyclic voltammogram results (figure not shown), the effective area of bare GCE was  $0.2 \text{ mm}^2$  and f-MWCNT film modified GCE was  $0.22 \text{ mm}^2$ . This result shows that the presence of f-MWCNTs on GCE enhances the effective area of electrode by  $0.4 \mu\text{m}^2 \mu\text{g}^{-1}$  which in turn can enhance the electrocatalytic activity.



**Figure 3.** EIS of bare GCE and f-MWCNTs modified GCE in  $5 \text{ mM Fe(CN)}_6^{3-}/\text{Fe(CN)}_6^{4-}$  in PBS. Amplitude:  $5 \text{ mV}$ , frequency:  $0.1 \text{ Hz}$  to  $1 \text{ MHz}$ . Inset shows the Randles circuit for the above electrodes.

The electrochemical impedance spectroscopy was carried out to study the charge transfer resistance of bare GCE and f-MWCNT film modified GCE. Fig. 3 shows the impedance spectra represented as Nyquist plots ( $Z_{im}$  vs.  $Z_{re}$ ) for bare GCE and f-MWCNT film modified GCE using  $5 \text{ mM Fe(CN)}_6^{3-}/4-$  as electrolyte. Inset of Fig. 3 represents the Randles equivalent circuit model used to fit the experimental data, where  $R_s$  is electrolyte resistance,  $R_{ct}$  charge transfer resistance,  $C_{dl}$  double layer capacitance and  $Z_w$  Warburg impedance.



**Figure 4.** (A) Cyclic voltammograms of f-MWCNTs film modified GCE in various pH solutions containing 0.1 mM acetaminophen (scan rate  $50 \text{ mVs}^{-1}$ ), where a to g is pH 5 to 8. The inset is the formal potential vs. pH from 5 to 8. (B) Plot of  $I_{pa}$  of acetaminophen vs. pH.

The semicircle appeared in the Nyquist plot indicates the parallel combination of charge transfer resistance and double layer capacitance resulting from electrode impedance [42-44]. Both the above said modified and unmodified electrodes exhibit semicircles with various diameters in the frequency range 0.1 Hz to 1 MHz. The results show that the area of semicircle for bare GCE is greater than f-MWCNT film modified GCE. In order to find the electron transfer efficiency of the electrodes,  $R_{et}$  values were obtained for both modified and unmodified electrodes by fitting the Nyquist plot



results with Randles equivalent circuit model. The obtained  $R_{et}$  values of bare GCE and f-MWCNT film modified GCE were 671.4 and 8.4  $\Omega$  respectively. These values reveal that the charge transfer resistance for f-MWCNT film modified GCE is lower than bare GCE. The decrease in charge transfer resistance in presence of f-MWCNTs is 13.26  $\Omega \mu\text{g}^{-1} \text{cm}^{-2}$ . This proves that f-MWCNTs present on GCE enhanced the electron shuttling between reactant and the electrode surface. All these above electrochemical studies revealed that the f-MWCNT film modified GCE has excellent electrochemical properties such as high effective area and electron transfer rate. These good electrochemical properties can be useful for the effective electrocatalysis of analytes.

### 3.3. Electrocatalysis of acetaminophen at f-MWCNT film modified GCE

The effect of pH on the electrochemical behavior of acetaminophen at f-MWCNT film modified GCE was studied. The cyclic voltammograms of f-MWCNT film modified GCE were obtained in various pH aqueous buffer solutions in the presence of 0.1 mM acetaminophen (Fig. 4). In these experiments, f-MWCNT film modified GCE was prepared as mentioned in section 2.3 and washed with deionized water before transferring it in to each pH solution containing acetaminophen. The results show that the redox reaction of acetaminophen is stable in the pH range between 5 and 8.

