Full Paper

Electrochemical Determination of Acetaminophen by using Modified Screen Printed Carbon Electrode

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Abstract- In the present work, a rapid and sensitive method for electrochemical determination of acetaminophen (AC) based on the modified screen printed carbon electrode (MSPCE) developed. Cyclic voltammetry was used to study the electrochemical behavior of AC and its determination was conducted by applying square wave voltammetry (SWV). The MSPCE in comparison with bare SPCE exhibited enhanced electrocatalytic activity toward the oxidation of AC. A single irreversible oxidation peak was observed at potentials of 590 mV and 480 mV on the MSPCE and bare SPCE, respectively. Based on the results, the linear oxidation peak current was 0.5–220 µM and the correlation coefficient was obtained to be 0.9973. According to the three times standard deviation ($3S_b$) of the blank, the limit of detection was calculated 0.1 µM. The MSPCE was used for quantitative analysis of acetaminophen in AC ampule and AC tablet samples and the results indicate the feasibility of the amperometric method for AC analysis in routine detection.

Keywords- Acetaminophen determination, Magnetic core shell nanoparticles, Screen-printed carbon electrode

1. INTRODUCTION

Drug analysis plays an important role in drug quality control, and has a great impact on public health [1]. Acetaminophen (N-acetyl-P-aminophenol or paracetamol, AC) is a long-established substance being one of the most extensively employed drugs in the world [2]. It is

an antipyretic and analgesic drug commonly used to treat many conditions such as headache, muscle aches, arthritis, backache, toothaches, colds and fevers [3]. In the therapeutic doses, it is a very effective and safe analgesic and is considered as a substitute of aspirin. However, it has been associated with liver necrosis in humans and experimental animal softer high dose exposure [4]. Overdoses of AC can lead to the accumulation of toxic metabolites, causing severe and sometimes fatal hepatotoxicity and nephrotoxicity [1,5].

Therefore, monitoring the AC is important due to the concerns of public health care and drug safety. Accordingly, the development of analytical methods for fast, low-cost, simple and large-scale determination is required. Many methods have been reported so far for its determination, such as titrimetry [6], spectrophotometry [7], capillary electrophoresis [8], fluorimetry [9], flow injection [10] and high-performance liquid chromatography [11]. However, some of these techniques are costly, complicated, time taking process and operated by highly skilled technicians. Incidentally, electrochemical methods provide a simple, rapid, selective detection with low-cost of systems and eco-friendly [12].

Recently, the electrochemical analysis methods are investigated for its simplicity, reproducibility and cost efficiency [13]. With the help of modified electrodes, efficient and enhanced electrochemical analysis platform for determining the AC is expected.

Over the past decades, there has been an increasing trend towards miniaturization of biological and chemical sensors, and their integration with miniaturized sample pre-processing and analysis systems [14, 15]. These devices offer several advantages, including the ability to analyze small volumes of samples, faster analysis time, suitability for automation procedures, and increased reliability and repeatability [16]. Recently, intensive research activity has been focused on developing miniaturized electrochemical sensors for microscale or submicroscale devices intended for extracellular fluid measurement, clinical diagnosis and micro total analysis [17].

The screen-printed electrodes (SPEs) have been designed especially for miniaturization of electrochemical analytical systems [18]. SPEs are highly-versatile, easy to use, cost-effective analytical tools, also suitable to miniaturization [19]. Furthermore, a screen printed electrode avoids the cleaning process, unlike conventional electrodes such as a glassy carbon electrode (GCE) [20].

Nowadays, it continues to be of interest in the developments of new materials capable to change the electrode surface with better analytical properties, including graphene, nanoparticles, and carbon nanotubes [21–29]. Nanomaterials, because of their unique properties, have been extensively developed. Nanoparticles can act as conduction centers facilitating the transfer of electrons and provide great catalytic surface areas. Among them, nanosized metal particle modified electrodes have emerged as a promising alternative for the electroanalysis of organic and inorganic compounds [30-34].

Metal nanoparticles have some distinct advantages such as higher mass transport, lower influence of the solution resistance, low detection limit, and better signal-to noise ratio over the conventional macroelectrodes [35-37].

