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High-efficient determination of niclosamide in tablet based on multiple-walled carbon nanotubes/cyclodextrins composite modified glassy carbon electrode

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Niclosamide (NA) is a commonly used teniacide against cestodes infecting humans. In order to realize the high-efficient determination of NA, an electrochemical sensor was fabricated with the multiple-walled carbon nanotubes/cyclodextrins composite modified glassy carbon electrode (MWCNT/CD/GCE), which was applied to analyze the NA residual. Multiple-walled carbon nanotubes (MWCNT) showed a one-dimensional nanorod structure with high electrical conductivity and large specific surface area, and cyclodextrins (CD) with good molecular recognition performance could promote the uniform dispersion of MWCNT. The fabricated MWCNT/CD/GCE sensor gave full play to their respective advantages of MWCNT and CD, which effectively improved the determination performance of NA. Under the optimal conditions, the fabricated MWCNT/CD/GCE sensor exhibited good determination performance of NA with a low detection limit of 19.5 nM in a great linear NA concentration of 0.06-0.8 μM and 1-15 μM. Moreover, the MWCNT/CD/GCE sensor showed a good practicability for the determination of NA in tablet.

Keywords: Multiple-walled carbon nanotubes; Cyclodextrins; Niclosamide determination; Electrochemical sensor; Tablet

1. INTRODUCTION

As one kind of teniacide, niclosamide have played a significant role in the elimination of cestodes, thus seriously affecting individual life and health. World Health Organization reported that this teniacide could be applied as the molluscicides for the prevention and control of schistosomiasis [1-3]. According to the type of worm and age of patient, the appropriate dose can be determined for the optimal

insecticidal effect. However, what is worth noting is that the excessive use of NA has a negative impact on the human health and ecological environment [4]. It is imperative as well as logical to develop a simple, low-cost, and high-efficient analytical technique. At present, conventional analytical methods such as HPLC, GC, and GC-MC were applied to confirm the accurate content [5-7], but they demonstrate certain disadvantages such as high cost, low sensitivity, and time-consuming.

In order to improve the analysis efficiency, scientific researchers have developed a series of electrochemical sensors [8-10]. These electrochemical detection technologies show various advantages such as low cost, simple fabrication, and high detection efficiency. The need to pay attention to is that the determination performance of electrochemical sensors has much to do with modification materials [11, 12]. According to the existing literatures, the electrochemical sensors can be optimized by modifying the electrode surface with other materials such as carbon materials, metal nanoparticles, transition metal oxides, and its composites [13-21]. These modification materials are beneficial to improve the electrical conductivity and surface affinity the surface/interface of the fabricated electrodes. Among the above modification materials, carbon nanotubes have high electrical conductivity, large specific surface area, and one-dimensional nanotube morphology, which can improve the charge transfer efficiency and surface adsorption performance [20-22]. It has been confirmed in plenty of works the important function of MWCNTs as high-performance modification material for the optimization of electrochemical sensors. Furthermore, it was reported that cyclodextrins (CD) with good molecular recognition performance could promote the uniform dispersion of MWCNTs because of the Van der Waals force and hydrogen-bonding interaction of CD molecules [23, 24]. The further introduction of CD is conducive to the significant improvement of electrochemical detection performance [25].

Herein, an electrochemical sensor was fabricated with the multiple-walled carbon nanotubes/cyclodextrins composite modified glassy carbon electrode (MWCNT/CD/GCE), which was applied to analyze the NA residual. Multiple-walled carbon nanotubes (MWCNT) possessed one-dimensional nanorod structure with high electrical conductivity and large specific surface area, and cyclodextrins (CD) with good molecular recognition performance could promote the uniform dispersion of MWCNT. The fabricated MWCNT/CD/GCE sensor gave full play to their respective advantages of MWCNT and CD, which effectively improved the determination performance of NA. The determination performance of NA at the MWCNT/CD/GCE sensor was investigated in detail.

