A novel sensitive doxorubicin hydrochloride electrochemical sensor based on nickel hexacyanoferrate/Ni–Al–LDH modified gold electrode

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Abstract

The highly sensitive and selective electrochemical sensor has been fabricated by electrodepositing of nickel hexacyanoferrate (NiHCF) on Ni–Al layered double hydroxides (Ni–Al–LDH) modified Au electrode for the quantification of doxorubicin hydrochloride (DOX). The characterization of synthesized nanomaterials has been conducted by scanning electron microscopy, energy dispersive X–ray spectroscopy and electrochemical methods. The synergistic effect of NiHCF and Ni–Al–LDH not only excellently improves the performance of DOX electro–reduction but also promotes the electron transfer between DOX and the NiHCF/Ni–Al–LDH/Au sensor. The differential pulse voltammetric response of NiHCF/Ni–Al–LDH/Au sensor shows a linear relationship with the concentration of DOX in the range of $1.0 \times 10^{-8} - 6.2 \times 10^{-6}$ mol L$^{-1}$, limit of detection of $1.9 \times 10^{-9}$ mol L$^{-1}$ (S/N=3) and a sensibility of 14.71 A mol L$^{-1}$ cm$^{-2}$. The developed sensor exhibits good sensitivity, reproducibility, anti–interference and long–term stability property. Furthermore, the NiHCF/Ni–Al–LDH/Au sensor has successfully applied to determine DOX in biological samples, human blood serum sample.

Keywords: Electrochemical sensor, doxorubicin hydrochloride, nickel hexacyanoferrate, double hydroxides.
Introduction

Doxorubicin hydrochloride (DOX, Scheme 1) as an anthracycline drug is extensively used in the treatment of many different types of cancers, such as leukemia, neuroblastoma, sarcomas and carcinoma, etc. However, the excess DOX can cause serious side effects, e.g., cardiac and liver toxicity as well as drug resistance, limiting its clinical application in a certain degree. Therefore, it is of great significance to explore a reliable and sensitive detection method for the trace amounts of DOX in biological samples. Till now, several analytical techniques including spectrometry, mass spectrometry, high performance liquid chromatography, liquid chromatography–mass spectrometry, and electroanalytical techniques have been developed to detect DOX in different biological samples. Among these techniques, due to the rapid, simple, low cost as well as high sensitivity, electrochemical analysis methods based on the modified electrodes have been attracted great attention and proven to be convenient for determining DOX because it contains electroactive quinone and hydroquinone groups. At present, modified electrodes such as polymerization of magnetic graphene oxide grafted with chlorosulfonic acid modified electrode (PS/Fe₃O₄–GO–SO₃H/GCE), poly–arginine modified glassy carbon electrode (PARG/GCE), oxidized multiwalled carbon nanotube modified glassy carbon electrode (OMWCNT/GCE) as well as molecular imprinted polymer modified Au electrode (MIP/Au electrode) have been used for determining DOX. However, the preparations of these modified electrodes are complicated and time–consuming. Therefore, it is necessary to fabricate a more simple, stable, sensitive and efficient electrochemical sensor for detection of the target.

Scheme. I here

Layered double hydroxides (LDH), named anionic clays or hydrotalcite–like compounds,
have been received much attention recently because of their potential applications in catalysis and adsorption, such as high adsorption capacity, high chemical stability, catalytic activity, etc. The LDH composition can be denoted as \([M^{2+}_{1-x}M^{3+}_x(OH)_2]_y[A^{n-}]_x\cdot zH_2O\) formula, of which \(M^{2+}\) and \(M^{3+}\) refer to the common divalent and trivalent metal ions, \(A^{n-}\) is any type of anion.\(^{16-18}\) LDHs as weakly conductive solids restrict its electrochemical performance.\(^{19}\) However, because of the higher anion exchange capacity and larger specific surface area, it can be served as support material for immobilizing some molecules with negative charge and electroactivity.\(^{20,21}\) The electrochemical sensors based on electroactive molecules immobilized onto LDH surface, for example, Fe(III)/Fe(II) couple in nickel hexacyanoferrate ([Fe(CN)\(_6\)]\(_2\)Ni\(_2\), denoted as NiHCF), have been greatly enhanced the catalytic performances.\(^{22,23}\) NiHCF, an important inorganic polymeric compound, has received great attention for its advantages, \(i.e.,\) open zeolite–like structure, interesting magnetic, and so on. Because of the reversibility of its redox reactions,\(^{24,25}\) NiHCF as electron transfer mediator has been extensively applied to modify electrode surface in the analytical applications.\(^{26-28}\)

In this work, the NiHCF/Ni–Al–LDH/Au sensor is fabricated by electrodeposition technique, which exhibits a considerable electrocatalytic activity for the detection of DOX using differential pulse voltammetry (DPV) method. This proposed method for determining DOX exhibits a wide linear range and low detection limit. Moreover, the fabricated sensor was used to detect DOX in human blood serum samples, which provides a novel platform for analyzing DOX in biological sample.