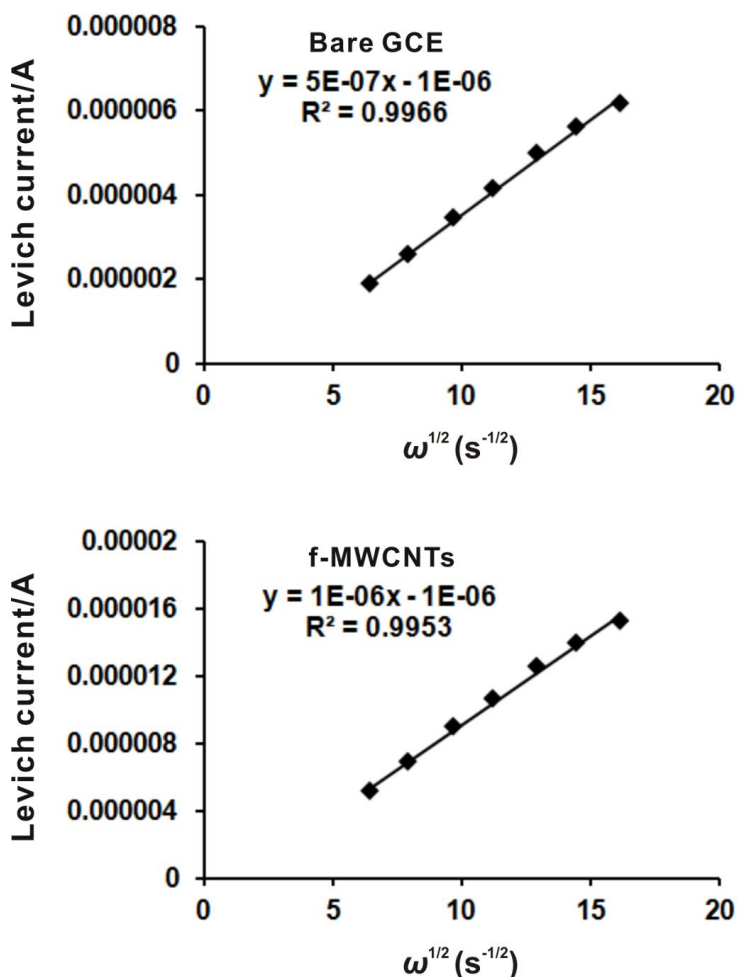
The redox reaction exhibits higher peak current in pH 7.0 PBS. Similarly, the oxidation peak current of acetaminophen is higher than the reduction peak current which implies that f-MWCNT film modified GCE catalyses the electrochemical oxidation of acetaminophen. Further, the acetaminophen's redox peaks ( $E_{pa}$  and  $E_{pc}$ ) depends on the pH of buffer solution. The response from the plot of acetaminophen's formal potential vs. pH has the slope of 59.5 mV  $\text{pH}^{-1}$ , which is close to that given by Nernstian equation for equal number of electrons and protons transfer in a redox reaction.

The cyclic voltammograms of 0.1 mM acetaminophen at f-MWCNT film modified GCE in pH 7.0 PBS at different scan rates show that the anodic and cathodic peak currents of acetaminophen's redox couple increased linearly with the increase in scan rate (figure not shown). Similarly, the  $\Delta E_p$  at each scan rate shows that the peak separation of acetaminophen's redox couple increases as the scan rate increases. These observations and the ratio of  $I_{pa}/I_{pc}$  for acetaminophen at f-MWCNT film modified GCE demonstrate that the redox process is diffusion controlled, where the  $I_{pc}$  is lower than  $I_{pa}$ .

A detailed study on acetaminophen oxidation by bare and f-MWCNT modified GCEs were carried out using RDE technique. In these experiments, the electrocatalytic oxidation of acetaminophen was studied at different rotation speeds (400 to 2500 rpm) in PBS. From these voltammogram results the Levich plots were obtained for both bare and f-MWCNT modified GCEs (Fig. 5).

If the electron transfer process of the f-MWCNT film is assumed to be fast, in tune with the experimental conditions, then the rate determining step must have been one of the following: (i) mass transfer process of acetaminophen in the solution, (ii) catalytic process at the film/solution interface or (iii) electron diffusion within the film.