2. EXPERIMENTAL DETAILS

The MWCNT/CD/GCE sensor was successfully prepared via a drop-coating process. Typically, a certain amount of MWCNT (Aladdin, >95%) was dispersed in dimethylformamide (DMF, Aladdin, AR, 99.5%). After ultrasonic dispersion for 60 mins, the uniform suspension could be obtained. Subsequently, CD (Aladdin, 98%) was uniformly dispersed into the above MWCNTs-DMF suspension with further ultrasonic treatment. In order to fabricate the MWCNT/CD/GCE sensor, the glassy carbon electrode (GCE) was subsequently treated through the precise polishing and ultrasonic cleaning process. The MWCNT-CD-DMF suspension (5 μL) was drop-coated on the surface of GCE. After drying for 15

mins by using the infrared lamp, the MWCNT/CD/GCE sensor was fabricated after the evaporation of DMF.

In order to confirm the phase structure, surface morphology and particle size distribution, COOH-CNT were studied by X-ray diffraction (XRD) and scanning electron microscopy (SEM), respectively. The determination performance of MP at the fabricated MWCNT/CD/GCE sensor was performed by means of CHI660E electrochemical workstation. The working electrode, counter electrode, and reference electrode were MWCNT/CD/GCE electrode, platinum wire, saturated calomel electrode (SCE), respectively. The phosphate buffer solution (0.1 M, PBS) was prepared by using a certain amount of NaH_2PO_4 and Na_2HPO_4 solution.

3. RESULTS AND DISCUSSION

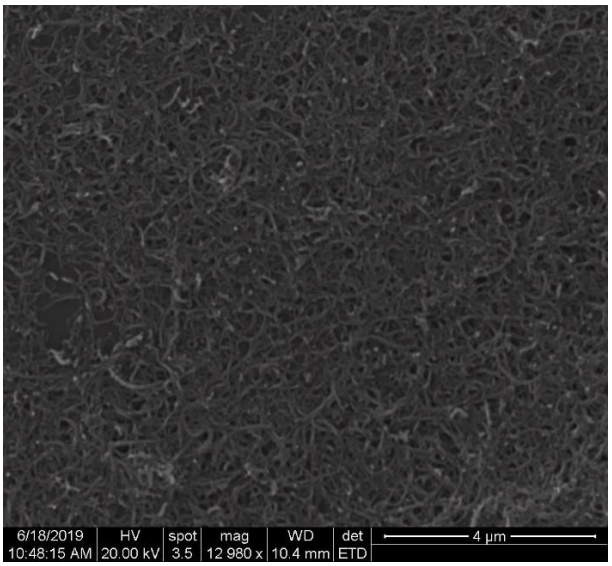

Figure 1. SEM image of the MWCNT/CD composite.

Figure 1 demonstrates the SEM image of the MWCNT/CD composite. It can be found that the MWCNT/CD composite presents one-dimensional nanotube morphology. With help of CD, MWCNT shows relatively uniform distribution, forming the carbon nanotube-based interlaced conductive network structure. These results suggest that the MWCNT/CD composite possesses excellent electrical conductivity, high surface affinity, and good absorption ability because of one-dimensional nanotube structure, interlaced carbon network structure, large specific surface area, good molecular recognition performance [20, 21, 26]. These factors can contribute to the significant improvement of NA determination performance [27].

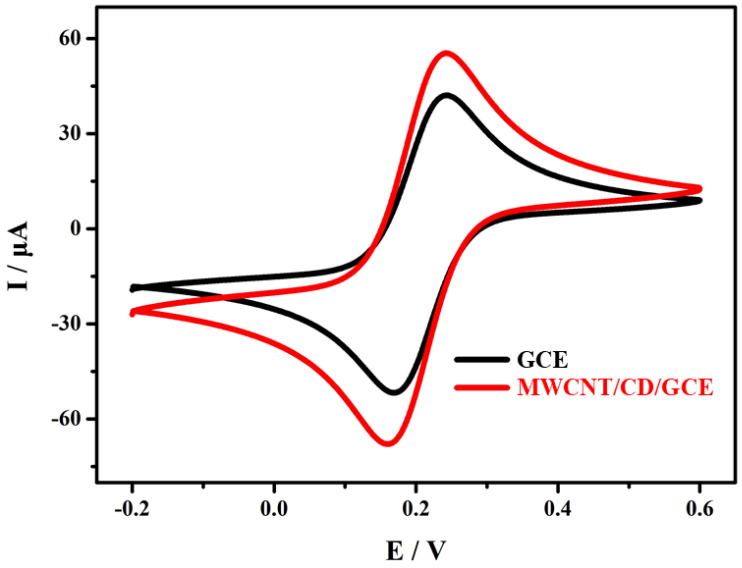

Figure 2. CV curves of the GCE and MWCNT/CD/GCE sensors in 5 mM $K_3[Fe(CN)_6]/K_4[Fe(CN)_6]$ solution containing 0.1 M KCl at a scan rate of 40 mV s^{-1}.