**Experimental**

*Reagents and chemicals*

Doxorubicin hydrochloride (DOX) was obtained from Hefei Bomei Biotechnology (Hefei, China). Al(NO\(_3\))\(_3\)·9H\(_2\)O, K\(_4\)[Fe(CN)\(_6\)], NaNO\(_3\), Ni(NO\(_3\))\(_2\)·6H\(_2\)O, K\(_3\)[Fe(CN)\(_6\)] and KNO\(_3\) were
purchased from Tianjin Guangfu Fine Chemical Research Institute. All chemical reagents were of analytical grade, and the ultrapure water used throughout in all experiments.

**Apparatus**

The electrochemical experiments were employed with CHI660E electrochemical analyzer (CH Instruments Inc., Shanghai, China) with a common three–electrode system under ambient temperature. The bare/modified Au electrode (\(\phi = 2 \text{ mm}\)), Ag/AgCl (sat. KCl) and platinum wire were employed as working electrode, reference electrode and auxiliary electrode, respectively. During the measurement, all solutions were purged with nitrogen to eliminate oxygen reduction waves. The pH measurements were conducted on the PHS–3C exact digital pH meter (Leici Instrumental Factory, Shanghai, China). Scanning electron microscopy (SEM) images were collected on a JSM–7500F (JEOL, Japan), equipped with energy dispersive X–ray spectrometry (EDX).

**Preparation of Blood plasma samples**

The blood plasma samples were obtained from Shuozhou Modern Hospital. For preparation of serum samples, adding 1.2 mL acetonitrile to 2 mL healthy plasma sample. The mixture was centrifuged for about 15 min at 10000 rpm to eliminate the serum proteins. Then, 100 \(\mu\text{L}\) supernatant was diluted to 10 mL with phosphate buffer solution (PBS, \(\text{pH} = 7.4\)). The recovery percent was conducted by DPV technique and standard addition method.

**Fabrication of modified electrodes**

Before using, bare Au electrode was burnished with 0.3 and 1.0 \(\mu\text{m}\) alumina powder, respectively, and then was rinsed successively with the ultrapure water, ethanol, HNO\(_3\) (v/v=1:1) and ultrapure water. Then the bare Au electrode was activated in 0.5 mol L\(^{-1}\) H\(_2\)SO\(_4\) solution by cycling in the potential range of 0 – 1.6 V for 20 circles, and dried at room temperature. Additionally, Ni–Al–LDH modified Au electrode (Ni–Al–LDH/Au) and
NiHCF/Ni–Al–LDH/Au electrode were fabricated according to the literature, of which the general formula Ni–Al–LDH is $\left[\text{Ni}^{2+}_{1-x}\text{Al}^{3+}_x(\text{OH})_2\right]\left[\text{NO}_3^{n^-}\right]_{\frac{x}{n}} z\text{H}_2\text{O}$.

**Electrochemical measurements**

0.2 mol L$^{-1}$ PBS was selected as the electrolyte solution for detecting DOX in all experiments. Cyclic voltammograms (CV) of DOX were tested by the potential range from $-0.8$ V to $0.3$ V at $0.05$ V s$^{-1}$. The differential pulse voltammograms (DPV) of DOX was recorded by the potential range from $-0.8$ V to $-0.5$ V. The modified electrode was immersed into PBS after electrochemical measurement and performed by the potential range from $-0.8$ V to $0.3$ V for 10 cycles at $0.05$ V s$^{-1}$.

