Au Quantum Dot/Nickel Tetraminophthalocyanine–Graphene Oxide-Based Photoelectrochemical Microsensor for Ultrasensitive Epinephrine Detection
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ABSTRACT: Owing to the importance of epinephrine as a neurotransmitter and hormone, sensitive methods are required for its detection. We have developed a sensitive photoelectrochemical (PEC) microsensor based on gold quantum dots (Au QDs) decorated on a nickel tetraminophthalocyanine–graphene oxide (NiTAPc-Gr) composite. NiTAPc was covalently attached to the surface of graphene oxide to prepare NiTAPc-Gr, which exhibits remarkable stability and PEC performance. In situ growth of Au QDs on the NiTAPc-Gr surface was achieved using chemical reduction at room temperature. The synthesized materials were characterized by Fourier transform infrared spectroscopy, ultraviolet–visible spectroscopy, X-ray photoelectron spectroscopy, scanning electron microscopy, transmission electron microscopy, and electrochemical impedance spectroscopy. Au QDs@NiTAPc-Gr provided a much greater photocurrent than NiTAPc-Gr, making it suitable for the ultrasensitive PEC detection of epinephrine. The proposed PEC strategy exhibited a wide linear range of 0.12–243.9 nM with a low detection limit of 17.9 pM (S/N = 3). Additionally, the fabricated PEC sensor showed excellent sensitivity, remarkable stability, and good selectivity. This simple, fast, and low-cost strategy was successfully applied to the analysis of human serum samples, indicating the potential of this method for clinical detection applications.

INTRODUCTION
Epinephrine (EP), an important neurotransmitter and hormone, can improve the survival rate of cardiac arrest patients by increasing the force and rate of heart contractions.1,2 However, excess EP or subcutaneous injection of EP into a vein can be deadly, as it can cause a sudden rise in blood pressure, cerebral hemorrhage, or even ventricular fibrillation.3,4 For this reason, the use of EP in sports is banned by the World Anti-Doping Agency. Therefore, it is very important to realize the ultrasensitive sensing of EP. Some conventional detection techniques, such as colorimetry,5 fluorescence spectrophotometry,6 and high-performance liquid chromatography (HPLC),7 have been successfully used for the determination of EP. Recently, electrochemical analysis,8 capillary electrophoresis,9 and chemiluminescence10 have been shown to be applicable to the detection of EP. Furthermore, photoelectrochemical (PEC) analysis is a rapidly developing method that can provide high precision, remarkable sensitivity, and easy integration using simple equipment based on appropriate photoactive materials.11–15 Various organic semiconductors16,17 and inorganic semiconductors18,19 have been used owing to their unique functions and photochemical activity.

Phthalocyanine metal derivatives have been widely used in applications in the spin-dyeing industry, medicine, and electrocatalytic analysis owing to their attractive features and functions.20–22 Nickel tetraminophthalocyanine (NiTAPc) is a phthalocyanine metal derivative well known for its excellent optical properties, chemical stability, and low cost.23,24 Moreover, high electrocatalytic activity can be achieved owing to the large number of amino groups in NiTAPc.25 Significantly, NiTAPc shows strong absorption in the region of 600–800 nm and high molar extinction coefficients in the near-infrared region, which has been exploited for PEC analysis.26,27 Recently, graphene oxide (GO) has been exploited in the field of PEC analysis.28 GO, which is usually prepared from graphite by oxidation using a strong acid, consists of sheets bearing carboxyl, hydroxyl, and epoxy groups and exhibits photoelectric activity.29 GO has good water solubility and excellent mechanical stability, which make it suitable for use as a template to form composites with various
nanoparticles (NPs) or amino polymers for chemical analysis. Previous studies have shown that NiTAPc, which is rich in amino groups, can be covalently attached to the surface of GO via chemical reaction with carboxyl groups to form nickel tetraminophthalocyanine-functionalized graphene oxide (NiTAPc-Gr). NiTAPc-Gr exhibits the advantages of both its constituent materials, showing not only excellent PEC properties and high mechanical stability but also a large specific surface area. This structure with an enhanced adsorption capacity has been successfully used for supercapacitors and micromolecule detection.

As unique functional materials, metallic NPs have been widely researched in various fields. To date, metallic NPs have been extensively applied in photodetectors, energy applications, and medical diagnosis and therapy. Notably, localized surface plasmon resonance in Au quantum dots (QDs) can be excited, which facilities the absorption of visible and even near-infrared photons, effectively boosts the rate of electron–hole formation, and promotes the separation of photogenerated charge carriers near the semiconductor, which can be transformed into a strong and stable electrical signal.