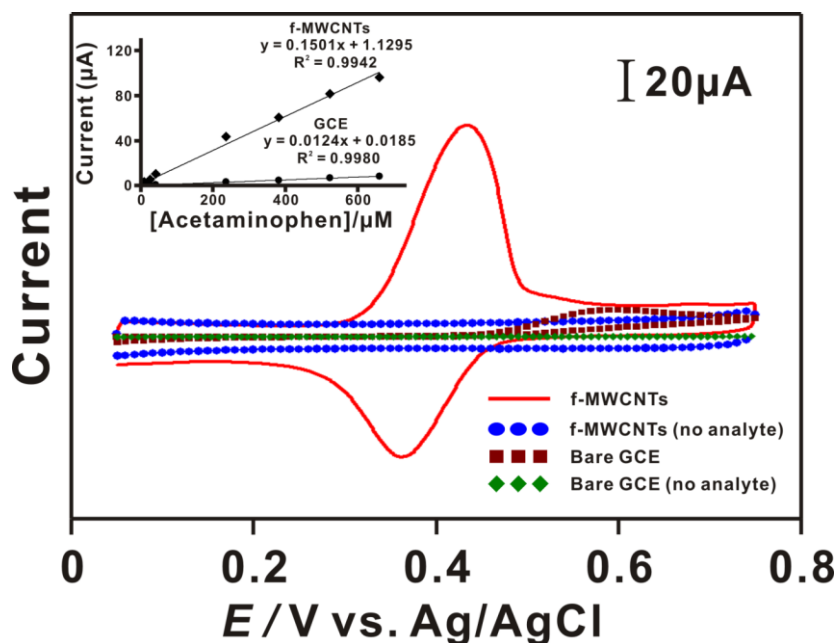


**Figure 5.** Plots of Levich current of acetaminophen vs. rotation rate for bare and f-MWCNTs modified GCEs.

In case, the oxidation of acetaminophen at f-MWCNT film controlled solely by mass transfer process in the solution, then the relationship between the limiting current and rotating speed should obey the following Levich equation,

$$I_L = 0.62nFAD^{2/3}\omega^{-1/2}\nu^{-1/6}c_0 \quad (2)$$

Where,  $n$  is the number of electrons (for acetaminophen  $n = 2$ ) [45],  $F$  faraday constant,  $A$  area of disk electrode ( $0.16 \text{ cm}^2$ ),  $D$  diffusion coefficient,  $\omega$  angular velocity of the electrode,  $\nu$  kinematic viscosity,  $c_0$  bulk concentration of acetaminophen ( $21.5 \text{ }\mu\text{M}$ ). The diffusion coefficients of acetaminophen at bare and f-MWCNT modified GCEs were calculated and they are  $4.2 \times 10^{-10}$  and  $1.2 \times 10^{-9} \text{ cm}^2 \text{ s}^{-1}$  respectively. These above electrochemical characterization results reveal that f-MWCNT film modified GCE can be used for the electrocatalysis of acetaminophen oxidation.