**Results and Discussion**

**Characterization of the NiHCF/Ni–Al–LDH/Au sensor**

*Morphological characterization.* The surface morphologies of the bare Au and modified electrodes are characterized by SEM technique, as shown in Figs. 1A–1C. It is noticed clearly that the Ni–Al–LDH layer (Fig. 1B) is uniformly distributed over the surface of bare Au electrode (Fig. 1A). And the NiHCF nanoparticles (23–38 nm) have been modified on the surface of Ni–Al–LDH layer to generate 3D structure (Fig. 1C), thus exhibiting higher electrochemical activity and stronger accumulation abilities, which can be reflected by the increase of active surface area and the peak current of DOX. In addition, the EDX spectroscopy analyses are conducted for the Ni–Al–LDH/Au electrode (curve 1) and NiHCF/Ni–Al–LDH/Au electrode (curve 2) to confirm the chemical composition of obtained nanomaterial (Fig. 1D). The curve 1 exhibits peaks for N, O, Ni, Al and Au elements, of which N, O, Ni and Al elements should be originated from the Ni–Al–LDH, and Au element is derived from Au electrode. The curve 2 exhibits additional peaks for Fe and C apart from the above elements. The above results suggest that NiHCF are effectively electrodeposited on bare Au electrode surface with Ni–Al–LDH.
Fig. 1 here

Electrochemical characterization. Cyclic voltammetry method is employed to verify the composition of the resulting NiHCF/Ni–Al–LDH nanocomposite film and characterize its electrochemical behaviour. Fig. 2A depicts the CVs of bare Au electrode and Ni–Al–LDH/Au electrode in 0.5 mol L$^{-1}$ KOH solution. The Ni–Al–LDH/Au electrode exhibits a pair of redox peaks with a potential range from 0.3 to 0.5 V, while the bare Au electrode does not display any electrochemical response. The redox peaks in Fig. 2A (curve 2) is attributed to the reversible redox of Ni$^{III}$/Ni$^{II}$, indicating that Ni–Al–LDHs are successfully electrodeposited on Au electrode.

Fig. 2 here

Furthermore, in order to demonstrate that NiHCF is electrodeposited on the surface of Ni–Al–LDH/Au electrode, the electrodeposition process of NiHCF is shown in Fig. 2B. It is observed that two pairs of redox peaks appear in the range of 0.4 – 0.6 V and the peak currents increase significantly with increasing the deposition cycles, indicating the growth of NiHCF layers during the CV scanning. In other words, NiHCF has been successfully modified on the surface of Ni–Al–LDH/Au electrode. Additionally, according to the previous reports, two pairs of redox peaks refer to the two different forms of NiHCF, Ni$_{1.5}$[Fe$^{III}$(CN)$_6$] (peak 1) and K$_2$Ni[Fe$^{II}$(CN)$_6$] (peak 2).

Electrochemical impedance spectroscopy (EIS) is recorded to provide detailed information on the impedance property of the modified electrodes. Fig. 2C presents the Nyquist diagrams of the bare Au electrode and modified electrodes in 0.1 mol L$^{-1}$ KCl containing 1 mmol L$^{-1}$
K₃[Fe(CN)₆]/K₄[Fe(CN)₆]. A small diameter of semicircle for the bare Au electrode suggests the lower interface electron transfer resistance (curve 1). The modification of Ni–Al–LDH film on Au electrode surface results in the significant increase of the impedance, indicating that the weak–conductive Ni–Al–LDH film hinders the electron transfer (curve 2). In addition, the semicircle diameter is drastically decreased at the NiHCF/Ni–Al–LDH/Au electrode, which indicates that the participation of NiHCF presents lower electron transfer resistance and significantly increases the electron transfer rate, and the Ni–Al–LDH provides a large surface area for the deposition of NiHCF. On the whole, the semicircle diameters of the electrodes follows the order of bare Au < NiHCF/Ni–Al–LDH/Au < Ni–Al–LDH/Au. The above result indicates that improved conductivity was obtained by the NiHCF deposited in Ni–Al–LDH film.

Further, the DPV experiment is performed to examine the electrochemical response of each sensor to DOX. Fig. 2D displays the DPV response of $3.0 \times 10^{-6}$ mol L⁻¹ DOX at the different electrodes. It is obviously noticed that the peak current of NiHCF/Ni–Al–LDH/Au electrode is greater than that of bare Au and Ni–Al–LDH/Au electrodes. This phenomenon proves that the NiHCF/Ni–Al–LDH composite is efficient to promote the accumulation of DOX on the surface of modified electrode, so as to improve the sensitivity. Besides, according to the Randles–Sevcik theory, the calculated electrochemical active area of NiHCF/Ni–Al–LDH/Au electrode is 0.5833 cm², which is much larger than bare Au electrode (0.0246 cm²) and Ni–Al–LDH/Au electrode (0.1509 cm²). Thus, the NiHCF/Ni–Al–LDH/Au electrode is selected as the optimal sensor in this work.

