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Application of multiwalled carbon nanotubes/ionic liquid modified electrode for amperometric determination of sulfadiazine

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A highly sensitive amperometric sulfadiazine sensor based on coating multiwalled carbon nanotubes (MWCNTs) and N-octyl-pyridinium-hexafluorophosphate ($OPPF_6$) ionic liquid composite on a glassy carbon (GC) electrode is described. The MWCNTs/$OPPF_6$ composite contributed new properties to electrochemical sensors by combining the advantages of both ionic liquids and MWCNTs. Compared with bare GC electrode, the electrocatalytic activity of MWCNTs/$OPPF_6$ generated a greatly improved electrochemical detection of sulfadiazine including low oxidation potential, high current responses, and good anti-fouling performance. The oxidation peak currents of sulfadiazine obtained on the MWCNTs/$OPPF_6$ coated GC electrode were proportional to the concentration of sulfadiazine within the range of 3.3-35.4 μM with a detection limit of 0.21 μM. Copyright © 2011 John Wiley & Sons, Ltd.

Keywords: sulfadiazine; electrochemical; multiwalled carbon nanotubes; ionic liquid

Introduction

Sulfonamides are commonly used as antibiotics for the therapy of urinary-tract infections, chronic bronchitis and several other bacterial infections.[1] Recently, sulfonamides have been extensively incorporated in animal feedstuff for prophylactic and therapeutic purposes due to their low cost and broad-spectrum bactericidal properties. Overdosage of veterinary sulfonamide drugs or improper medication during withdrawal time (WDT) always results in excessive drug residues found in animal derived food. However, the risk of sulfonamide drug residues existing in food products may cause undesired effects on consumers such as allergy, disorder of the hemopoietic system, carcinogenic, teratogenic action [2] and bacterial resistance.[3] Therefore, the presence of sulfonamide residues in food is a safety concern. Governmental agencies have set limitations on the levels of residues on the basis of toxicological data. Indeed, it is important to develop a sensitive and convenient method for routine analysis of trace sulfonamide residues and their metabolites in agriculture and food samples. Several methods have been developed for the evaluation of the drug residues including gas chromatography (GC),[4] high performance liquid chromatography coupled with fluorimetric detection (HPLC-Fluo),[5,6] or ultra-violet detection (HPLC-UV),[7] enzyme-linked immunosorbent assay (ELISA) method,[8–10] mass spectrometry,[11–13] and time-resolved fluoroimmunoassay (TRFIA).[14] Although these methods have the advantage of high sensitivity and accuracy, they also have drawbacks: expensive instruments are needed, tedious samples preparation, skilled laboratory personnel are required, and so on. Consequently, searching for simple, convenient, low-cost and sensitive analytical methods for rapid detection of sulfonamide residues in animal derived food is of particular significance.

Electrochemical detection methods have the advantage of being simple, low cost and easy to use.[15] Up to now, modified electrodes, such as amperometric DNA-peroxidase sensors,[16] bismuth film electrodes,[17] boron-doped electrodes,[18,19] carbon nanotube-Nafion modified electrodes[20] and metalloporphyrin modified electrodes,[21] were designed for sulfonamide antibiotics determination. And the results show advantages of high determination sensitivity, good stability, and promising selectivity. Obviously, electrochemical determination method will be a new avenue for sulfonamide antibiotics detection.

Recently, electrochemical detection based on carbon nanotubes (CNTs) modified electrodes has become an attractive research area. CNTs are new kinds of porous carbon materials possessing properties such as high chemical stability, huge surface area, and fast electron transfer reactions.[22,23] As electrode materials, CNTs exhibit good current responses, have low overpotential and promising surface anti-fouling capability.[24] Another important material for modified electrodes is ionic liquids (ILs). Due to their good solvating properties, high electrical conductivity, large potential window, and good

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electrochemical stability, ILs are suitable for electrochemical application in particular. In recent years, CNT-modified electrodes made by using ILs as a binder for analytical purposes have been reported, which contribute new functions to electrochemical sensors by combining the advantages of both ILs and CNTs.[25,26] CNTs can be considerably untangled in ILs so as to greatly increase the effective area of the electrode, which will result in high current response and low background current.[27]

In the present work, a voltammetric sensor for trace sulfadiazine determination was fabricated using N-octyl-pyridinium-hexafluorophosphate ($OPPF_6$) ionic liquid as the binder and multiwalled carbon nanotubes (MWCNTs) as the conductive material. Compared with bare glassy carbon (GC) electrode, the MWCNTs and $OPPF_6$ composite modified electrode exhibited several advantages of robust electrocatalytic activity, high current response, low oxidation potential, and good anti-fouling performance.