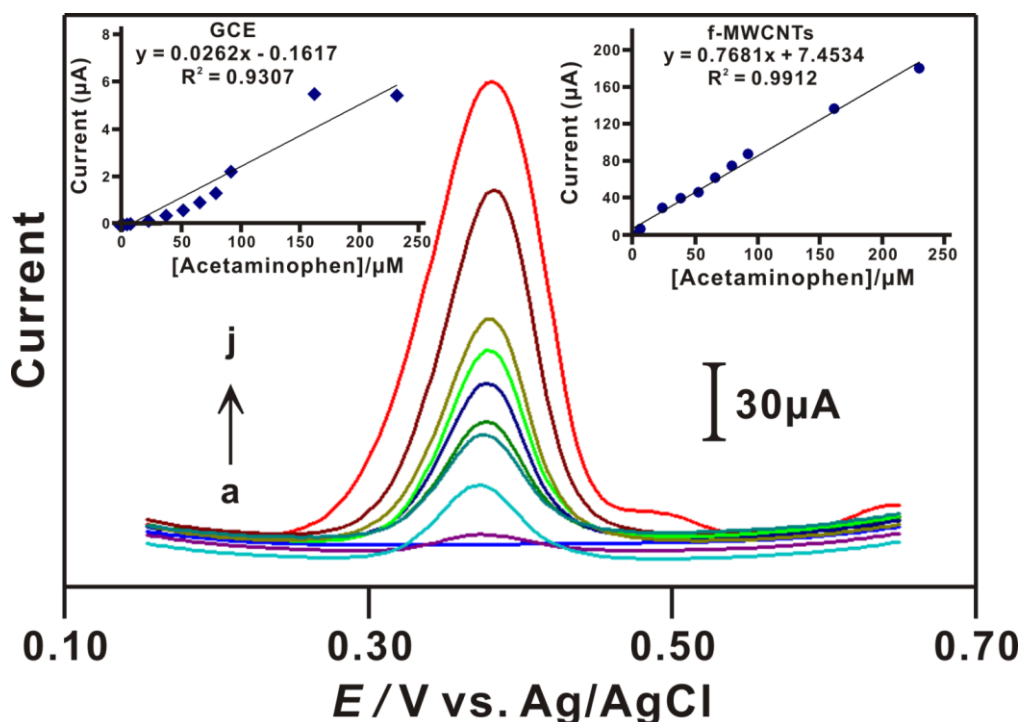
**Figure 6.** Cyclic voltammograms of acetaminophen (0.66 mM) at bare GCE and f-MWCNTs modified GCE in PBS at  $50 \text{ mV s}^{-1}$ ; where both electrodes are shown with and without 0.66 mM acetaminophen. The inset is the plot of peak current ( $I_{pa}$ ) vs. concentration of acetaminophen at bare GCE and f-MWCNTs modified GCE.

### 3.4. Electroanalysis of acetaminophen at bare and f-MWCNT film modified GCEs

The f-MWCNT film was synthesized on GCE at similar conditions given in section 2.3. Then the f-MWCNT film modified GCE was washed carefully with deionized water and transferred to PBS for the electroanalysis of acetaminophen using CV. All the cyclic voltammograms were recorded at the constant time interval of 1 min with  $\text{N}_2$  purging before the start of each experiment. Fig. 6 shows the electrocatalytic oxidation of acetaminophen at f-MWCNTs modified and unmodified GCEs with scan rate of  $50 \text{ mV s}^{-1}$ , where both the electrodes are shown with highest concentration (0.66 mM) and in the absence of acetaminophen. The cyclic voltammogram of f-MWCNT film does not exhibit reversible redox couple in the absence of acetaminophen, and upon addition of acetaminophen a new growth in the oxidation peak of acetaminophen appears at 416 mV ( $E_{pa}$ ). Similarly, the ( $E_{pa}$ ) of acetaminophen for bare GCE appeared at 596 mV. This result shows that the f-MWCNTs reduce the overpotential of acetaminophen's oxidation. In these electrocatalysis experiments an increase in concentration (0.19  $\mu\text{M}$  to 0.66 mM) of acetaminophen simultaneously produces a linear increase from 0.74  $\mu\text{M}$  to 0.66 mM in the oxidation peak current ( $I_{pa}$ ) at f-MWCNT film modified GCE. At bare GCE the linear increase of ( $I_{pa}$ ) is from 0.9  $\mu\text{M}$  to 0.66 mM.