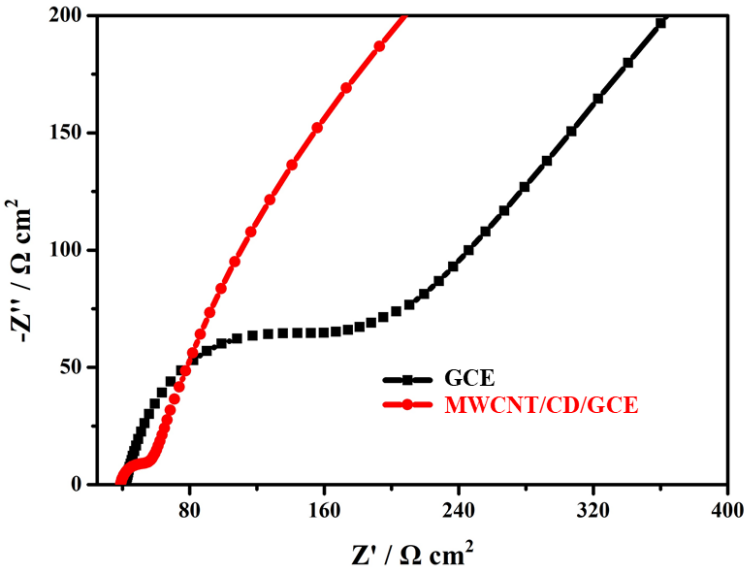

Figure 3. Nyquist plots of the GCE and MWCNT/CD/GCE sensors in 5 mM $K_3[Fe(CN)_6]/K_4[Fe(CN)_6]$ solution containing 0.1 M KCl.

Figure 2 shows the cyclic voltammetry (CV) curves of the unmodified GCE and MWCNT/CD/GCE sensors. Notably, the unmodified GCE sensor presents relatively weak redox peaks in the CV curve, suggesting an undesirable electrochemical sensing performance. For the fabricated MWCNT/CD/GCE sensor, the CV curve presents a pair of quite apparent redox peaks with a higher peak current response, indicating the excellent electrochemical sensing performance [9, 28]. This positive result is mainly contributed to the one-dimensional nanotube morphology and carbon nanotube-based interlaced conductive network structure, which plays a significant role in the improvement of charge transport.

Figure 3 displays the EIS results of the unmodified GCE and MWCNT/CD/GCE sensors. The positive effect of the MWCNT/CD composite can be further confirmed based on the analysis of EIS

results. As shown here, there are a semicircle (high to medium frequency region) and a slope (low frequency region) in the Nyquist plots. According to the existing literatures, the semicircle in the high to medium frequency region corresponds to the charge transfer resistance (R_{ct}), which is closely related to the electrochemical performance [11, 14]. As shown here, the unmodified GCE sensor presents a relatively large R_{ct} value, suggesting an undesirable electrochemical performance. By contrast, the MWCNT/CD/GCE sensor presents a lower R_{ct} value than that of the unmodified GCE sensor, which indicates the positive modification role of the MWCNT/CD composite. According to the reported work, CD with good molecular recognition performance could promote the uniform dispersion of MWCNT. With the one-dimensional nanotube morphology and uniform distribution of the MWCNT/CD composite, the carbon nanotube-based interlaced conductive network is formed, which electrical conductivity in the surface/interface between electrolyte and MWCNT/CD electrode [20, 26, 28].