Owing to their high specific surface area, excellent photocatalytic activity, and good biocompatibility, Au QDs have been applied as efficient light-harvesting enhancers in PEC analysis; for instance, TiO$_2$–MoS$_2$-Au NPs and CdS-Au QDs. Au NPs integrated with ZnAgInS QDs have been used for specific purposes. The development of novel photoelectrodes is inevitable because of shortcomings during the inception phase.

In this work, we report the PEC analysis of EP using a heterostructure composite consisting of Au QDs decorated on NiTAPc-Gr (Au QDs@NiTAPc-Gr) as a signal indicator. This PEC sensor has significant advantages: (1) The Au QDs@NiTAPc-Gr composite material with specific structural features and a high specific surface area was synthesized by coupling the photoactive template material NiTAPc-Gr and a signal enhancer (Au QDs), which not only provided stability and increased the photoelectric catalytic activity but also reduced the self-aggregation of Au QDs, leading to an enhanced electrical signal output. (2) The sensitivity of the PEC sensor is comparable to that of enzymes; however, unlike enzyme sensors, the PEC sensor does not suffer from inactivation. (3) The Au QDs@NiTAPc-Gr heterostructure is ultrasensitive to visible and even near-infrared light, suggesting that the PEC sensor has broad applicability for the clinical detection of small molecules owing to the strong penetrability of the near-infrared light into cell tissues. However, such sensors have general disadvantages such as relatively short lifetimes, usually requiring replacement after 1–3 years. Moreover, the electrolytic solution should be carefully maintained and replenished regularly. Nevertheless, the PEC sensor was successfully applied to ultrasensitive EP detection, exhibiting rapid response, high stability, wide linear detection range, and selectivity. These findings provide insights into the development of heterostructures for PEC analysis and new methods for EP detection.

**RESULTS AND DISCUSSION**

**Characterization of PEC Materials.** X-ray photoelectron spectroscopy (XPS) was used for the elemental analysis of the Au QDs@NiTAPc-Gr composite material (Figure 1A). The high-resolution Ni 2p XPS spectrum showed two peaks at 855.7 and 870.0 eV (Figure 1B), assigned to Ni 2p$_{3/2}$ and Ni 2p$_{1/2}$ of NiTAPc-Gr, respectively. In Figure 1C, the O 1s peaks at 531.7 and 533.2 eV were attributed to C–O and C=O bonds, respectively. The N 1s XPS spectra (Figure 1D) of the Au QDs@NiTAPc-Gr composite material indicated that the peaks of nitrogen functionalities appeared at 399.2 eV (the N in C=O bonds), 400.5 eV (the N in N=H bonds), and 401.6 eV (the N in C=N bonds). The C 1s peaks at 284.8, 286.0, and 287.9 eV corresponded to C–C, C–O, and C=O, respectively (Figure 1E). Furthermore, the peaks located at 85.2 and 88.8 eV were attributable to Au 4f (Figure 1F). These findings imply the successful preparation of the Au QDs@NiTAPc-Gr composite material.

Furthermore, the PEC materials GO, NiTAPc, NiTAPc-Gr, and Au QDs@NiTAPc-Gr were characterized using Fourier transform infrared (FTIR) spectroscopy, as shown in Figure 1G. The FTIR spectra confirmed the successful preparation of the composite material.
1F. GO exhibited absorption peaks at 1724 and 1618 cm$^{-1}$ (curve a), which are related to the symmetric and asymmetric telescopic vibrations of $\text{-COO}^-$. NiTAPc showed a bending vibration at 1609 cm$^{-1}$ (curve b) related to the presence of $\text{-NH}_2$. In NiTAPc-Gr, NiTAPc, which is rich in amino groups, was covalently bound to the surface of GO via reactions with carboxyl groups. As a result, NiTAPc-Gr exhibited a strong absorption peak corresponding to C=O in amido linkages at 1694 cm$^{-1}$ (curve c). Furthermore, the symmetric telescopic vibration of GO at 1724 cm$^{-1}$ disappeared, which could be attributed to the p$-\pi$-conjugated effect of amido linkages, resulting in a shift of the C=O absorption frequency toward lower wavenumbers. In the case of Au QDs@NiTAPc-Gr, Au QDs were in situ grown on the surface of NiTAPc-Gr, and characteristic peaks of amido linkages and L-cysteine were observed at 1687, 1644, and 1613 cm$^{-1}$.

The PEC materials in dimethylformamide (DMF) were characterized using ultraviolet–visible (UV–vis) spectroscopy (Figure 1G). The absorption spectrum of NiTAPc showed two intense Q bands at $\sim$637 and 715 nm (curve b), whereas the Q bands of NiTAPc-Gr appeared at $\sim$629 and 683 nm (curve c). After further modification with Au QDs, which can absorb a range of visible light, the PEC material exhibited an increased absorbance at 623 nm, indicating the successful modification of Au QDs on NiTAPc-Gr.