**Electrochemical behavior of DOX on the NiHCF/Ni–Al–LDH/Au electrode**

**Effect of scan rate.** For the purpose of expounding the electrochemical mechanism of DOX on the surface of NiHCF/Ni–Al–LDH/Au sensor, the effect of scan rate ($\nu$) on the response of DOX is investigated by CV method in PBS solution containing $1.0 \times 10^{-6}$ mol L⁻¹ DOX, as
presented in Fig. 3A. It can be observed that DOX has a pair of quasi-reversible redox peaks and the peak currents increase with the scan rates. Because the reduction peak current \( I_{pc} \) is much higher than the corresponding oxidation peak current \( I_{pa} \), so the reduction peak is studied in this work. It is pertinent to note that the reduction peak currents of DOX are proportional to the scan rates by following the linear regression equation of \( I_{pc} \) (μA) = \(-2.451 - 30.23v \) (V s\(^{-1}\)) \( (R^2 = 0.9967) \) as shown in Fig. 3B. The above result suggests an adsorption–controlled electrode process of DOX at NiHCF/Ni–Al–LDH/Au sensor, thus promoting the accumulation of DOX onto the NiHCF/Ni–Al–LDH/Au electrode surface for further quantitative analysis.

**Fig. 3 here**

In addition, it is also observed that the reduction peak potentials \( E_{pc} \) of DOX shifted to negative direction with the increasing of scan rate. The linear relationship of \( E_{pc} \) and the logarithm of scan rate (logv) \( (R^2 = 0.9982) \) can be expressed as:

\[
E_{pc} (V) = -0.6991 - 0.0498\log v
\]

The slope of \( E_{pc} – \log v \) plot is equivalent to \( 2.303RT/\alpha nF \), of which \( \alpha \) refers to the electron transfer coefficient and \( n \) corresponds to the transfer electron number. Based on the above linear regression equation, the value of \( n \) is equal to 2 for the reduction reaction of DOX, when assuming \( \alpha = 0.5 \) for quasi-reversible reaction.

**Effect of pH values.** The effect of pH on the determination of DOX at NiHCF/Ni–Al–LDH/Au sensor is studied by CV method. Fig. 4A presents the CVs of DOX on the modified electrode in PBS with different pH values. It is noticed that the reduction peak currents of DOX increase gradually from 5.23 μA to 7.28 μA with the change of pH from 5.8 to 8.2 (Fig. 4B). Considering that the pH value of physiological is 7.4, so pH 7.4 is used as the pH value of supporting electrolyte to determine DOX.
In addition, the reduction peak potential of DOX is going negatively as pH value increases. Such behaviour suggests that the proton of DOX is participated the electrochemical reaction. The corresponding linear equation $E_{pc} (V) = -0.2258 - 0.0565pH (R^2 = 0.9968)$ is obtained through analyzing the relationship of $E_{pc}$ and pH, as shown in Fig. 4C. According to Nernst equation, the slope of linear equation $-0.0565$ V pH$^{-1}$ is close to the theoretical value of $-0.059$ V pH$^{-1}$, which suggests that electrochemical reaction of DOX at NiHCF/Ni–Al–LDH/Au electrode should be a two protons and two electrons process, which is consistent with previous reports. The reasonable reduction mechanisms of DOX at the NiHCF/Ni–Al–LDH/Au electrode can be depicted as Scheme 2.

**Scheme 2 here**

*Differential Pulse Voltammetric Determination of DOX.* The quantificational determination of DOX is conducted by DPV method under the optimal conditions. Fig. 5 depicts the DPV responses of NiHCF/Ni–Al–LDH/Au sensor toward the different concentrations of DOX. It can be noticed that there is a good linear relationship between the concentration of DOX and reduction peak current. The corresponding regression equation is $I$ (μA) = $-2.2543 - 1.8479c$ ($R^2 = 0.9980$), with linear range of $1.0 \times 10^{-8} - 6.2 \times 10^{-6}$ mol L$^{-1}$, LOD of $1.9 \times 10^{-9}$ mol L$^{-1}$ (S/N=3) and sensibility of 14.71 A mol L$^{-1}$ cm$^{-2}$. Additionally, compared to the reported DOX sensors in the aspect of detection performance,$^8$–$^{11,32}$ the present sensor exhibits the wider linear range and lower LOD, as listed in Table S1.
Practical application of the NiHCF/Ni–Al–LDH/Au sensor. The selectivity of the proposed DOX sensor is one of the most important indicators for an analytical method, especially in the presence of coexisting species in the real sample. Hence, interference test is examined by the CV response of NiHCF/Ni–Al–LDH/Au sensor in $3.0 \times 10^{-6}$ mol L$^{-1}$ DOX and presence of $3.0 \times 10^{-4}$ mol L$^{-1}$ possible interferents, as shown in Fig. 6A.