Experimental

Materials

Sulfadiazine was purchased from Aldrich. MWCNTs crude material (diameter: 10–30 nm, length: 5–15 μm, purity: >95%) was obtained from Shenzhen Nanotech Port (Shenzhen, China). $OPPF_6$ was purchased from Shanghai Chenjie Chemical Co. Ltd (Shanghai, China). All chemicals were of analytical grade and used without further purification. The whole electrochemical detection procedure was carried out in different pH values using sulfuric acid solution or sodium acetate buffer solution. All solutions were prepared by using double-distilled water.

Apparatus

Electrochemical measurements were performed by CHI 660A electrochemical workstation (CH Instruments, Austin, Texas, USA) integrated with a three-electrode system. A bare GC electrode (3.0 mm diameter) or a MWCNTs/$OPPF_6$ composite coated GC electrode was used as the working electrode. An AgCl/Ag electrode (saturated potassium chloride) and a platinum wire were used as the reference electrode and the auxiliary electrode, respectively. The potential of all electrochemical measurements in this study is given with respect to the AgCl/Ag reference electrode. A pHs-3B meter (Dazhong, Shanghai, China) was used for measuring the pH value of the supporting buffers.

Preparation of the MWCNTs/$OPPF_6$ composite

MWCNTs crude material was pretreated before use according to the literature method.[28] In brief, 100 mg of MWCNTs crude material were refluxed in 2.6 M of nitric acid for 48 h at 80 °C. Then the purified MWCNTs were rinsed to neutral with double-distilled water. After drying in a vacuum drying oven at 60 °C, the nitric-acid-purified MWCNTs were dispersed in a mixture of concentrated sulfuric and nitric acids (3:1, 98% and 70%, respectively) with the aid of ultrasonic agitation and then sonicated for 6 h. Then the functionalized MWCNTs were rinsed to neutral with double-distilled water and dried at 60 °C in a vacuum drying oven. A suspension of MWCNTs was prepared by mixing functionalized MWCNTs and $OPPF_6$ (m/m = 1:9) and grinding well in an agate mortar for 20 min to form a black gel; 2 mg of this black gel was dispersed into 2 ml of dimethylformamide (DMF) through ultrasonication and a black suspension was obtained.

Fabrication of modified electrode

Prior to the modification, the GC electrode was polished to a mirror-like surface with 0.05 μm alumina slurry, thoroughly rinsed with double-distilled water, and then sonicated in anhydrous ethanol and double-distilled water (each for 3 min). Then, 2 μl of the black suspension was cast onto the surface of the cleaned GC electrode and dried in ambient temperature to fabricate the MWNTs/$OPPF_6$-GC electrode. Before use, the modified electrode was scanned in 0.1 M disodium carbonate until overlapping cyclic voltammograms were obtained.

Results and discussion

Characterization of the modified electrode

GC electrodes, which were unmodified, modified with $OPPF_6$, or modified with MWCNTs/$OPPF_6$, were characterized by cyclic voltammetric scanning with ferricyanide as the probe to investigate the changes of electrode behaviour. Figure 1 represents the cyclic voltammograms of bare GC (solid line), $OPPF_6$/GC (dotted line) and MWCNTs/$OPPF_6$-GC electrodes (dashed line), which were recorded in a 0.5 mM $[Fe(CN)_6]^{3-/4-}$ solution containing 0.1 M KCl at 50 mV s^{-1}. As is shown, well-defined oxidation and reduction peaks due to $[Fe(CN)_6]^{3-/4-}$ redox couple are observed. It can be seen that the peak current obtained on $OPPF_6$/GC electrode is shrunken compared with that of bare GC electrode because of a decreasing in electroactive surface area of $OPPF_6$/GC electrode, which may own to the $OPPF_6$ layer formed on the surface of the electrode. However, the MWCNTs/$OPPF_6$-GC electrode exhibits the maximum peak current, illustrating that the modified electrode possesses the highest electrocatalytic activity resulting from its huge electroactive surface area.