From both fundamental and industrial points of view, many different synthetic procedures have been developed for the preparation of metal nanoparticles (NPs). Nanoscale materials are attractive targets due to their large surface-to-volume ratio, they exhibit properties that can be significantly different from those of bulk materials [38].

In the present work, we synthesized magnetic core-shell manganese ferrite nanoparticles (MCSNP) [39] and screen printed carbon electrodes were modified with MCSNP. To the best of our knowledge, no study has been reported so far on the determination of acetaminophen by using MCSNP/SPCE.

2. EXPERIMENTAL

2.1. Apparatus and Chemicals

The electrochemical measurements were performed with an Autolab potentiostat/galvanostat (PGSTAT 302N, Eco Chemie, Netherlands). The experimental conditions were controlled with General Purpose Electrochemical System software. Screen printed electrodes were purchased from DropSens (Oviedo, Spain). The pH values were measured using a pH-meter (Metrohm 692 model, Herisau, Switzerland). Acetaminophen and all the other reagents were analytical grade and were obtained from Merck (Darmstadt, Germany). The buffer solutions were prepared from orthophosphoric acid and its salts in the pH range of 2.0–9.0. Magnetic core-shell manganese ferrite nanoparticles were synthesized in our laboratory as reported previously [39].

2.2. Preparation of the electrode

The bare screen-printed electrode was coated with MCSNP as follows. A stock solution of MCSNP in 1 mL aqueous solution was prepared by dispersing 1 mg MCSNP with ultrasonication for 1 h, and a 2 μL aliquot of the MCSNP/H_2O suspension solution was casted on the carbon working electrodes, waiting until the solvent was evaporated in room temperature.

2.3. Preparation of Real Samples

Five tablets of AC (labeled 325 mg per each tablet) were completely ground and homogenized. 200.0 mg of this powder was accurately weighed and dissolved with ultrasonication in 10 mL of water. Finally the mixture was filtered and the clear filtrate was transferred into a 100 mL volumetric flask and diluted to the mark with using 0.1 mol L^{-1} PBS with pH 7. The sample of the AC ampule was prepared by the appropriate dilution with

0.1 M PBS solution (pH 7.0) and directly used for determination of AC. Finally, a suitable volume of the resultant solutions were transfer to electrochemical cell and the resulting solution was used for the analysis of AC.

The samples were spiked with different amounts of AC and contents were analyzed by using the standard addition method in order to prevent any matrix effect. The amount of unknown AC in the AC ampule and tablet can be detected by extrapolating the plot.

3. RESULTS AND DISCUSSION

3.1. Electrochemical behavior of acetaminophen at the surface MCSNP/SPCE

The electrochemical behavior of AC is dependent on the pH value of the aqueous solution. Therefore, pH optimization of the solution seems to be necessary in order to obtain the best results for electrooxidation of AC. Thus the electrochemical behaviors of AC were studied in 0.1 M PBS in different pH values (2.0–9.0) at the surface of MCSNP/SPCE by voltammetry. It was found that the electro-oxidation of AC at the surface of MCSNP/SPCE was more favored under neutral conditions than in acidic or basic medium. Thus, the pH 7.0 was chosen as the optimum pH for electro-oxidation of AC at the surface of MCSNP/SPCE.

Fig. 1 depicts the CV responses for the electro-oxidation of 30.0 μM AC at surface of unmodified SPCE (curve a) and MCSNP/SPCE (curve b). The peak potential due to the oxidation of AC occurs at 480 mV, which is about 110 mV more negative than unmodified SPCE.

