

Synthesis of a Schiff Base for Carbon Sphere Modification and Cd²⁺ Electrochemical Determination

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In this work, a novel carbon paste electrode was chemically modified by 2-(2-hydroxyphenyl)-2,5-diaza-4,6-dimethyl-8-hydroxy-1,5,7-nonatriene (SB)-coated carbon spheres, which showed excellent performance in the detection of cadmium via square-wave anodic stripping voltammetry (SWASV) with exceptional speed, simplicity, accuracy, selectivity, and sensitivity. Cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS) measurements were then carried out for the characterization of this modified electrode. Our proposed electrode was successfully used for the detection of Cd(II) in human plasma specimens. For Cd(II), the limit of detection (LOD) was calculated as 4.6 pM (based on a signal to noise ratio of 3), and the linearity range was found to be 10–250 pM.

Keywords: Schiff bases; Electrochemical determination; Cd ions; Human serum; Carbon sphere

1. INTRODUCTION

In surface and sensor science fields, the development of modified electrodes has recently gained substantial attention [1-5]. Conventionally, electrodes are modified by a substrate (metal substrates, carbon materials, etc.) [6]. Many techniques have been applied for these surface modifications, such as amine oxidation [7], decoration with self-assembled monolayers [8], polymerization [9], and electrochemical reduction of diazonium salts [10]. Recent studies have reported the application of some important metal substrates, including gold [11], platinum [12] and iron [13]. Further studies are expected to be carried out on the modification of carbon materials (e.g., graphene [14] and glassy carbon [15]). Extensive applications, including drug analysis [16], sensor

applications [17], metal determination [18], food analysis [19] and the determination of biological molecules [20, 21], have been found for modified electrodes.

It has been found that metal ions have significant effects on living organisms, necessitating the studies of their detection. Environmental resources that contain some metal ions (zinc [22], arsenic [23, 24], mercury [24, 25], chromium [26-29], lead [30-32] and cadmium, etc.) have been considered to pose great risks for living organisms. In addition, the above metal ions could lead to toxic effects and poisoning for humans [33]. A survey of the literature shows that a wide variety of techniques, including inductively coupled plasma-mass spectrometry [34], flame-atomic absorption spectrometry [35] and spectrophotometric methods [36], have been applied for the detection of cadmium ions. However, the above techniques suffer from several drawbacks, including a high cost of materials and device and time-consuming extraction procedures for the elimination of the contaminants, excipients, and interference ions. Fortunately, low-cost and facile electrochemical strategies could address the abovementioned disadvantages due to their rapidity and excellent sensitivity [37].

This work proposed a newly synthesized Schiff base, 2-(2-hydroxyphenyl)-2,5-diaza-4,6-dimethyl-8-hydroxy-1,5,7-nonatriene-modified carbon paste electrode with carbon spheres to detect trace levels of Cd^{2+} using SWASV. It was found that the proposed strategy provided excellent performance in detecting trace levels of metal ions in different real specimens due to its distinct selectivity.

2. EXPERIMENTS

2.1. Chemicals and apparatus

All experimental reagents were of analytical grade and were used without additional purification. Double-distilled water was used throughout for the preparation of all solutions. Carbon spheres were commercially obtained from Shenzheng Tiancai Graphite Ltd. Co. Infrared spectra were obtained using a Fourier transform infrared (FTIR) spectrometer (FT-IR, Perkin Elmer, spectrum 100). Voltammetric measurements were performed on a potentiostat/galvanostat (Autolab PGSTAT302 N) linked to a computer with Nova version 1.7 software. The CVs and square-wave voltammograms (SWVs) were obtained using a three-electrode configuration consisting of a modified carbon paste electrode (CPE) working electrode, a saturated Ag/AgCl reference electrode, and a platinum wire auxiliary electrode. For electrochemical impedance spectroscopy analysis, a multi-impedance test configuration was used in which the AC amplitude was 10 mV and the frequency ranged from 10 kHz to 10 mHz.

2.2. Synthesis of the Schiff base

2,6-Pentanedione and 1,2-propylene diamine were added in a 1:1 ratio to dichloromethane, followed by refluxing for 3 h in a water bath. After vacuum distillation, an oily condensation product

with a yellow colour was obtained. Then, 2-hydroxy acetophenone was added to this product (1:1) in chloroform, followed by refluxing for 5 h in a water bath to yield “an asymmetric Schiff base”, which was then distilled in vacuum and separated. To remove the unreacted reactants, a further distillation was carried out for the ethanol solution of the as-prepared product to yield the final Schiff base (SB) product.