Electrochemical response of sulfadiazine

The electrochemical behaviour of sulfadiazine on GC and MWCNTs/$OPPF_6$-GC electrodes was investigated by cyclic voltammetry (CV) method. Curve A in Figure 2 shows the cyclic voltammogram of 0.1 mM sulfadiazine obtained on bare GC electrode with 0.1 M sulfuric acid as the supporting solution. A weak oxidation current peak appears at 1.1 V while no corresponding reduction peak is found, indicating that the electrode reaction is absolutely irreversible. Although there is no

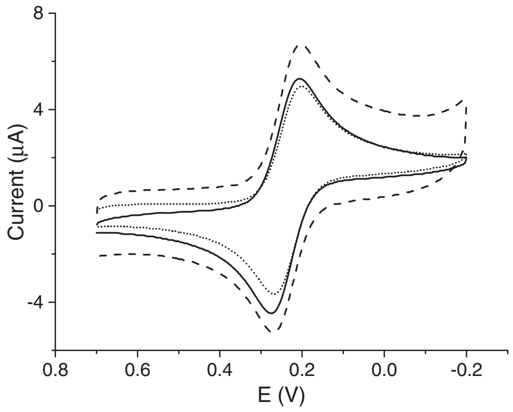

Figure 1. Cyclic voltammograms of 0.5 mM $[Fe(CN)_6]^{3-/4-}$ solution obtained on GC (solid line), $OPPF_6$/GC (dotted line) and MWNTs/$OPPF_6$-GC electrodes (dashed line).

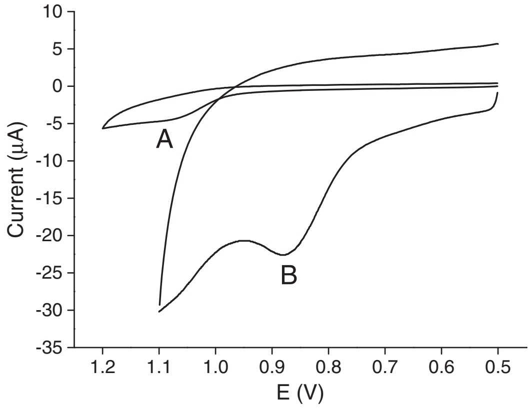

Figure 2. Cyclic voltammetric responses of 0.1 mM sulfadiazine in 0.1 M sulfuric acid solution on GC (A) and MWCNTs/OPPF$_6$-GC electrodes (B).

reduction current peak on the cyclic voltammogram obtained on MWCNTs/OPPF$_6$-GC electrode (Curve B in Figure 2), the oxidation current peak increases sharply. The enhanced current responses observed on MWCNTs/OPPF$_6$-GC electrode attribute to the increased active electrode surface area due to the MWCNTs coating. As shown in Figure 2, the oxidation peak potential shifts to 0.88 V, which is 220 mV lower than that obtained on bare GC electrode. This phenomenon probably owns to fast electron-transfer kinetics for electrochemical reactions of sulfadiazine on MWCNTs/OPPF$_6$-GC electrode. The enhanced sensibility of MWCNTs/OPPF$_6$-GC electrode suggests the possibility of sensitive determination of sulfadiazine at trace level.

The effect of accumulation potential and time were also evaluated. The accumulation potential was set at 0.6 V, 0.4 V, 0.2 V, 0 V, -0.2 V and −0.4 V, respectively. With the decreasing of accumulation potential, the oxidation currents of sulfadiazine changed little, but the background currents increased distinctly. When the accumulation time increased, the oxidation currents of sulfadiazine were also augmented gradually and then leveled off after 120 s. Consequently, accumulation time of 120 s in open circuit condition was selected for the following voltammetric experiments.

Optimization of modified electrode

To optimize the preparation of the modified electrodes, 0 μl, 2 μl, 5 μl, 10 μl of homogenously dispersed MWCNTs/OPPF$_6$ suspension were used as the modifier, respectively. And the amperometric responses of different modified electrodes were characterized by CV method in 0.1 M sulfuric acid solution containing 0.1 mM of sulfadiazine. Figure 3 shows the oxidation peak currents obtained on different modified electrodes. Compared with that of bare GC electrode (0 μl of modifier), the oxidation peak currents obtained on MWCNTs/OPPF$_6$-GC electrodes are amplified enormously. However, the oxidation peak currents increase indistinctively when the volume of modifier is greater than 2 μl. Consequently, 2 μl of MWCNTs/OPPF$_6$ suspension was used for preparation of modified electrodes in following electrochemical measurements.