Also, MCSNP/SPCE shows much higher anodic peak current for the oxidation of AC compared to unmodified SPCE, indicating that the modification of unmodified SPCE with MCSNP has significantly improved the performance of the electrode toward AC oxidation. The electrooxidation mechanism of AC was shown in Scheme 1.
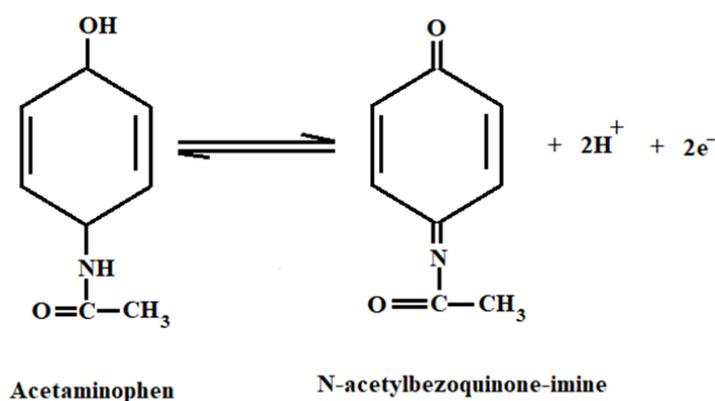
Scheme 1. The electrooxidation mechanism of AC at the 2FTNEMCNPPE electrode.
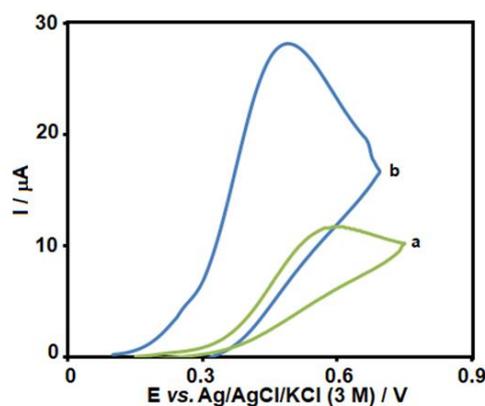
Fig. 1. Voltammograms of (a) unmodified SPE and (b) MCSNP/SPCE in the presence of 30.0 µM acetaminophen at pH 7 (at 50 mV s^{-1}).

3.2. Effect of Scan Rate

The effect of potential scan rates on the oxidation current of AC (Fig. 2) have been studied. The results showed that increasing in the potential scan rate induced an increase in the peak current. In addition, the oxidation processes are diffusion controlled as deduced from the linear dependence of the anodic peak current (I_p) on the square root of the potential scan rate ($\upsilon^{1/2}$).
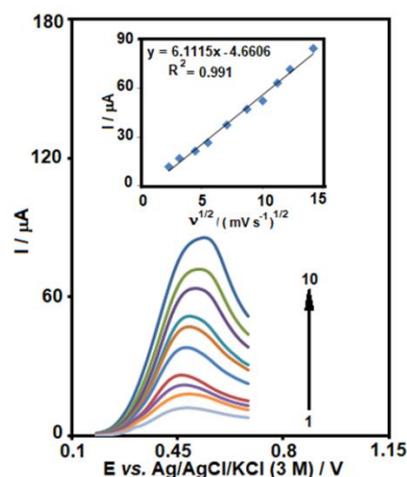

Fig. 2. LSVs of MCSNP/SPCE in 0.1 M PBS (pH 7.0) containing 5.0 µM acetaminophen at various scan rates; numbers 1-10 correspond to 5, 10, 20, 30, 50, 75, 100, 125, 150 and 200 mV s^{-1}, respectively. Inset: Variation of anodic peak current *vs*. square root of scan rate

Tafel plot was drawn from data of the rising part of the current voltage curve recorded at a scan rate of 10 mVs^{-1} for AC (Fig. 3). This part of voltammogram, known as Tafel region, is affected by electron transfer kinetics between substrate (AC) and MCSNP/SPCE. Tafel slope

of 0.0808 V was obtained which agree well with the involvement of one electron in the rate determining step of the electrode process [40] assuming charge transfer coefficients, $\alpha=0.27$ for AC.
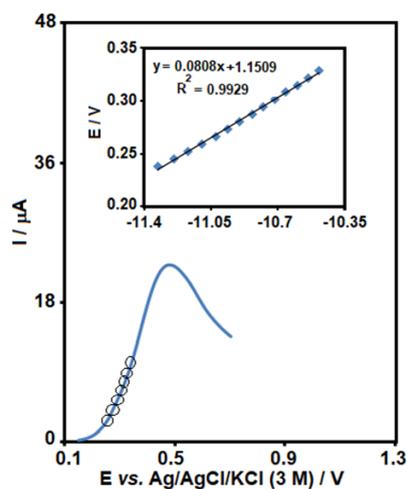