It is obvious that the f-MWCNT film modified GCE shows higher electrocatalytic activity for acetaminophen than bare GCE. In detail, the enhanced electrocatalytic activity of f-MWCNT film modified GCE can be explained in terms of both lower overpotential and higher peak current of acetaminophen than at bare GCE. Where, the  $I_{pa}$  of acetaminophen at f-MWCNT film modified GCE is 416 mV and bare GCE is 596 mV. The increase in peak current and decrease in overpotential, both are

considered as electrocatalytic activity [46]. From the slopes of linear calibration curves (Fig.6 inset) the sensitivities are calculated:  $0.16 \mu\text{A } \mu\text{M}^{-1} \text{cm}^{-2}$  for bare GCE and  $1.88 \mu\text{A } \mu\text{M}^{-1} \text{cm}^{-2}$  for f-MWCNT modified GCE. The correlation coefficient for bare GCE was 0.9980 and for f-MWCNTs modified GCE was 0.9942. It is obvious that the sensitivity of f-MWCNT film for acetaminophen determination was higher when compared to bare GCE. From the same results, limit of detection (LOD) of acetaminophen at bare and f-MWCNT modified GCEs at a signal to noise ratio of 3 is calculated and they are 0.74 and  $0.63 \mu\text{M}$  respectively. In these results too f-MWCNT film modified GCE shows lower LOD than at bare GCE. The overall view of these results reveals that f-MWCNT film is efficient for acetaminophen analysis.



**Figure 7.** Differential pulse voltammograms of acetaminophen (a to j = 74.1 nM to 0.23 mM) at f-MWCNTs modified GCE in PBS. Insets represent the plot of peak current ( $I_{\text{pa}}$ ) vs. concentration of acetaminophen at bare GCE and f-MWCNTs modified GCE.

### 3.5. DPV and selectivity studies of acetaminophen at bare and f-MWCNT modified GCEs

Fig. 7 shows the differential pulse voltammograms recorded for the addition of different acetaminophen concentrations at f-MWCNT film modified GCE in PBS. After each successive acetaminophen addition, pre-purified  $\text{N}_2$  gas was purged into PBS for 1 min before starting the next voltammogram. Differential pulse voltammograms of acetaminophen at bare GCE were also carried out at similar conditions (figure not shown). From the corresponding differential pulse voltammograms the  $I_{\text{pa}}$  values were plotted against acetaminophen concentrations as shown in insets of Fig. 7. From these inset plots it is obvious that f-MWCNT film exhibits a steady state response towards the addition of various acetaminophen concentrations when comparing bare GCE. The oxidation peak current of

acetaminophen increased linearly from 38.1  $\mu\text{M}$  to 0.16 mM for bare GCE; and 74.1 nM to 0.23 mM for f-MWCNT film. From the slopes of linear calibration curve the sensitivities are calculated and they are 0.33  $\mu\text{A } \mu\text{M}^{-1} \text{ cm}^{-2}$  for bare GCE and 9.6  $\mu\text{A } \mu\text{M}^{-1} \text{ cm}^{-2}$  for f-MWCNT modified GCE. The correlation coefficient for bare GCE was 0.9307 and f-MWCNT modified GCE was 0.9912. Similarly, LOD of acetaminophen at bare and f-MWCNT modified GCEs at a signal to noise ratio of 3 was 0.2  $\mu\text{M}$  and 39.8 nM respectively. These electroanalytical results obtained using DPV were better than CV results. In general, DPV results disclose that f-MWCNT film modified electrode is more efficient for acetaminophen determination. The comparison of f-MWCNT film modified GCE with that of previously reported electrodes in Table. 1 highlights the advantages of f-MWCNTs such as lower in over potential, lower detection limit, higher sensitivity and the detection of acetaminophen in neutral pH.

**Table. 1.** Comparison of electroanalytical results of acetaminophen at various modified electrodes in various conditions.