Effect of pH

The effect of pH value on the electrochemical oxidation of sulfadiazine with MWCNTs/OPPF$_6$-GC electrode as the working electrode was studied by CV method. Several kinds of solutions such as 0.1 M sulfuric acid, 0.1 M hydrochloric acid, pH 1.8 Britton-Robinson solution (containing 0.04 M of phosphoric acid, acetic acid and boric acid), 0.2 M sodium acetate buffer and 0.2 M phosphate buffer at pH values ranged from 0.7 to 7.0, were used as the supporting electrolytes, respectively. It was found that the oxidation potential of sulfadiazine was pH dependent. As shown in Figure 4, a decrease in oxidation peak potential is observed with pH value increasing. The shift of oxidation peak potential toward more negative indicates the participation of protons in electrode reaction process. An inflexion point at about pH 2.0 is observed for sulfadiazine oxidation, which is attributed to the deprotonation of the amine group of sulfadiazine molecule. The slope of E *vs* pH plot for the pH ranged from 0.7 to 1.8 was 107 mV pH^{-1}, indicating that sulfadiazine molecule could be electrochemically oxidized at –NH$_2$ group effectively with different number of electrons and protons participating in the reaction.

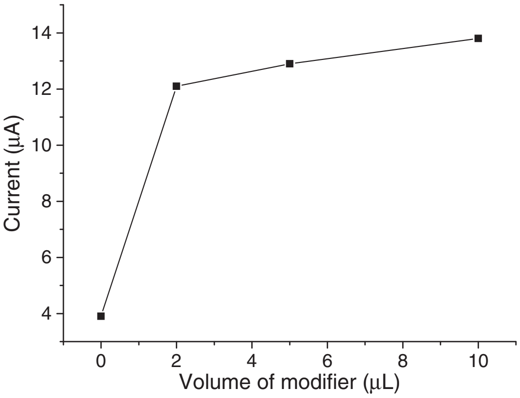

Figure 3. Peak currents obtained on MWCNTs/OPPF$_6$-GC electrodes prepared with different volume of modifier.

Additionally, the oxidation peak currents were also pH dependent (Figure 5). With increasing of pH value, the oxidation peak currents decreased sharply. Eventually, the oxidation current peak disappeared when the pH value was higher than 7.0. A maximum current response was obtained in 0.1 M sulfuric acid solution, which meant the involvement of protons during the oxidation of sulfadiazine. Consequently, 0.1 M sulfuric acid was selected as the supporting electrolyte for the following electrochemical measurements.

Effect of scan rate on the oxidation of sulfadiazine

The effect of scan rate on the electrochemical behaviour of sulfadiazine on MWCNTs/OPPF$_6$-GC electrode was studied by CV

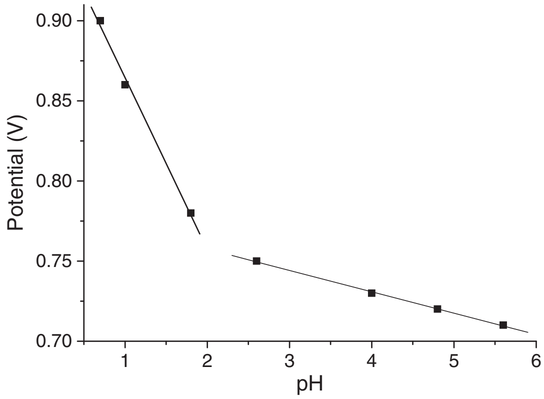

Figure 4. Plot of the oxidation peak potentials *vs*. pH value obtained on the MWCNTs/OPPF$_6$-GC electrode (The concentration of sulfadiazine was 0.1 mM.).

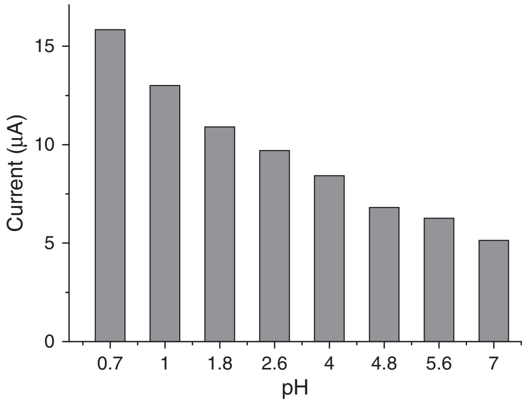

Figure 5. pH dependence of the oxidation peak currents on the MWCNTs/OPPF$_6$-GC electrode (The concentration of sulfadiazine was 0.1 mM.).