It is noticed that the prepared NiHCF/Ni–Al–LDH/Au sensor delivers a good response to $3.0 \times 10^{-6}$ mol L$^{-1}$ DOX, and the addition of 100-fold concentrations of vitamin B6 (VB6), vitamin C (VC), L-lysine (LYS), L-serine (SER), glycine (GLY), glucose (GLU) and sodium citrate (SC) have no influence on the response of DOX, suggesting that the coexisting species mentioned above are almost no interference on the determination of DOX. That is to say, the proposed NiHCF/Ni–Al–LDH/Au sensor has an excellent anti-interference for DOX.

The reproducibility of the NiHCF/Ni–Al–LDH/Au sensor is evaluated by detecting the reduction peak current of $1.0 \times 10^{-6}$ mol L$^{-1}$ DOX for five parallel measurements using CV method. The obtained relative standard deviation (RSD) is 4.2%, indicating that the NiHCF/Ni–Al–LDH/Au possesses good reproducibility. Additionally, the stability of the NiHCF/Ni–Al–LDH/Au sensor is determined by monitoring of its DPV responses towards $1.0 \times 10^{-6}$ mol L$^{-1}$ DOX during 10 days (cf. Fig. 6B). Apparently, the current response of NiHCF/Ni–Al–LDH/Au sensor still retains about 86.4% of its initial value after 10 days, revealing the good stability of NiHCF/Ni–Al–LDH/Au sensor.
In order to evaluate its performance in real samples, analytical response of DOX in the human blood serum is analysed using a standard addition method, as depicted in Figs. 6C and 6D. The corresponding regression equation is $I (\mu A) = -2.9919 - 1.7420c \ (R^2 = 0.9989)$, and the linear range and sensibility for the real sample on NiHCF/Ni–Al–LDH/Au sensor are calculated to be $1.0 \times 10^{-8} - 6.0 \times 10^{-6}$ mol L$^{-1}$ and 13.86 A mol L$^{-1}$ cm$^{-2}$, respectively. The LOD is evaluated to be $2.5 \times 10^{-9}$ mol L$^{-1}$ (S/N=3), respectively.

Additionally, the recovery of DOX is varied from 96.02% to 101.50% (cf. Table 1) with a RSD between 2.35% and 4.21%, suggesting the good accuracy of this method. The results illuminate that the proposed NiHCF/Ni–Al–LDH/Au sensor is satisfactory for detecting DOX in human blood serum.

Conclusions

In this study, the sensitive electrochemical sensor for detecting DOX based on NiHCF/Ni–Al–LDH modified Au electrode is fabricated using electrochemical deposition method. The modified electrode exhibits excellent electrocatalytic activity towards the DOX. Under the studied conditions, DOX is determined at NiHCF/Ni–Al–LDH/Au sensor using DPV in standard samples and in human blood serum with a wide linear range and low detection limit. The fabricated NiHCF/Ni–Al–LDH/Au sensor is sensitive with good stability, low cost and large surface area, and presents good selectivity for the direct detection of DOX. As a convenient operation sensor, it seems to be of great practical value for some real applications, such as pharmacokinetic studies in cancer patients.

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Supporting Information

(A table is listed in the material). This material is available free of charge on the Web at http://www.jsac.or.jp/analsci/.
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Tables

**Table 1** Recovery studies of DOX in blood serum samples.

| Added (μmol L⁻¹) | Found (μmol L⁻¹) | Recovery (%) | RSD (%) |
|------------------|------------------|--------------|---------|
| 1.00             | 0.96             | 96.02        | 4.21    |
| 2.00             | 2.01             | 100.51       | 2.51    |
| 3.00             | 2.98             | 99.33        | 2.35    |
| 4.00             | 4.06             | 101.50       | 2.73    |
Figures

Scheme. 1. The molecular structure of doxorubicin hydrochloride.

Fig. 1 The SEM images of bare Au electrode (A), Ni–Al–LDH/Au electrode (B) and NiHCF/Ni–Al–LDH/Au electrode (C), as well as the EDX spectra of Ni–Al–LDH/Au and NiHCF/Ni–Al–LDH/Au electrodes (D).