Electrodes	pH	$E_{pa}$ (V)	Linear range	Sensitivity	LOD	Ref.
f-MWCNTs	7.0	0.416	74.1 nM to 0.23 mM	$9.6 \mu\text{A } \mu\text{M}^{-1} \text{ cm}^{-2}$	39.8 nM	This work
CNTPE	5.5	0.58	0.15 to 126 $\mu\text{M}$	$I_{pa}=4.72 \times 10^{-8} + 0.0179c$ ( $I_{pa}$ : A, c: M)	43 nM	[47]
L-cysteine	6.2	0.43	0.1 $\mu\text{M}$ to 0.2 mM	$I_{pa} (\mu\text{A}) = 3.29 + 14.51c$ ( $\mu\text{M}$ )	50 nM	[45]
PEDOT	5.0	0.5	4 to 400 $\mu\text{M}$	$I_{pa} (\mu\text{A}) = 0.1252 c (\mu\text{M}) + 2.5292$	3.7 $\mu\text{M}$	[48]
MWCNTs	6.0	0.46	0.4 $\mu\text{M}$ to 0.15 mM	$I_{pa} (\text{A}) = 1.2216 \times 10^{-8} + 0.10063c$ ( $I_{pa}$ : A, c: M)	0.12 $\mu\text{M}$	[49]
MWCNTs- PANIFAD	2.3	0.73	2 to 60 $\mu\text{M}$	$3.3 \text{ mA mM}^{-1} \text{ cm}^{-2}$	-	[50]

The DPV experiments for selectivity studies were carried out using various analytes such as ascorbic acid, acetic acid, uric acid and dopamine[51-57]. In selectivity experiments the concentration of acetaminophen was kept constant at 1 mM, and then each analyte was added at 10  $\mu\text{M}$ . The interference of the analytes during acetaminophen determination was calculated from the variation between  $I_{pa}$  values of acetaminophen before and after the addition of analytes (Table. 2). The  $I_{pa}$  values in above mentioned table show that there is not much interference of analytes during acetaminophen determination.

The results also show the presence of analytes decreases the  $I_{pa}$  of acetaminophen. These selectivity experimental results suggest that f-MWCNT film can be efficiently used for acetaminophen determination in real samples.

**Table 2.** Interference of various compounds during acetaminophen determination at f-MWCNTs film modified GCE.

Analyte	Interference <sup>a</sup> ( $\mu\text{A mM}^{-1}$ )
Ascorbic acid	No interference
Acetic acid	No interference
Uric acid	-1.21
Dopamine	-9.01

<sup>a</sup> Change in  $I_{pa}$  of acetaminophen (1 mM) at f-MWCNTs film after the addition of respective analyte (10  $\mu\text{M}$ ).

### 3.6. Analysis of panadol tablet

The performance of f-MWCNT film modified GCE was tested by applying it to the determination of acetaminophen present in panadol tablet. The technique used for the determination was DPV, and the experimental conditions were similar to that of DPV studies given in section 3.5. The panadol tablets were obtained from a Taiwan's pharmaceutical company. The tablet's labeled composition was 100 mg  $\text{g}^{-1}$  of acetaminophen and 13 mg  $\text{g}^{-1}$  of caffeine anhydrous. The concentrations added in the experiment, found and relative standard deviation (RSD) obtained from the experiments are given in Table. 3. From the results given in Table. 3 the recovery of acetaminophen is  $\approx 106\%$ . The analysis shows that f-MWCNT film is efficient for acetaminophen determination.

**Table 3.** Electroanalytical values obtained from the acetaminophen determination in panadol tablet using DPV in PBS by f-MWCNTs film modified GCE.

Added ( $\mu\text{M}$ )	Found ( $\mu\text{M}$ )	Recovery (%)	%RSD
5.63	5.98	106	0.82
52.3	56.2	107	
162	170	105	

## 4. CONCLUSIONS

A functionalized MWCNT film modified GCE was prepared for the electroanalysis of acetaminophen. The prepared f-MWCNTs film for the electroanalysis combines the advantages of ease of fabrication and good reproducibility. The FT-IR and TEM results confirmed the presence of functional groups in f-MWCNTs and have shown the difference in surface morphology between pristine MWCNTs and f-MWCNTs. Further, f-MWCNT film has excellent functional properties along with good electrocatalytic activity on acetaminophen. The experimental methods of CV and DPV with f-MWCNT film presented in this article provide an opportunity for qualitative and quantitative characterization of acetaminophen sensor.