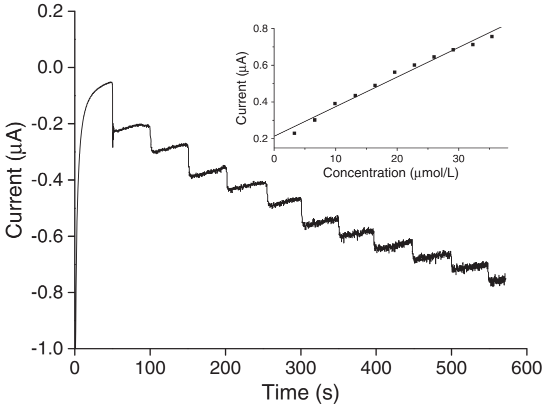

Figure 7. Current-time plot with the addition of 3.3 μM sulfadiazine at each step. Inset: calibration curve of sulfadiazine.

method in 0.1 M sulfuric acid solution (Figure 6). The oxidation peak currents were proportional to the scan rates within the range of 20–350 mV·s^{-1} with a linear correlation coefficient of 0.991, indicating an adsorption controlled electrochemical step.

Analytical properties

Electrochemical measurements of sulfadiazine were carried out by amperometric *i-t* curve method with the oxidation potential of 0.9V. As shown in Figure 7, the amperometric response is enhanced with the successive addition of sulfadiazine. When an aliquot of sulfadiazine was added, the oxidation currents increased steeply to reach a stable value in less than 3 s. Further, the current responses were linearly proportional to the concentration of sulfadiazine within the range of 3.3–35.4 μM with a satisfactory correlation coefficient (R = 0.991) and the linear equation was i (μA) = 0.2135 + 0.0161·C (μM). The detection limit of 0.21 μM was calculated according to the 3S$_b$/m,[29] where m was the slope of the linear range of the respective calibration plot, and S$_b$ was estimated as the standard deviation of the signals obtained in a blank solution. Compared with other methods of sulfadiazine determination in Table 1, the linear range obtained with MWCNTs/OPPF$_6$-GC electrode is similar to that of other electroanalytical methods, but narrower than that of HPLC methods conjugated with amperometric detector (AD). Although the detection limit of this work is still inferior to HPLC methods, it is the lowest in all electroanalytical methods listed in Table 1.

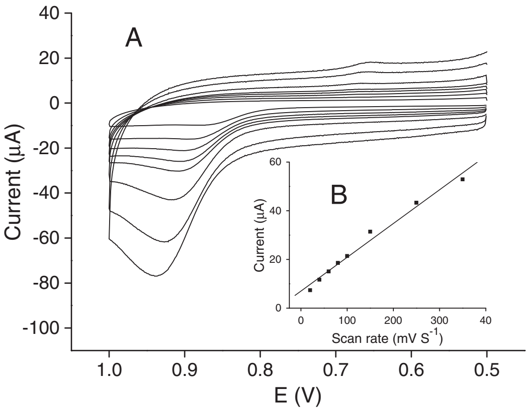

Figure 6. Cyclic voltammograms of the MWCNTs/OPPF$_6$-GC electrode in 0.1 M sulfuric acid containing 0.1 mM sulfadiazine at different scan rates. Inset: the relationship between scan rates and oxidation peak currents.

The repeatability of five measurements for solutions of 9.9 μM sulfadiazine was excellent with relative standard deviations (RSD) of 4.5%. The proposed MWCNTs/OPPF$_6$-GC electrode was stored in air at ambient conditions and its sensitivity was checked every day. The current response of the modified electrode was maintained almost the same as its initial response after 8 days' testing (RSD = 6.2%), indicating that the stability of the new electrode was good. Hence, the authors considered that the MWCNTs/OPPF$_6$-GC electrode had a good stability and reproducibility for sulfadiazine determination in solution condition.