2.3. Immobilization of 2-(2-hydroxyphenyl)-2,5-diaza-4,6-dimethyl-8-hydroxy-1,5,7-nonatriene (SB) onto carbon spheres

For the preparation of the carbon sphere phase-bounded chloropropyl derivative moiety (NSPBCP), carbon spheres were reacted with CPTS as a silylation agent. A suspension, prepared by suspending a sample of activated carbon spheres (10.0 g) in dry toluene (50.0 cm³), was mixed with CPTS (10.66 Mm). This was followed by refluxing this mixed solution for 72 h in a dry nitrogen atmosphere. Then, the modified silica was filtered off, followed by washing using ethanol and toluene two times, and vacuum drying at ambient temperature. For the synthesis of the SB-modified carbon sphere phase, dry toluene (50.0 mL) was mixed with 5.0 g of the as-prepared NSPBCP. NSPBCP was added to SB (5.0 g) dissolved in ethanol. Then, the reaction mixture was refluxed and stirred for 72 h to yield a solid phase. After filtration, ethanol washing, and vacuum drying for 24 h at ambient temperature, the final product was obtained as SB-C. The modified electrode was denoted as SB-C/CPE.

3. RESULTS AND DISCUSSION

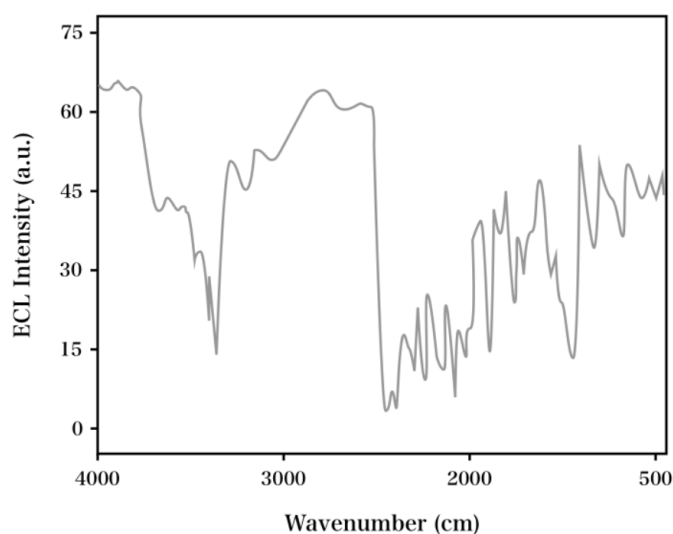


Figure 1. FTIR spectrum of the unsymmetrical Schiff base, 2-(2-hydroxyphenyl)-2,5-diaza-4,6-dimethyl-8-hydroxy-1,5,7-nonatriene.

As shown in the IR spectra of the initial compounds, the typical peaks at 3358 cm⁻¹ (N–H groups) and 1700 cm⁻¹ (>C=O groups) disappeared. As shown in the FTIR spectrum of the Schiff base

presented in Figure 1, a new peak was observed at 1614 cm^{-1} ($>\text{C}=\text{N}-$ group). These results indicated the formation of the Schiff base.

As shown in Figure 2, two irreversible oxidation peaks were observed, suggesting the electrochemical reactions of SB-C at bare CPE at 1490 and 1820 mV, with the less positive peak corresponding to the oxidation occurring on the nitrogen atom in the imidazole ring [38]. As the number of potential cycles increased, a decrease in these two irreversible oxidation peaks was observed, with a plateau state reached for the currents after several cycles. The differential decrease of the peak current indicated that the SB-C was formed on the CPE. The carboxylic and alcoholic functionalities were formed with the extension of the switching potential to the oxygen-evolution potential range, which led to the oxidization of the CPE surface [7] almost at the same level. Therefore, the modification is a reaction between the surface hydroxyl functionalities and the oxidation product through the aromatic p-carbon. The remaining water on the surface of the electrode possibly gave rise to the formation of the above oxygen-containing functionalities [39].