Fig. 3. Tafel plot derived from LSV of MCSNP/SPCE in 0.1 M PBS (pH 7.0) containing 5.0 µM acetaminophen at scan rate of 10 mV/s
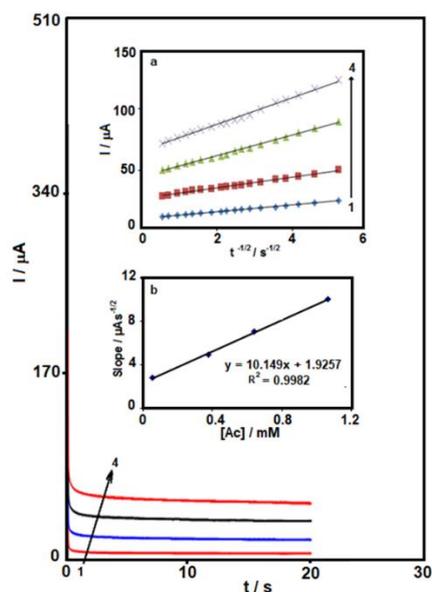

Fig. 4. Chronoamperograms obtained at MCSNP/SPCE in 0.1 M PBS (pH 7.0) for different concentration of acetaminophen. The numbers 1–4 correspond to 0.1, 0.35, 0.65 and 1.1 mM of acetaminophen. Insets: Plots of I *vs.* $t^{-1/2}$ obtained from chronoamperograms 1–4 (a), and Plot of the slope of the straight lines against acetaminophen concentration (b)

3.3. Chronoamperometric Measurements

Chronoamperometric measurement of AC at MCSNP/SPCE was carried out by setting the working electrode potential at 0.7 V *vs*. Ag/AgCl/KCl (3.0 M) for the various concentrations of AC (Fig. 4) and in PBS (pH 7.0). For electroactive materials (AC) with a diffusion coefficient of D, the current observed for the electrochemical reaction at the mass transport limited condition is described by the Cottrell equation [40]:

$$I = nFAD^{1/2} C_b \pi^{-1/2} t^{-1/2} \tag{1}$$

Where D and C_b are the diffusion coefficient ($cm^2 s^{-1}$) and the bulk concentration (mol cm^{-3}), respectively. Experimental plots of I *vs*. $t^{-1/2}$ were employed, with the best fits for different concentrations of AC (Fig. 4a). The slope of the resulting straight lines was then plotted *vs*. AC (Fig. 4b) concentrations. From the resulting slope and Cottrell equation the mean value of the D was found to be 3.5×10^{-7} cm^2/s for AC.
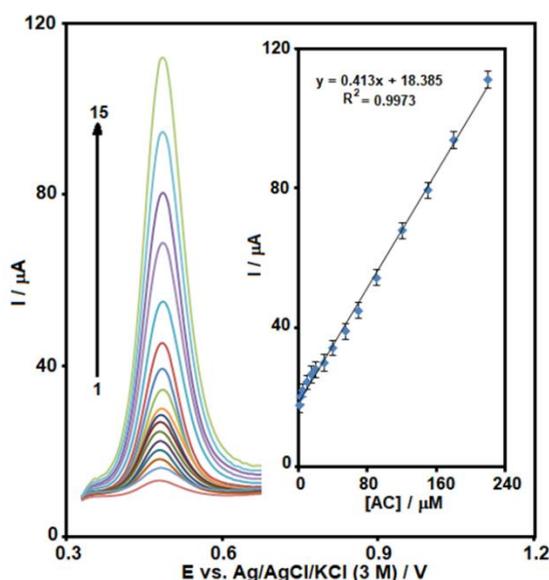

Fig. 5. SWVs of MCSNP/SPCE in 0.1 M PBS (pH 7.0) containing different concentrations of acetaminophen (0.5, 1, 5, 10, 15, 20, 30, 40, 55, 70, 90, 120, 150, 180 and 220 μM). Inset: The plot of the peak current as a function of acetaminophen concentration in the range of 0.5-220 μM