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## References

1. J.E. Wallace, *Anal. Chem.* 39 (1967) 531.
2. F.M. Plakogiannis, A.M. Saad, *J. Pharmaceutical Sci.* 64 (1975) 1547.
3. J.F. van Staden, M. Tsanwani, *Talanta* 58 (2002) 1095.
4. M. Oliva, R.A. Olsina, A.N. Masi, *Talanta* 66 (2005) 229.
5. K.K. Verma, A.K. Gulati, S. Palod, P. Tyagi, *Analyst* 109 (1984) 735.
6. M.K. Srivastava, S. Ahmad, D. Singh, I.C. Shukla, *Analyst* 110 (1985) 735.
7. S.M. Sultan, I.Z. Alzamil, A.M.A. Alrahman, S.A. Altamrah, Y. Asha, *Analyst* 111 (1986) 919.
8. F.A. Mohamed, M.A. AbdAllah, S.M. Shammatt, *Talanta* 44 (1997) 61.
9. R.N. Goyal, S.P. Singh, *Electrochim. Acta* 51 (2006) 3008.
10. J.M. Zen, Y.S. Ting, *Anal. Chim. Acta* 342 (1997) 175.
11. M. Boopathi, M.S. Won, Y.B. Shim, *Anal. Chim. Acta* 512 (2004) 191.
12. X. ShangGuan, H. Zhang, *Anal. Bioanal. Chem.* 391 (2008) 1049.
13. F.S. Felix, C.M.A. Brett, L. Angnes, *J. Pharm. Biomed. Anal.* 43 (2007) 1622.
14. M.L.S. Silva, M.B.Q. Garcia, J.L.F.C. Lima, E. Barrado, *Anal. Chim. Acta* 573 (2006) 383.
15. P. Fanjul-Boaldo, P.J. Lamas-Ardiansa, D. Hernandez-Santos, A. Costa-Garcia, *Anal. Chim. Acta* 638 (2009) 133.
16. M.S.M. Quintino, K. Araki, H.E. Toma, L. Angnes, *Electroanalysis* 14 (2002) 1629.
17. Y. Li, X. Shi, J. Hao, *Carbon* 44 (2006) 2664.
18. J. Wang, M. Musameh, *Anal. Chim. Acta* 511 (2004) 33.
19. H. Cai, X. Cao, Y. Jiang, P. He, Y. Fang, *Anal. Bioanal. Chem.* 375 (2003) 287.
20. A. Erdem, P. Papakonstantinou, H. Murphy, *Anal. Chem.* 78 (2006) 6656.
21. H. Beitollahi, M.M. Ardakani, H. Naeimi, B. Ganjipour, *J. Solid State Electrochem.* 13 (2009) 353.
22. B. Gao, Q. Fu, L. Su, C. Yuan, X. Zhang, *Electrochim. Acta* 55 (2010) 2311.
23. B. Gao, C. Yuan, L. Su, S. Chen, X. Zhang, *Electrochim. Acta* 54 (2009) 3561.
24. E.J. Park, J.Y. Lee, J.H. Kim, C.J. Lee, H.S. Kim, N.K. Min, *Talanta* 82 (2010) 904.
25. J. Kathi, K.Y. Rhee, *J. Mater. Sci.* 43 (2008) 33.
26. D. Tasis, N. Tagmatarchis, A. Bianco, M. Prato, *Chem. Rev.* 106 (2006) 1105.
27. A. Hirsch, *Angew Chem. Int. Edn. Engl.* 41 (2002) 1853.
28. A.R. Bhattacharyya, T.V. Sreekumar, T. Liu, S. Kumar, L.M. Ericson, R.H. Hauge, R.E. Smalley, *Polymer* 44 (2003) 2373.
29. L. Chen, G. Lu, *Sens. Act. B:Chem.* 121 (2007) 423.
30. F. Qu, M. Yang, J. Jiang, G. Shen, R. Yu, *Anal. Biochem.* 344 (2005) 108.
31. Y.H. Zhu, Z.L. Zhang, D.W. Pang, *J. Electroanal. Chem.* 581 (2005) 303.
32. P.Y. Chen, P.C. Nien, C.W. Hu, K.C. Ho, *Sens. Act. B:Chem.* 146 (2010) 466.
33. G.A. Rivas, M.D. Rubianes, M.C. Rodriguez, N.F. Ferreyr, G.L. Luque, M.L. Pedano, S.A. Miscori, C. Parrado, *Talanta* 74 (2007) 291.
34. H. Su, R. Yuan, Y. Chai, Y. Zhuo, C. Hong, Z. Liu, X. Yang, *Electrochim. Acta* 54 (2009) 4149.
35. D.R.S. Jeykumari, S.S. Narayanan, *Biosen. Bioelectron.* 23 (2008) 1404.
36. A. Misra, P.K. Tyagi, M.K. Singh, D.S. Misra, *Diam. Rel. Mat.* 15 (2006) 385.
37. S.D. Oh, S.H. Choi, B.Y. Lee, A. Gopalan, K.P. Lee, S.H. Kim, *J. Ind. Eng. Chem.* 12 (2006) 156.
38. W.H. Chang, I.W. Cheong, S.E. Shim, S. Choe, *Macromol. Res.* 14 (2006) 545.
39. D.S. Bag, R. Dubey, N. Zhang, J. Xie, V.K. Varadan, D. Lal, G.N. Mathur, *Smart Mater. Struct.* 13 (2004) 1263.
40. H. Peng, L.B. Alemany, J.L. Margrave, V.N. Khabashesku, *J. Am. Chem. Soc.* 125(2003) 15174.