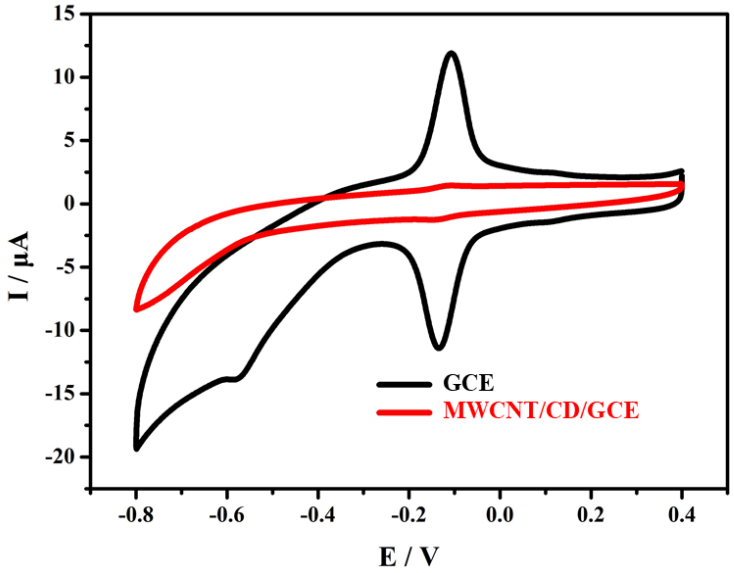

Figure 4. CV curves of the GCE and MWCNT/CD/GCE sensors in 0.1 M PBS containing 40 μM NA.

Figure 4 presents the CV results of the unmodified GCE and MWCNT/CD/GCE sensors in 0.1 M PBS containing 40 μM NA. The pH value is controlled around 7.0 with the scanning rate controlled at a scan rate of 40mV s^{-1}. It can be found that the unmodified GCE sensor presents not very obvious CV curve with relatively small peak current response. This poor electrochemical sensing performance suggests that it is difficult to achieve the sensitivity determination of NA via the unmodified GCE sensor. For the MWCNT/CD/GCE sensor, the electrochemical sensing performance is completely different from that of the unmodified GCE sensor. There are obvious irreversible reduction peak and a pair of obvious reversible redox peaks in the CV curve of the fabricated MWCNT/CD/GCE sensor, which mainly correspond to the irreversible reduction from nitro group to hydroxylamine group and reversible redox reaction of hydroxylamine group [4, 29, 30]. The above results indicate that the MWCNT/CD composite plays a significant role in the improvement of NA determination performance.

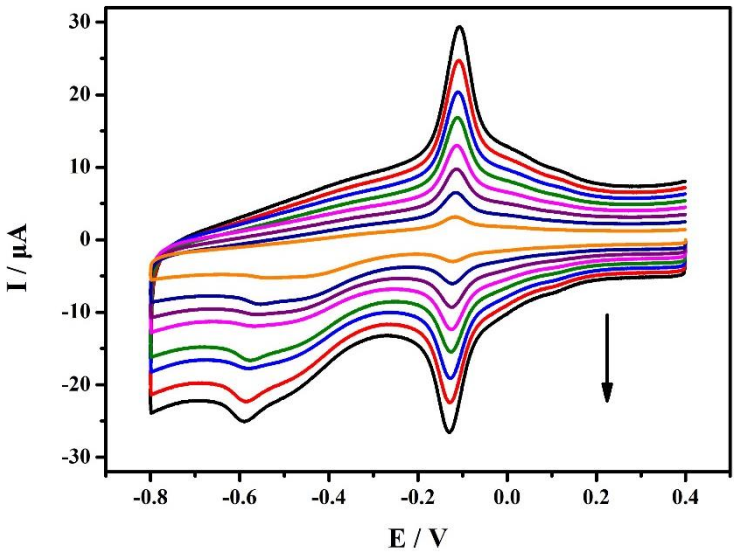

Figure 5. CV curves of the MWCNT/CD/GCE sensor in 0.1 M PBS containing 40 μM MP at a scan rate of 30-240 mV s^{-1}.