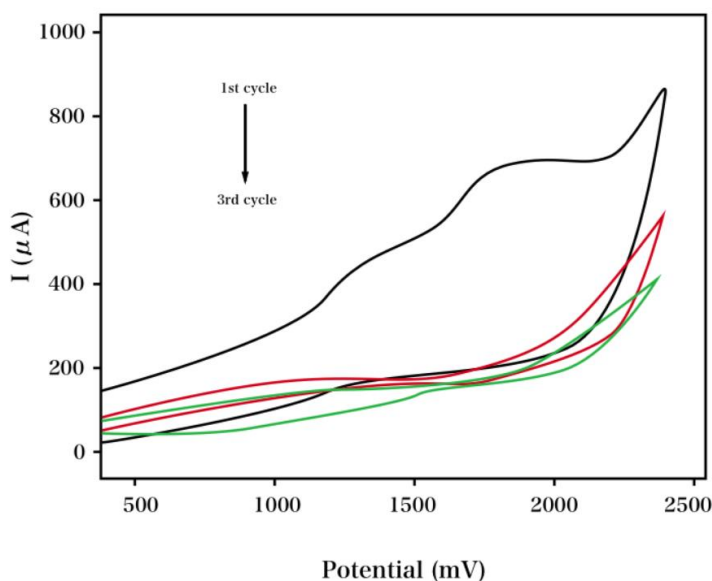


Figure 2. Modification voltammogram of SB-C on a CPE, scan rate: 100 mV/s.

The redox probes registered on the SB-C-modified CPE were characterized via CVs in $\text{K}_3[\text{Fe}(\text{CN})_6]$ (1.0 mM) and aqueous KCl (0.1 M). Compared to the bare CPE, the SB-C-modified CPE showed considerable reversible redox peaks of $\text{K}_3[\text{Fe}(\text{CN})_6]$, indicating that the involvement of SB-C led to an enhanced charge transfer rate (Figure 3). The peak current obtained on the CPE was much higher than that obtained on the SB-C/CPE. Due to a high number of graphitic edges on the surface of the electrode and the high electron conductivity of graphene, the electron transfer kinetics on the CPE were remarkably enhanced [40, 41].

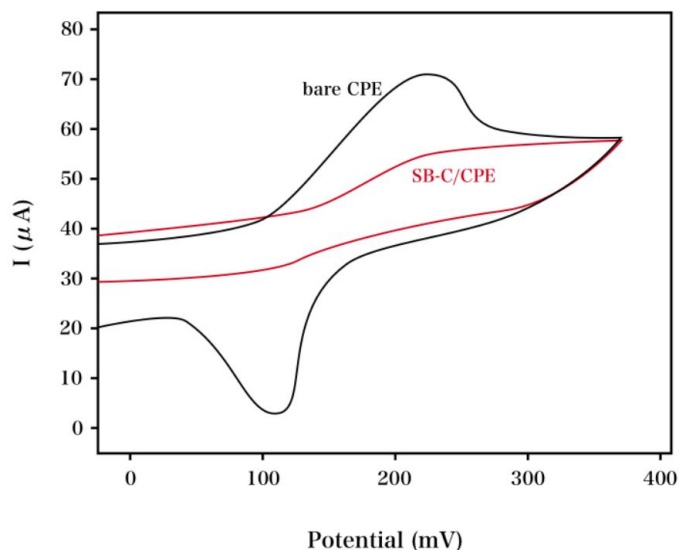


Figure 3. CVs recorded for potassium ferricyanide (1.0 mM) in 0.1 M KCl at the SB-C/CPE.

Impedance measurements were carried out to evaluate the performance for electron transfer kinetics. As shown in Figure 4, the bare CPE and SB-C modified CPE were characterized via Nyquist diagrams. The bare CPE was further characterized via the impedance plot shown in the inset of Figure 4, where a straight line was observed. On the other hand, a semicircle was observed for the SB-C-modified CPE in the high-frequency region, suggesting the blocking of charge transfer between the SB-C-modified CPE and $[\text{Fe}(\text{CN})_6]^{3-/4-}$ (1.0 mM). As shown in Figure 4, the constant phase element, the charge transfer resistance (R_{ct}), and the solution resistance (R_s) constitute the equivalent circuit. Based on the impedance plots of $[\text{Fe}(\text{CN})_6]^{3-/4-}$ (1.0 mM) at the bare CPE and the SB-C-modified CPE, the R_{ct} and R_{ct}^0 were obtained as 422.0 and 89.0 k Ω , respectively. Compared to the bare CPE, the SB-C-modified CPE showed higher R_{ct} , suggesting that the film was passivated.