The morphologies of synthesized PEC materials were characterized by scanning electron microscopy (SEM) and transmission electron microscopy (TEM). As shown in Figure 2A, after reacting with GO, Hovenia dulcis thunb-like structures were clearly observed on the surfaces of the GO sheets (Figure 2B,C). Furthermore, TEM images revealed that NiTAPc-Gr was modified with Au QDs (Figure 2D) and the Au QDs on the NiTAPc-Gr surface possessed dispersed lattice planes with an average size of approximately 4 nm. These results indicated that the Au QDs@NiTAPc-Gr composite was successfully prepared.

**PEC Characterization of Modified Electrodes.** Electrochemical impedance spectroscopy (EIS) measurements were carried out at a potential of 0.2 V to characterize the fabricated PEC sensor in a solution of 3 mM $[\text{Fe(CN)}_6]^{3-/-4-}$ containing...
0.1 M KCl. As shown in Figure 3A, the charge-transfer resistance (Ret) of bare indium tin oxide (ITO) was approximately 49.9 Ω (curve a). A decrease in Ret was observed after modification with NiTAPc (∼41.8 Ω, curve b), which was attributed to the excellent conductivity of this material. An increased Ret was observed for the GO-modified ITO electrode (∼82.4 Ω, curve c). Additionally, the Ret of Au QDs@NiTAPc-Gr (∼279.3 Ω, curve e) was much larger than that of NiTAPc-Gr (∼233.6 Ω, curve d) owing to additional scattering at the surface of NiTAPc-Gr when the electron mean free path became comparable to the thickness of the metal film.56 These results indicated that Au ions were reduced in the HAuCl₄ aqueous solution during the preparation of Au QDs@NiTAPc-Gr, resulting in the successful modification of the NiTAPc-Gr surface with Au QDs. In addition, cyclic voltammetry (CV) tests of various electrodes were conducted in the same aqueous solution between −0.2 and 0.8 V at a scan rate of 100 mV/s. As shown in Figure 3C, the anodic peak current for bare ITO was approximately 820.8 μA. When the electrode surface was modified with NiTAPc, the anodic peak current increased to 908.2 μA because of the good conductivity of this material. The GO-, NiTAPc-Gr-, and Au QDs@NiTAPc-Gr-modified electrodes exhibited lower anodic peak currents (782.1, 601.7, and 537.9 μA, respectively) owing to steric hindrance and electronic repulsion. Furthermore, Nyquist plots showing the effect of dark conditions and light illumination on the charge-transfer behavior in Au QDs@NiTAPc-Gr/ITO are displayed in Figure 3B. The corresponding EIS measurements were performed in 0.1 M pH 8.0 phosphate-buffered saline (PBS) buffer with or without EP.
(150 nM) at an applied potential of 0.2 V. The Ret for the PEC sensor under light illumination was lower than that in dark conditions, indicating that the separation efficiency of electron–hole (e\(^{-}/h^{+}\)) pairs was enhanced under light irradiation.

Subsequently, the photocurrent responses of various PEC sensors were characterized as shown in Figure 3D. Photocurrent vs time plots were plotted for the PEC sensors at a potential of −350 mV in the presence of 150 nM EP in 0.1 M pH 8.0 PBS. The photocurrent responses of NiTAPc/ITO, GO/ITO, and NiTAPc-Gr/ITO were 0.8, 0.3, and 1.0 μA, respectively, within 20 s. In the case of Au QDs@NiTAPc-Gr/ITO, the photocurrent increased to 4.5 μA. The photocurrent of Au QDs@NiTAPc-Gr was 4.5 times higher than that of NiTAPc-Gr, which could be attributed to the effects of Au QDs toward enhancing the response of NiTAPc-Gr. These results indicated that the Au QDs@NiTAPc-Gr composite can be selected as a photocatalytic material for fabricating PEC sensors.

**Optimization of Experimental Conditions.** To obtain high sensitivity for the determination of EP, two relevant experimental conditions, namely, the pH of the supporting electrolyte and the applied potential (V), were examined. In the presence of 150 nM EP, the photocurrent response increased with the increase in pH from 4.0 to 8.0, with the maximum value obtained at pH 8.0 (Figure 4B). Thus, pH 8.0 PBS buffer was chosen as the optimum condition. Additionally, the effect of V on the PEC sensor was examined, as shown in Figure 4C. The photocurrent response increased linearly with the increase in V in range from 0 to −350 mV, which can be described by the linear equation \( I(\mu A) = -0.0087V (mV) + 1.26, R^2 = 0.9924 \) (Figure 4D). At V higher than −350 mV, the photocurrent began to decrease. Therefore, an applied potential of −350 mV was used in subsequent experiments.