Interference studies were carried out using amperometric method in a homogeneously stirred 0.1 M sulfuric acid solution at an applied potential of 0.9V. Ascorbic acid (AA), acting as a reductant, is widely existing in biological tissue and pharmaceuticals. The oxidation potential of AA is about 0.35V in 0.1 M sulfuric acid, which means AA will be oxidized simultaneously at applied potential of 0.9V during amperometric *i-t* monitoring. Hence, determination of sulfadiazine with AA coexisting was carried out by background subtraction. We got 0.08 μA for a solution containing 5 μM AA and 3.3 μM sulfadiazine when 0.4V was applied. The observed current was due to the oxidation of AA. However, when 0.9V was applied to the same solution, the current was 0.18 μA due to the oxidation of AA and sulfadiazine. Subtracting of current obtained for AA (0.08 μA) from the total current gave the current of 0.1 μA for sulfadiazine alone. This current was consistent with the current obtained for the individual addition of 3.3 μM sulfadiazine in Figure 7. After the addition of 100-fold excess of glucose, NH_4^+, Ca^{2+}, Mg^{2+}, Cl^- and NO_3^- separately in each step to sulfadiazine, the current was not changed. These results indicate that MWCNTs/OPPF$_6$-GC electrode can be successfully used for the determination of sulfadiazine.

Applications

Sulfadiazine suspension (Hainan Pharmaceutical Factory, Wuzhishan, China), a commercial pharmaceutical product containing 10% sulfadiazine was independently analyzed by voltammetric method using MWCNTs/OPPF$_6$-GC electrode following the above-described electroanalytical methodology. The sample solution was prepared as follows. After shaking vigorously, 1.00 ml of sulfadiazine suspension was pipetted and transferred into a volumetric flask. The pipet was washed several times and the washings were collected in the same volumetric flask. Then the sulfadiazine suspension sample was diluted to a desired concentration with 0.1 M sulfuric acid.

Table 1. Comparison of different methods for determination of sulfadiazine

Method	Reaction	Linear range (μM)	Detection limit (μM)	Reference
HPLC (AD)	Oxidation	0.05–50	0.05	Rao *et al.*[30]
HPLC (AD)	Oxidation	0.2–400	0.044	Preecharoworapun *et al.*[31]
DPV (GCE)	Oxidation	15–60	5.4	Carrazon *et al.*[32]
SWV (BDDE)	Oxidation	8.01–119	2.19	Souza *et al.*[18]
DPP (HgE)	Reduction	2.0–32	4.9	Diaz *et al.*[33]
SWV (P3MT/GCE)	Reduction	20–3200	4.0	Msagati *et al.*[34]
SWV (GCE)	Reduction	62.7–340	10.9	Braga *et al.*[35]
DPV (BiFE)	Reduction	3.2–20	2.1	Campestrini *et al.*[17]
i-t (CNT/IL/GCE)	Oxidation	3.3–35.4	0.21	This work

DPV=differential pulse voltammetry, DPP=differential pulse polarography, SWV=square wave voltammetry, AD=Amperometric Detector, GCE=glassy carbon electrode, BDDE=boron doped diamond electrode, HgE=mercury electrode, P3MT=poly (3-methylthiophene), BiFE=bismuth film electrode.

Table 2. Determination and recovery results in commercial pharmaceutical products on the MWCNTs/OPPF$_6$-GC electrode

Sample	Number	Added (mg/ml)	Found (mg/mlL)	RSD (%) (n=5)	Recovery (%)
Sulfadiazine Suspension	1	0	88.2	4.9	–
	2	20	103	3.1	95.2
	3	40	124	2.5	96.7

Amperometric method with the oxidation potential of 0.9V was selected for the determination and the unknown concentrations were evaluated from the calibration curve. The results obtained were in good agreement with the declared content and showed a high degree of precision (RSD=4.9%). A standard addition method was employed to assess the reliability. The results were summarized in Table 2. The recoveries of the sulfadiazine added were acceptable.

Conclusions

MWCNTs/OPPF$_6$ composite was successfully deposited onto the surface of GC electrode to form MWCNTs/OPPF$_6$-GC electrode. The synergistic effect of MWCNTs and OPPF$_6$ provides the modified GC electrode with the advantages of strong catalytic activity, large surface area and preventing MWCNTs from leaking. The stable, selective, and sensitive MWCNTs/OPPF$_6$-GC electrode exhibits good catalytic activity for sulfadiazine oxidation and will be promising for sensitive determination of trace sulfadiazine.

Acknowledgements

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