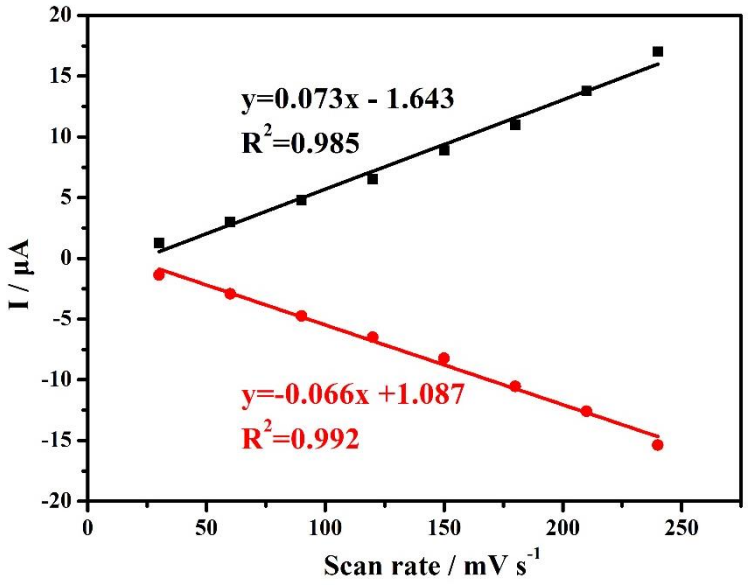

Figure 6. Relation of peak current vs. scan rate at the MWCNT/CD/GCE sensor in 0.1 M PBS containing 40 μM NA.

The effect of scan rate on the NA determination performance at the MWCNT/CD/GCE sensor was investigated, as shown in Figure 5. The corresponding scan rate is 30, 60, 90, 120, 150, 180, 210, 240 mV s^{-1}, respectively. It can be found that the scan rate has a great impact on the peak current response. As the scan rate increases, the current responses of irreversible reduction peak and reversible redox peaks showed gradually increasing trend. These results suggest that the scan rate has a great impact on the NA determination performance of the fabricated MWCNT/CD/GCE sensor. Figure 6 presents the relationship of peak current with scan rate. As shown here, the peak current responses depend linearly on the scan rate with regression equations of I_O(μA)=0.073v-1.643 (R^2=0.985) and

$I_R(\mu A)$=-0.066v+1.087 (R^2=0.992), respectively, which suggests the adsorption-controlled process of the NA determination at the fabricated MWCNT/CD/GCE sensor [9, 28].

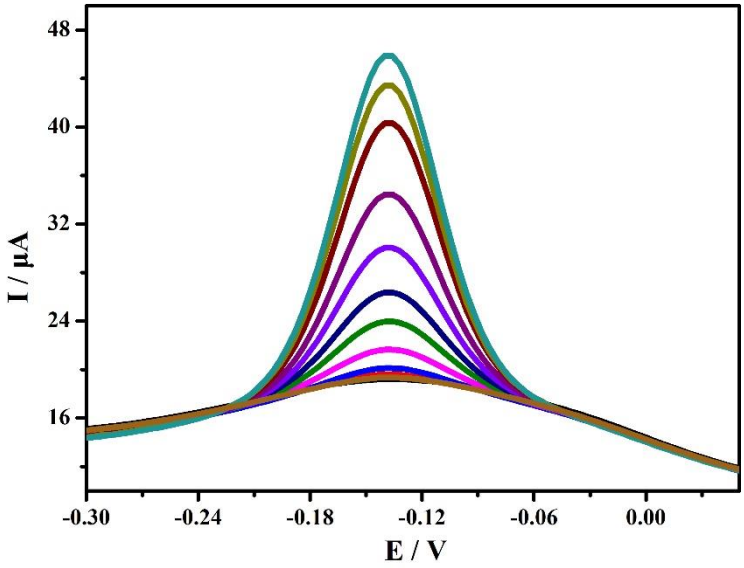

Figure 7. DPVs for the MWCNT/CD/GCE sensor in 0.1 M PBS containing different NA concentrations ranging from 0.06 to 15 μM.

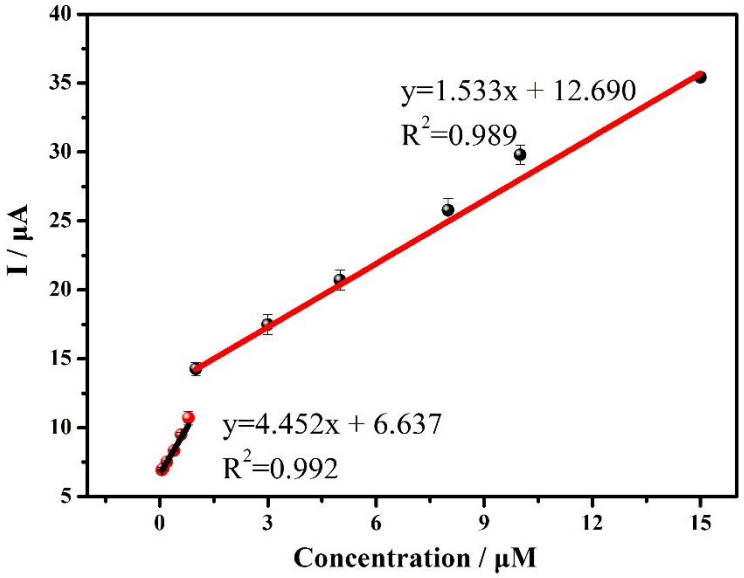

Figure 8. Relationship between oxidation current and NA concentration at the MWCNT/CD/GCE sensor in 0.1 M PBS containing different NA concentrations ranging from 0.06 to 15 μM.