**Detection of EP.** Under optimal sensing conditions, the photocurrent responses of the PEC sensor to different concentrations of EP were recorded (Figure 5A), with each test repeated four times. The photocurrent increased with the increase in EP concentration and a good linear relationship was observed, which can be expressed as \( I(\mu A) = 0.0195C (nM) + 1.72, R^2 = 0.9992 \) (Figure 5B), with a limit of detection (LOD) of 17.9 pM.

In the Au QDs@NiTAPc-Gr structure, the NiTAPc-Gr network and Au QD sensitizer possess different absorption bands owing to their different energy gaps, allowing adequate utilization of the energy of the excitation light.\(^{27,58,59}\) Au QDs and NiTAPc-Gr exhibit cascade band-edge levels that can promote the ultrafast transfer of charge and effectively inhibit the recombination of negatively charged electrons (e\(^{-}\)) and positively charged holes (h\(^{+}\)) when red excitation light is transmitted through the photosensitive Au QDs@NiTAPc-Gr material. Therefore, the photocurrent response is obviously enhanced. Under light irradiation, the photogenerated electrons in the valence band (VB) are injected in the conduction band (CB) through a cascade starting from the Au NP to form the electron–hole pairs. EP as an electron donor can block the recombination of the photogenerated holes and facilitate the transfer of electrons from the conduction band of Au QDs to NiTAPc-Gr and then to the surface of the ITO electrode, resulting in the oxidation of EP to EP\(^{+}\) in the electrolyte and the generation of a strong current response.\(^{27,58,59}\)

The presence of EP enhances the electron transfer between the photosensitive materials, resulting in an increase of photocurrent. Thus, different concentrations of EP affect the magnitude of the photocurrent. A schematic diagram of the PEC detection on the sensor is shown in Figure 4A.

Additionally, using several analytical parameters, the performance of the PEC sensor was compared with that of some of the previously reported strategies for EP detection. As shown in Table 1, the current PEC strategy provides a much lower LOD and a somewhat wider linear range, which can be attributed to the large specific surface area and excellent stability and photoelectric conversion capacity of Au QDs@NiTAPc-Gr under red-light illumination. Thus, the proposed PEC sensor has great potential for the determination of EP.

**Stability, Reproducibility, and Selectivity of the PEC Sensor.** To investigate the stability of the proposed PEC sensor, the photocurrent response during continuous detection of EP was recorded under periodic light irradiation for 650 s. Good short-term stability was observed with a relative standard deviation (RSD) of 1.09%. Subsequently, the PEC sensor was stored in a refrigerator at 4 °C and monitored occasionally. After 1 month, 90.8% of the initial photocurrent value was recorded, revealing that the PEC sensor has long-term stability. Furthermore, the photocurrents of five newly modified working electrodes tested in the same experiment gave an RSD of 1.62%, reflecting the good reproducibility of PEC sensor. The photocurrent response of the PEC sensor was also investigated in the presence of several possible interferents at a 100-fold higher concentration than EP (75.0 vs 7.5 × 10\(^{-3}\) nM). As shown in Figure 5D, the initial photocurrent response increased rapidly after EP was added without interferents, and the subsequent addition of interferents, including Cu\(^{2+}\), K\(^{+}\), Mg\(^{2+}\), Ca\(^{2+}\), Fe\(^{3+}\), glucose, noradrenaline (NA), uric acid (UA), l-Cys, dopamine (DA), and tyrosine, did not cause a significant change in the photocurrent. These results

| material/method                        | linear range (μM) | LOD (μM) | RSD (%) | R     | ref  |
|----------------------------------------|-------------------|----------|---------|-------|------|
| Au-MWCNT-PANI-RuO\(_2\)/EC            | 7.69 × 10\(^{-2}\)−4.9 | 0.18     | 0.9760  | 60    |      |
| MIPs/MWCNTs/EC                        | 0.30−1 × 10\(^3\)  | 0.03     | 1.30    | 61    |      |
| Chit-fCNT bio-nanocomposite/EC         | 0.05−10           | 0.03     | 4.50    | 62    |      |
| GCPE(centri-voltammetry)/EC           | 0.20−20           | 1.30 × 10\(^{-2}\) | 2.53    | 0.9975 | 63    |      |
|                                        | 50−500            | 4.30 × 10\(^{-2}\) | 0.9980  |       |      |
| GQD-CS/EC                             | 0.36−380          | 3.00 × 10\(^{-4}\) | 2.80    | 0.9983 | 64    |      |
| caffeic acid/EC                       | 2−80              | 0.20     |         | 0.9987 | 65    |      |
| β-NiSi@rGO/Au nanocomposites/EC       | 2−1 × 10\(^6\)    | 0.54     | 2.04    | 0.9924 | 66    |      |
| UPLC-MS/MS                            | 2 × 10\(^{-3}\)−14 | 1.00 × 10\(^{-4}\) |       | 0.9999 | 67    |      |
| EP−MIP/CL                             | 5 × 10\(^{-5}\)−10 | 3.00 × 10\(^{-3}\) |       | 0.9980 | 68    |      |
| AuNPs@NiTAPc-Gr/PEC                   | 1.20 × 10\(^{-4}\)−0.2439 | 1.79 × 10\(^{-5}\) | 1.36    | 0.9996 | this work |
demonstrated the potential applicability of the PEC sensor for complex sample analysis.