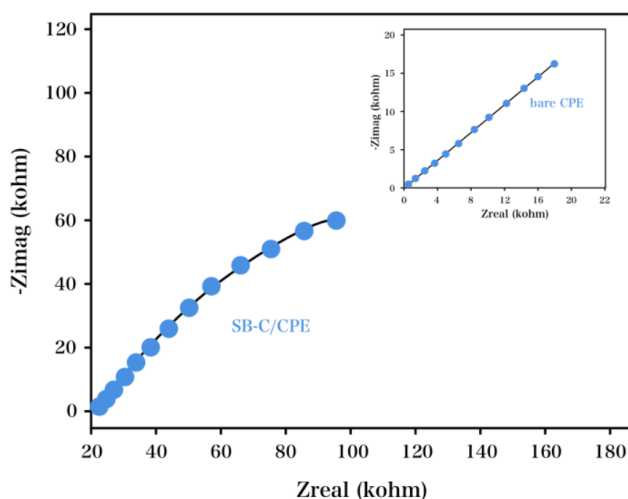


Figure 4. Fitting of the impedance spectrum for $[\text{Fe}(\text{CN})_6]^{3-/4-}$ (1.0 mM; 1:1) in 0.1 M KCl at SB-C/CPE with Randall's equivalent circuit/ Inset: impedance plot for the bare CPE.

The voltammetric responses of the SB-C-modified CPE towards Cd(II) ion solutions (0.25 nM) were obtained after incubation for 25 min in various supporting electrolytes at various pH values. As shown in Figure 5A, in pH 5.0 sodium acetate/acetic acid solution, the highest and most proper voltammogram shape and peak current were observed. The incubation time was optimized by immersing the SB-C-modified CPE in pH 5.0 sodium acetate/acetic acid solution in the presence of Cd(II) ions (0.25 nM) for 5, 15, 25, 35 and 45 min. A hyperbolic increase in the adsorptive stripping voltammograms (ASVs) was observed with the incubation time increasing to 25 min, followed by a plateau reached with further increases in the time.

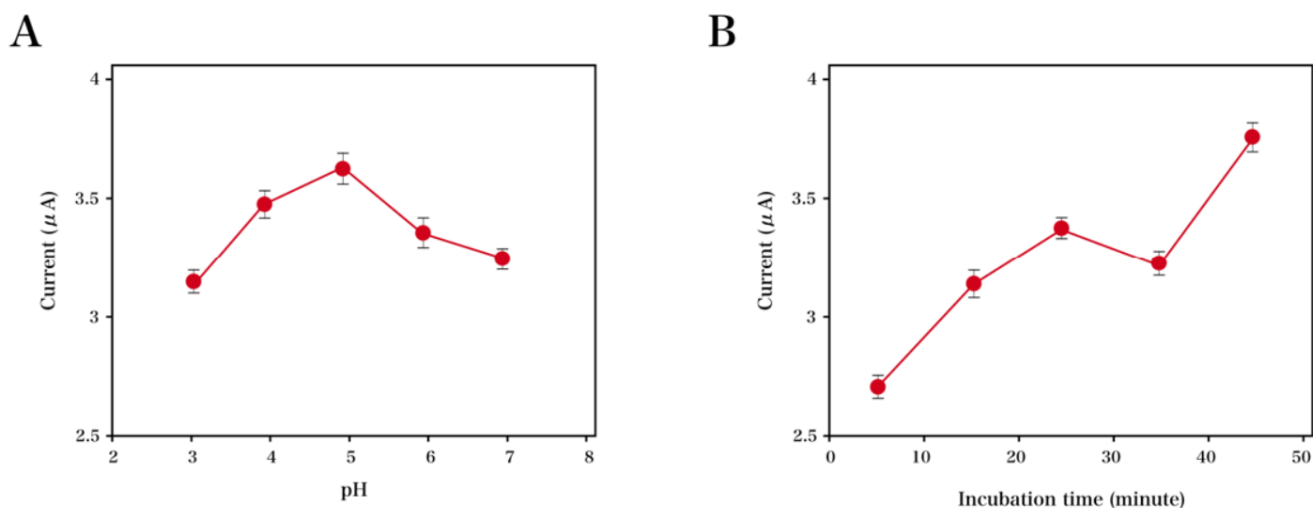


Figure 5. Voltammetric responses of SB-C/CPE towards Cd(II) ions (0.25 nM) at various (A) pH values and (B) incubation times.

The cadmium collected in human plasma specimens was determined using the as-prepared SB-C-modified CPE. The ASVs were obtained over the Cd(II) ions concentration range of 0.01 nM - 0.25 nM, as shown in Figure 6. Five different measurements were conducted for each point of the calibration curve. $LOQ = 10 S/m$, where (LOQ is the limit of quantification, S is the standard deviation of the intercept and m the slope of the regression line) was used to measure the LOQ . For Cd(II), the LOQ was calculated as 12 pM. On the other hand, the equation of $LOD = 3.3 S/m$ was used to measure the limit of detection (LOD). The LOD was calculated as 4.6 pM for Cd(II). Table 1 compares the analytical features of our developed biosensor to those obtained in the previous studies.