Figure 7 presents the DPV curves of NA at the MWCNT/CD/GCE sensor, which was investigated at the NA concentration ranging from 0.06 to 15 μM in 0.1M PBS. As shown here, the peak current response presents a growing trend with the increasing of the concentration of NA. Figure 8 shows

the relationship between oxidation current and NA concentration at the MWCNT/CD/GCE sensor in 0.1 M PBS containing different NA concentrations ranging from 0.06 to 15 μM. It can be found that the peak current response increases linearly with the MP concentration of 0.06-0.8 μM and 1-15 μM. The corresponding regression equation is I(μA)=12.690+1.533C (R^2=0.999, High concentration) and I(μA)=6.637+4.452C (R^2=0.992, Low concentration). The two linear ranges in the calibration curves can be attributed to the fact that the NA molecules are moved very fast to the electrode surface when the addition of lower concentrations and the movement of NA molecules were quite slow when the addition of higher concentrations. According to the analysis results, the MWCNT/CD/GCE sensor shows a low detection of limit of 19.5 nM (S/N=3). Table 1 lists the NA determination of other reported works and this work. Compared with other reported works, the fabricated MWCNT/CD/GCE sensor shows relatively good MP determination performance, which has much to do with the one-dimensional nanotube morphology and carbon nanotube-based interlaced conductive network structure, which plays a significant role in the improvement of charge transport [21, 22, 27]. Moreover, CD cyclodextrins (CD) with good molecular recognition performance can further enhance the surface affinity toward NA [23, 24].

Table 1. Comparison of the performance the existing reports and this work.

Electrode	Detection limit (nM)	Linear range (μM)	Reference
PEDOT:PSS-PVA-GR-COOH	50	0.168-84	[31]
GCE	20.5	0.05-1	[29]
PGE	15	0.05-10	[32]
MWCNT/CD/GCE	19.5	0.06-0.8 1-15	This work

Table 2 lists the NA determination performance of the MWCNT/CD/GCE sensor in pharmaceutical tablet. In order to more accurately reflect the NA determination performance, this real sample were divided into three parts. To study the precision of NA determination, the corresponding relative standard deviation (RSD) and recovery were analyzed. According to the measurement results, the MWCNT/CD/GCE sensor presented quite satisfactory RSD values and recoveries of MP, which suggest the good practical feasibility of the MWCNT/CD/GCE sensor for the determination of NA.

Table 2 Determination of NA in tablet using the MWCNT/CD/GCE sensor.

Sample	MP spiked (μM)	MP found (μM)	Recovery (%)	RSD (%)
Tablet	5.00	4.93	98.60	2.01
	10.00	10.02	100.20	1.95
	15.00	14.97	99.80	2.62

4. CONCLUSION

To summarize, an electrochemical sensor was fabricated using the multiple-walled carbon nanotubes/cyclodextrins composite modified glassy carbon electrode (MWCNT/CD/GCE), which was applied to analyze the NA residual. Multiple-walled carbon nanotubes (MWCNT) displayed the one-dimensional nanorod structure with high electrical conductivity and large specific surface area, and cyclodextrins (CD) with good molecular recognition performance could promote the uniform dispersion of MWCNT. The fabricated MWCNT/CD/GCE sensor gave full play to their respective advantages of MWCNT and CD, which effectively improved the determination performance of NA. The fabricated MWCNT/CD/GCE sensor showed good determination performance of MP with a low detection limit of 19.5 nM in a great NA concentration of 0.06-15 μM. This work could provide an important reference for the development of high-performance NA electrochemical sensor.

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AUTHORS CONTRIBUTIONS
Cuiling Wang and Jiateng Zhong performed the experiments and collected the data, Gaiping Zhang and Jianhe Hu formulated the research and provided the facilities to carry out the research. All the authors contributed to the manuscript.

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