Practical Applications. To verify the practical applicability of the proposed PEC sensor, different amounts of EP were added to human serum samples (final concentrations of 5, 100, and 200 nM). These human serum samples were analyzed by the standard recovery method using the PEC sensor. As shown by the analysis results in Table 2, the recovery ranged from 98.80 to 99.44%. The parallel determination was performed five times (n = 5), and the RSD was less than 4%. These results indicated that the PEC sensor could be applied for EP detection in human serum samples.

Table 2. Results of the Detection of Epinephrine in Human Serum Samples (n = 5)

| added (nM) | found (nM) | RSD (%) | recovery (%) |
|-----------|-----------|---------|--------------|
| human serum 5 | 4.94 | 3.45 | 98.80 |
| 100 | 99.17 | 1.44 | 99.17 |
| 200 | 198.89 | 1.52 | 99.44 |

98.80 to 99.44%. The parallel determination was performed five times (n = 5), and the RSD was less than 4%. These results indicated that the PEC sensor could be applied for EP detection in human serum samples.

CONCLUSIONS

In this work, to construct a PEC sensor for EP, a novel Au QDs@NiTAPc-Gr composite was devised by uniformly growing Au QDs on the surface of NiTAPc-Gr via a chemical reduction method. The integration of Au QDs and NiTAPc-Gr produced synergetic effects that enhanced the photoelectric conversion capacity and absorption efficiency, thus increasing the photocurrent signal. The synthesized composite showed low self-aggregation of Au QDs, a large specific surface area, and excellent biocompatibility. This proposed PEC sensor based on Au QDs@NiTAPc-Gr exhibited a wide linear range (0.12–243.9 nM), a low LOD (17.9 pM), high stability, good reproducibility, and good selectivity for ultrasensitive EP detection. Finally, this PEC strategy was successfully applied to the biological analysis and detection of EP in human serum samples, with recoveries ranging from 98.80 to 99.44%. In view of these results, the PEC strategy has great potential for real-time monitoring of real samples.

EXPERIMENTAL SECTION

Materials and Reagents. Adrenaline hydrochloride, ascorbic acid (AA), L-cysteine, thionyl chloride, ammonium molybdate, and HAuCl4 were purchased from Aladdin Industrial Corporation (Shanghai, China). Graphite was purchased from Xilong Chemical Industry Co., Ltd. (Shenzhen, China). 4-Nitrophthalimide was obtained from Meryer Chemical Technology Co., Ltd. (Shanghai, China). Sodium sulfide nonahydrate (Na2S·9H2O) and carbamide were purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). Phosphate-buffered saline (PBS; 0.1 M, pH 7.0) buffer was prepared using KH2PO4, Na2HPO4, 12H2O, and KCl. The human serum sample was obtained from Chongzuo People’s Hospital (Guangxi, China).

Apparatus. SEM and TEM images were recorded using an EVO-18 microscope (ZEISS, Oberkochen, Germany) and an FEI Tecnai-G2 F30 microscope (FEI Co., Hillsboro, OR) spectrometer, respectively. XPS spectra were obtained using a K-α spectrometer (Thermo Fisher Scientific Co., Waltham, MA). The FTIR spectra were collected with a Spectrum 65 FTIR spectrophotometer (PerkinElmer Co., Ltd., Waltham, MA). The UV−vis absorption spectra were obtained using a Shimadzu UV-6100 UV−vis-NIR spectrophotometer (Shanghai Mapada Instruments Co., Ltd., Shanghai, China). Red excitation light was provided by a PEAC 200A system (Ada Hengsheng Technology Development Co., Ltd., Tianjin, China). The distance between the illumination source and the sample cell was maintained at 10 cm. PEC measurements were performed using an electrochemical workstation (CHI760e, Chenhua Instrument Co., Ltd., Shanghai, China). ITO slices (<6 Ω, South China Xiangcheng Technology Co., Ltd., Shenzhen, China) with an active surface area of 0.25 cm2 were used as the working electrode vs Ag/AgCl as the reference electrode.