41. T. Sainsbury, K. Erickson, D. Okawa, C.S. Zonte, J.M.J. Frechet, A. Zettl, *Chem. Mater.* 22 (2010) 2164.
42. H.O. Finklea, D.A. Snider, J. Fedyk, *Langmuir* 9 (1993) 3660.
43. Y. Li, J.-X. Wei, S.-M. Chen, *Int. J. Electrochem. Sci.* 6 (2011) 3385.
44. Y. Li, C.-Y. Yang, S.-M. Chen, *Int. J. Electrochem. Sci.* 6 (2011) 4829.
45. C. Wang, C. Li, F. Wang, C. Wang, *Microchim. Acta* 155 (2006) 365.
46. C.P. Andrieux, O. Haas, J.M. SavGant, *J. Am. Chem. Soc.* 108 (1986) 8175.
47. H. Xiong, H. Xu, L. Wang, S. Wang, *Microchim. Acta* 167 (2009) 129.
48. W.Y. Su, S.H. Cheng, *Electroanalysis* 22 (2010) 707.
49. L.S. Duan, F. Xie, F. Zhou, S.F. Wang, *Anal. Lett.* 40 (2007) 2653.
50. Y. Li, Y. Umasankar, S.-M. Chen, *Talanta* 79 (2009) 486.
51. S. M. Chen, K. T. Peng, *J. Electroanal. Chem.* 547 (2003) 179.
52. V.S. Vasantha, S.M. Chen, *J. Electroanal. Chem.* 592 (2006) 77.
53. S.M. Chen, K.C. Lin, *J. Electroanal. Chem.* 523 (2002) 93.
54. K.C. Lin, T.H. Tsai, S.M. Chen, *Biosensors and Bioelectronics* 26 (2010) 608.
55. S. Thiagarajan, T.H. Tsai, S.M. Chen, *Biosens. Bioelectron.* 24 (2009) 2712.
56. S. M. Chen, W. Y. Chzo, *J. Electroanal. Chem.*, 587(2006) 226.
57. K. C. Lin, C. Y Yin, S. M. Chen, *Int. J. Electrochem. Sci.* 6 (2011) 3951.