Fig. 2 CV curves of bare Au electrode and Ni–Al–LDH/Au electrode in 0.5 mol L$^{-1}$ KOH at 0.05 V s$^{-1}$ (A), electrodeposition process of NiHCF on Ni–Al–LDH/Au electrode, that is, CV curves of Ni–Al–LDH/Au electrode in 1.0 mmol L$^{-1}$ K$_3$[Fe(CN)$_6$] and 1.0 mol L$^{-1}$ KNO$_3$ solution at 0.05 V s$^{-1}$ (B), EIS of bare Au electrode, Ni–Al–LDH/Au electrode and NiHCF/Ni–Al–LDH/Au electrode in 0.1 mol L$^{-1}$ KCl containing 1 mmol L$^{-1}$ K$_3$[Fe(CN)$_6$]/K$_4$[Fe(CN)$_6$] solution (C), the DPV responses of 3.0×10$^{-6}$ mol L$^{-1}$ DOX in PBS buffer solution (pH 7.4) at the bare Au electrode, Ni–Al–LDH/Au electrode, and NiHCF/Ni–Al–LDH/Au electrode (D).

Fig. 3 CV curves of 1.0×10$^{-6}$ mol L$^{-1}$ DOX on NiHCF/Ni–Al–LDH/Au electrode with the scan rates from 0.01 to 0.4 V s$^{-1}$ (curves a–j, 0.01, 0.025, 0.05, 0.1, 0.15, 0.2, 0.25, 0.30, 0.35, and 0.40 V s$^{-1}$) in the PBS (A), the plot of peak current I vs. the scan rate ν (B), and the plot of the peak potential E vs. logν (C).

Fig. 4 CV curves of 2.0×10$^{-6}$ mol L$^{-1}$ DOX at NiHCF/Ni–Al–LDH/Au sensor in PBS with different pH value (pH 5.8, 6.2, 6.6, 7.0, 7.4, 7.8 and 8.2) with the scan rates of 0.05 V s$^{-1}$ (A), plot of peak current I vs. pH value (B), and plot of the peak potential E vs. pH value (C).
Scheme 2. The reduction mechanism of DOX at the NiHCF/Ni–Al–LDH/Au electrode.

Fig. 5 DPV response of NiHCF/Ni–Al–LDH/Au electrode with DOX concentration from $1.0 \times 10^{-8} - 6.2 \times 10^{-6}$ mol L$^{-1}$ (curves 1–16, 0.01, 0.05, 0.10, 0.15, 0.20, 0.50, 0.80, 1.10, 1.40, 1.70, 2.00, 2.30, 2.60, 3.80, 5.00, 6.20 μmol L$^{-1}$) in PBS (pH 7.4), and the inset shows the plot of current $I$ vs. the concentrations of DOX.

Fig. 6 The effect of potential interferents on detection of DOX for NiHCF/Ni–Al–LDH/Au electrode (A), current responses of NiHCF/Ni–Al–LDH/Au electrode toward $1.0 \times 10^{-6}$ mol L$^{-1}$ DOX day–to–day (B), DPV responses of NiHCF/Ni–Al–LDH/Au electrode with DOX concentration from $1.0 \times 10^{-8} - 6.0 \times 10^{-6}$ mol L$^{-1}$ (curves 1–14, 0.01, 0.025, 0.05, 0.075, 0.10, 0.25, 0.50, 0.75, 1.00, 2.00, 3.00, 4.00, 5.00 and 6.00 μmol L$^{-1}$) in the real sample (C), plot of current $I$ vs. concentrations of DOX (D).
Scheme 1

Fig. 1
Fig. 2

(A) 1. Au electrode
2. Ni-Al-LDH/Au electrode

(B) Increasing cycles

(C) 1. Au electrode
2. Ni-Al-LDH/Au electrode
3. NiHCF/Ni-Al-LDH/Au electrode

(D) 1. Au electrode
2. Ni-Al-LDH/Au electrode
3. NiHCF/Ni-Al-LDH/Au electrode

Fig. 3

(A) 1. Au electrode
2. Ni-Al-LDH/Au electrode
3. NiHCF/Ni-Al-LDH/Au electrode

(B) $R^2 = 0.9967$

(C) $R^2 = 0.9982$
Fig. 4

Scheme II

Fig. 5
Fig. 6

(A)  

(B)  

(C)  

(D) 

$R^2 = 0.9989$