Synthesis of NiTAPc. NiTAPc was prepared by the reduction of the corresponding nitro-substituted intermediate. Briefly, 4-nitrophthalimide (1.75 g), carbamide (10 g), ammonium molybdate (0.025 g), and NiCl2 (1.14 g) were mixed and then fused by heating to a temperature of 160 °C,
GO was synthesized from graphite by a modified Hummers’ method.70 NiTAPc-Gr was synthesized via the following steps. Coated area of the modified substrate were coated with NiTAPc, GO, and NiTAPc-Gr which was allowed to dry naturally in the air. In addition, ITO substrates were coated with NiTAPc-Gr, GO, and NiTAPc-Gr suspension (0.1 wt %) using a high-speed shaker for 1 h. Subsequently, 5 mL of L-cysteine aqueous solution (1 mM) and then 1 mL of NiTAPc-Gr suspension (0.1 wt %) were dissolved in DMF (50 mL) and heated at 70 °C for 6 h. Au QDs@NiTAPc-Gr was prepared via the in situ growth of Au QDs on the surface of NiTAPc-Gr, as described in a previous report from the Yuan group.71 NiTAPc-Gr was easily dispersed using a high-speed shaker for 1 h. Subsequently, 5 mL of HAuCl4 aqueous solution (0.3 mM) and 10 mL of AA aqueous solution (10 mL) and DMF (10 mL), stirred, and then heated for 96 h. The product was washed with ultrapure water several times and dried in a vacuum drying chamber at 70 °C for 2 h.

Preparation of the Au QDs@NiTAPc-Gr Composite. Au QDs@NiTAPc-Gr was synthesized from graphite by a modified Hummers’ method. GO was synthesized from graphite by a modified Hummers’ method. GO was synthesized via the following steps. GO (1 mg) was added to a mixture of thionyl chloride (10 mL) and DMF (10 mL), stirred, and then heated at 70 °C for 24 h. NiTAPc (200 mg) was added to the mixture after thionyl chloride was removed by vacuum distillation and heated for a further 96 h. The product was washed with ultrapure water and absolute ethyl alcohol several times, and then dried in a vacuum drying chamber at 70 °C for 6 h. Au QDs@NiTAPc-Gr was prepared via the in situ growth of Au QDs on the surface of NiTAPc-Gr, as described in a previous report from the Yuan group. NiTAPc-Gr was easily dispersed using a high-speed shaker for 1 h. Subsequently, 5 mL of HAuCl4 aqueous solution (0.3 mM) and 10 mL of AA aqueous solution (5 mM) were added to the mixture, which was stirred rapidly at room temperature for 3 h to give NiTAPc-Gr decorated with Au QDs. Finally, the product was washed with ultrapure water several times and dried in a vacuum drying chamber at 70 °C for 6 h. The synthesis mechanism is shown in Scheme 1.

Electrode Fabrication. The ITO slices were cleaned with acetone, ethanol, and ultrapure water and then dried under an infrared lamp. The ITO substrate was then coated with 5 μL of a dispersion of Au QDs@NiTAPc-Gr (1 mg) in DMF (1 mL), which was allowed to dry naturally in the air. In addition, ITO substrates were coated with NiTAPc, GO, and NiTAPc-Gr using dispersions with the same concentration and volume as mentioned above. Furthermore, a bare ITO electrode was prepared by coating an ITO substrate with 5 μL DMF. The coated area of the modified electrodes was 0.25 cm².