3.4. Calibration plots and limits of detection

The electro-oxidation peak current of AC at the surface of the MCSNP/SPCE can be used for determination of AC in solution. Since, square wave voltammetry (SWV) has the advantage of increase in sensitivity and better characteristics for analytical applications, therefore, SWV experiments (Initial potential=0.33 V, End potential=0.67 V, Step potential=0.002 V, Modulation Amplitude=0.01995 V) were performed using MCSNP/SPCE

in 0.1 M PBS containing various concentrations of AC (Fig. 5). The results showed that the electrocatalytic peak current of AC oxidation at the surface of MCSNP/SPCE was linearly dependent on the AC concentrations, over the range of 0.5×10^{-6}–2.2×10^{-4} M (with a correlation coefficient of 0.9973) and the detection limit (3s) was obtained 0.1×10^{-6} M. A comparison of the analytical performance of present work with other modified electrodes, is listed in Table 1. With respect to Table 1, linear dynamic range (LDR) and limit of detection (LOD) present work are comparable with values reported by other research groups for electrocatalytic oxidation of AC at the surface of chemically modified electrodes by other mediators.

Table 1. Comparison of the efficiency of electrochemical methods used in detection of AC.

Electrode	Modifier	LOD (µM)	LDR (µM)	Ref.
Screen printed electrode	Gold nanoparticles	68	99-1200	[41]
Graphite screen printed electrode	ZnO/Al$_2$O$_3$ nanocomposite	0.06	1-100	[42]
Glacy carbon electrode	Gold nanoparticles/MWCNTs	0.03	0.09-35	[43]
Carbon paste electrode	ZrO$_2$ Nanoparticles	0.91	1-2500	[44]
Carbon paste electrode	Graphen/CoFe$_2$O$_4$ nanocomposite	0.025	0.03-12	[45]
Carbon paste electrode	Graphen/NiFe$_2$O$_4$ nanocomposite	0.004	0.01-9	[46]
Carbon paste electrode	Silicon/palladium nanostructure	0.4	0.1-700	[47]
Carbon paste electrode	ZrO$_2$ nanoparticles	0.9	0.7-2000	[48]
Carbon paste electrode	5-amino-3′,4′-dimethoxy-biphenyl-2-ol/carbon nanotube	0.9	220-850	[49]
Screen printed electrode	magnetic core-shell manganese ferrite nanoparticles (MCSNP)	0.1	0.5-220	This work

3.5 Real Sample Analysis

Finally, MCSNP/SPCE was applied for determination of AC in AC ampule and AC tablet samples. For this purpose, the determination of AC in the real samples were carried out by using standard addition method to prevent any matrix effect. The results are shown in Table 2. Also, the recovery of AC from samples spiked with known amounts of AC was studied. The results were showed that, the added AC was quantitatively recovered from the real samples. These results demonstrate the applicability of the MCSNP/SPCE for determination of AC in the real samples. Also, the reproducibility of the method was demonstrated by the mean relative standard deviation (RSD).

The amounts of AC in ampule and tablet were found to be 326.5 mg/tablet and 9.98 mg/mL, respectively. It was found that there is no significant difference between the results obtained by the MCSNP/SPCE and the nominal value on the ampoule and tablet label (325.0

mg/tablet and 10.0 mg/mL, respectively). The t-test was applied to both sets of results and showed that there was no significant difference at the 95% confidence level.

Table 2. The application of MCSNP/SPE for determination of AC in real samples (n=5)

Sample	Spiked (μM)	Found (μM)	Recovery (%)	R.S.D. (%)
AC tablet	0.0	20.1	---	2.6
	10.0	29.8	97.0	3.2
	20.0	40.5	102.0	2.7
	30.0	49.6	98.3	2.8
AC Ampoule	0	15.5	---	3.1
	10.0	25.1	96.0	2.6
	20.0	35.8	101.5	2.9
	30.0	54.7	98.7	2.7

4. CONCLUSION

In this work, employing magnetic core shell nanoparticles as modifier in modification of SPCEs, a novel sensor has been developed that provides a sensitive method for the determination of AC. The proposed protocol demonstrated herein a novel, simple, portable, inexpensive and easy-to-use fabrication method for the measurement of AC concentration in AC ampule and AC tablet samples with good analytical performance. Due to the unique properties of magnetic core shell nanoparticles, the sensor exhibited remarkable electrochemical activity toward the oxidation of AC. Under optimized conditions, square wave voltammetry exhibited linear dynamic ranges from 0.5–220 μM with detection limit of 0.1 μM.

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