The selectivity of this method for the determination of heavy metal ions was evaluated for various heavy metal ions included in the Cd(II) solutions. Other metal ions can interfere if they compete for complexation. In the present work, interferences of other metal ions, such as Cr(II), Fe(II), Co(II), Hg(II), Cu(II), Pb(II) and Ag(I), were studied at different pH values. The current responses of Cd(II) ions were reduced by approximately 2.2% by the presence of 100-fold excesses of other metal ions in the entire pH range.

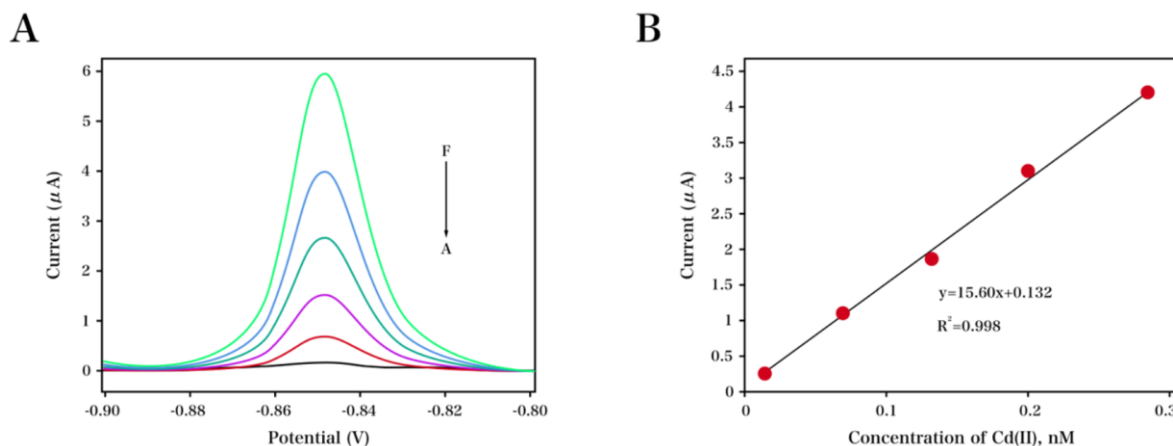


Figure 6. (A) Square-wave voltammograms on SB-C/CPE: (a) blank, (b) 0.01 nM, (c) 0.05 nM, (d) 0.1 nM, (e) 0.15 nM, (f) and 0.25 nM Cd(II); (B) Calibration curve of Cd(II).

The applicability of SB-C-modified CPE was studied by the detection of Cd(II) ions. As shown in Table 1, the comparison of the results was presented using the substitution strategy, i.e., atomic absorption spectrometry (AAS). The results from the SB-C-modified CPE and AAS were in good agreement with each other, with the recoveries for the specimen solutions shown in Table 2.

Table 1. Electrochemical determination of Cd(II) using SB-C/CPE and other reported references.

Electrode	Detection limit of Cd ²⁺ (µg/L)	Linear range of Cd ²⁺ (µg/L)	Reference
CNT arrays	1.8	1.5-4.5	[42]
Bismuth/poly(p-aminobenzene sulfonic acid)	0.63	1-110	[43]
Nitrogen-doped microporous carbon/Nafion/bismuth-film electrode	1.5	2-10	[21]
Bi/Au-GN-Cys/GCE	0.1	0.5-40	[44]
Bi/Nafion/PANI-MES/GCE	0.04	0.1-20	[45]
Clioquinol/HMDE	0.06	0-15	[46]
Carbon paste bulk-modified with antimony powder	0.9	2-20	[47]
Cu/Nafion/Bi	0.7	2-12	[48]
SPG	0.012	0.01-0.25	This work

Table 2. Recoveries of cadmium ion in human plasma specimens (n = 3).

Sample	Added (nM)	Found (nM)	ASS (nM)	Recovery (%)	RSD (%)
1	-	-	-	-	-
2	0.2	0.2018	0.1998	100.9	1.58
3	0.1	0.1087	0.1047	108.7	3.65
4	0.05	0.0496	0.0522	99.2	2.44

4. CONCLUSIONS

In this work, an inexpensive and facile preparation of SB-C-modified CPE was reported. This modified CPE showed distinct voltammetric behaviour and excellent quantification of cadmium ions in human plasma specimens. CV and EIS measurements were carried out for the characterization of our proposed electroanalytical sensor. In addition, this modified electrode was successfully used for the detection of Cd(II) in human plasma specimens.

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