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REFERENCES

1. Perkins, G. D.; Ji, C.; Deakin, C. D.; Quinn, T.; Nolan, J. P.; Scomparin, C.; Regan, S.; Long, J.; Slowther, A.; Pocock, H.; et al. A randomized trial of epinephrine in out-of-hospital cardiac arrest. N. Engl. J. Med. 2018, 379, 711–721.
2. Hansen, M.; Schmicker, R. H.; Newgard, C. D.; Grunau, B.; Scheuermeyer, F.; Cheskes, S.; Vithalani, V.; Alnajj, F.; Rea, T.; Idris, A. H.; et al. Time to epinephrine administration and survival from non-shockable out-of-hospital cardiac arrest among children and adults. Circulation 2018, 137, 2032–2040.
3. Hansen, M.; Eriksson, C.; Mah, N.; Meckler, G.; Guise, J. M. Accuracy of prefilled ‘code cart’ epinephrine syringes for direct administration of small doses. JAMA Pediatr. 2017, 171, 393–394.
4. Michael, J. R.; Guerci, A. D.; Koehler, R. C.; Shi, A. Y.; Tsitlik, J.; Chandra, N.; Niedermeyer, E.; Rogers, M. C.; Traystman, R. J.; Weisfled, M. L. Mechanisms by which epinephrine augments cerebral and myocardial perfusion during cardiopulmonary resuscitation in dogs. Circulation 1984, 69, 822–835.
5. Saraf, N.; Bosak, A.; Willenberg, A.; Das, S.; Willenberg, B. J.; Seal, S. Colorimetric detection of epinephrine using an optimized paper-based aptasensor. RSC Adv. 2017, 7, 49133–49143.
6. Cardoso, C. E.; Martins, R. O. R.; Telles, C. A. S.; Aucélio, R. Q. Sequential determination of hydrocortisone and epinephrine in pharmaceutical formulations via photochemically enhanced fluorescence. Microchim. Acta 2004, 146, 79–84.
7. Willemsen, J. J.; Ross, H. A.; Jacobs, M. C.; Lenders, J. W.; Thien, T.; Swinkels, L. M.; Benraad, T. J. Highly sensitive and specific HPLC with fluorometric detection for determination of plasma epinephrine and norepinephrine applied to kinetic studies in humans. Clin. Chem. 1995, 41, 1455.
8. Saraf, N.; Woods, E. R.; Papper, M.; Seal, S. Highly selective aptamer based organic electrochemical biosensor with pico-level detection. Biosens. Bioelectron. 2018, 117, 40–46.
9. Wei, S.; Song, G.; Lin, J.-M. Separation and determination of norepinephrine, epinephrine and isoproterenol by capillary electrophoresis in pharmaceutical formulation and human serum. J. Chromatogr. A 2005, 1098, 166–171.
10. Li, T.; Wang, Z.; Xie, H.; Fu, Z. Highly sensitive trivalent copper chelate-luminescence system for capillary electrophoresis detection of epinephrine in the urine of smoker. J. Chromatogr. B 2012, 911, 1–5.
11. Pang, Y.; Xu, G.; Zhang, X.; Lv, J.; Shi, K.; Zhai, P.; Xue, Q.; Wang, X.; Wu, Y. Photoelectrochemical properties and the detection mechanism of Bi2WO6 nanosheet modified TiO2 nanotube arrays. Dalton Trans. 2015, 44, 17784–17794.
12. Kecsenovitsy, E.; Endrödi, B.; Toth, P. S.; Zou, Y.; Raw, D.; Rajeshwar, K.; Janáky, C. Enhanced photoelectrochemical performance of cuprous oxide/graphene nanohybrids. J. Am. Chem. Soc. 2017, 139, 6682–6692.

Notes

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sensor for the detection of glibenclamide in urine and blood samples.

(31) Bu, H.; Yan, F.; Yang, J.; Yang, X. New photoelectrochemical detection platform for phthalocyanine-modified MWCNTs for sensitive detection of glucose in urine samples. J. Electroanal. Chem. 2018, 830, 278–285.

(32) Wang, Y.; Li, J.; Zhao, J.; Gao, Y.; Li, X. Electrochemical sensor for detection of L-Dopa based on carbon nanotube as catalyst. Biosens. Bioelectron. 2018, 106, 212–219.

(33) Wang, Y.; Li, J.; Zhao, J.; Gao, Y.; Li, X. Electrochemical sensor for detection of L-Dopa based on carbon nanotube as catalyst. Biosens. Bioelectron. 2018, 106, 212–219.

(34) Wang, Y.; Li, J.; Zhao, J.; Gao, Y.; Li, X. Electrochemical sensor for detection of L-Dopa based on carbon nanotube as catalyst. Biosens. Bioelectron. 2018, 106, 212–219.

(35) Wang, Y.; Li, J.; Zhao, J.; Gao, Y.; Li, X. Electrochemical sensor for detection of L-Dopa based on carbon nanotube as catalyst. Biosens. Bioelectron. 2018, 106, 212–219.

(36) Wang, Y.; Li, J.; Zhao, J.; Gao, Y.; Li, X. Electrochemical sensor for detection of L-Dopa based on carbon nanotube as catalyst. Biosens. Bioelectron. 2018, 106, 212–219.

(37) Wang, Y.; Li, J.; Zhao, J.; Gao, Y.; Li, X. Electrochemical sensor for detection of L-Dopa based on carbon nanotube as catalyst. Biosens. Bioelectron. 2018, 106, 212–219.
(47) Ibrahim, I.; Lim, H. N.; Abou-Zied, O. K.; Huang, N. M.; Estrela, P.; Pandikumar, A. Cadmium sulfide nanoparticles decorated with Au quantum dots as ultrasensitive photoelectrochemical sensor for selective detection of copper(II) ions. J. Phys. Chem. C 2016, 120, 22202–22214.

(48) Hu, Y.; Huang, Y.; Wang, Y.; Li, C.; Wong, W. L.; Ye, X.; Dong, S. A photoelectrochemical immunosensor based on gold nanoparticles/ZnAgIn3 quaternary quantum dots for the high-performance determination of hepatitis B virus surface antigen. Anal. Chim. Acta 2018, 1035, 136–145.

(49) Nesbitt, H. W.; Legrand, D.; Bancroft, G. M. Interpretation of Ni2p XPS spectra of Ni conductors and Ni insulators. Phys. Chem. Miner. 2000, 27, 357–366.

(50) Kwan, Y. C. G.; Ng, G. M.; Huan, C. H. A. Identification of functional groups and determination of carboxyl formation temperature in graphene oxide using the XPS O 1s spectrum. Thin Solid Films 2015, 590, 40–48.

(51) Zhu, J.; Li, Y.; Chen, Y.; Wang, J.; Zhang, B.; Zhang, J.; Werner, J. B. Graphene oxide covalently functionalized with zinc phthalocyanine for broadband optical limiting. Carbon 2011, 49, 1900–1905.

(52) Zhao, K.; Yan, X.; Gu, Y.; Kang, Z.; Bai, Z.; Cao, S.; Liu, Y.; Zhang, X.; Zhang, Y. Self-powered photoelectrochemical biosensor based on CdS/RGO/ZnO nanowire array heterostructure. Small 2016, 12, 245–251.

(53) Guo, W.; Chen, J.; Sun, S.; Zhou, Q. In situ monitoring the molecular diffusion process in graphene oxide membranes by ATR-FTIR spectroscopy. J. Phys. Chem. C 2016, 120, 7451–7456.

(54) Li, Y.; Wang, B.; Yu, Z.; Zhou, X.; Kang, D.; Wu, Y.; Chen, Z.; He, C.; Zhou, X. The effects of central metals on ammonia sensing of metallophthalocyanines covalently bonded to graphene oxide hybrids. RSC Adv. 2017, 7, 34215.

(55) Zhang, W. Q.; Lu, Y.; Zhang, T. K.; Xu, W.; Zhang, M.; Yu, S. H. Controlled synthesis and biocompatibility of water-soluble ZnO nanorods/Au nanocomposites with tunable UV and visible emission intensity. J. Phys. Chem. C 2008, 112, 19872–19877.

(56) Fuchs, K. The conductivity of thin metallic films according to the electron theory of metals. Math. Proc. Cambridge Philos. Soc. 1938, 34, 100.

(57) Asfaram, A.; Ghadiri, M.; Purkait, M. K. Novel synthesis of nanocomposite for the extraction of sildenafil citrate (viagra) from water and urine samples: process screening and optimization. Ultrasôn. Sonochem. 2017, 38, 463–472.

(58) Pang, Y.; Xu, G.; Zhang, X.; Lv, J.; Shi, K.; Zhai, P.; Xue, Q.; Wang, X.; Wu, Y. Photoelectrochemical property and its detection mechanism of Bi2WO6 nanosheet modified TiO2 nanotube arrays. Dalton Trans. 2015, 44, 17784.

(59) Zhang, Y.-H.; Li, M.-J.; Wang, H.-J.; Yuan, R.; Wei, S.-P. A sensitive photoelectrochemical aptasensor based on Bi, N-coded TiO2 sensitized by quantum dots. Anal. Chem. 2019, 91, 10864–10869.

(60) Tsele, T. P.; Adepkunle, A. S.; Fayemi, O. E.; Ebenso, E. E. Electrochemical detection of epinephrine using polyaniline nanocomposite films doped with TiO2 and RuO2 nanoparticles on multi-walled carbon nanotube. Electrochim. Acta 2017, 243, 331–348.

(61) Zhou, H.; Xu, G.; Zhu, A.; Zhe, Z.; Ren, C.; Nie, L.; Kan, X. A multipurpose electrochemical sensor for epinephrine recognition and detection based on molecularly imprinted polypyrrole. RSC Adv. 2012, 2, 7803–7808.

(62) Reddy, K. K.; Satyanarayana, M.; Goud, K. Y.; Gobi, K. V.; Kim, H. Carbon nanotube ensemble hybrid nanocomposite electrode for direct electrochemical detection of epinephrine in pharmaceutical tablets and urine. Mater. Sci. Eng., C 2017, 79, 93–99.

(63) Altuntas, D. B.; Oren, T.; Anik, U. Cyclic voltammetric detection of epinephrine. Anal. Methods 2016, 8, 6872–6876.

(64) Tashkhouri, J.; Nami-Ana, S. F.; Shamisipur, M. Designing a modified electrode based on graphene quantum dot-chitosan application to electrochemical detection of epinephrine. J. Mol. Liq. 2018, 266, 548–556.