

## Electrocatalytic performance of Au@Cu Nanoparticle Chains as Sensor for Determination of Piroxicam

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A chemical reduction technique at low temperature was employed to synthesize Au and Cu nanoparticle chains (Au@Cu NCs) with sodium citrate as the growth reducing agent, stabilizer and structure directing agent, chloroauric acid (HAuCl<sub>4</sub>) and copper chloride (CuCl<sub>2</sub>) as metal precursors. Then, the Au@Cu NCs were dropped on glassy carbon electrode (GCE) to prepare an electrochemical sensor (Au@Cu NCs/GCE) for sensing piroxicam. The electrochemical behaviors on Au@Cu NCs/GCE of piroxicam were investigated in detail. The electrochemical sensor for piroxicam exhibited a linear range of 0.04-1.00 mM at desired conditions. In particular, Au@Cu NCs/GCE was successfully applied for determination of piroxicam liniments samples with satisfactory recovery range (92.86-101.22 %) and relative standard deviation (RSD, 2.95-4.69 %), indicating its reasonability and feasibility for piroxicam determination.

**Keywords:** Nanoparticle chains; Au@Cu NCs; Piroxicam; Electrochemical sensor

### 1. INTRODUCTION

As a member of non-steroidal anti-inflammatory drugs (NSAIDs), piroxicam (C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>S, 4-hydroxy-2-methyl-3-(pyrid-2-yl-carbamoyl)-2H-1,2-benzothiazine 1,1-dioxide) usually has been in the treatment of various inflammatory diseases and arthropathies, such as rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, atherosclerosis, and musculoskeletal disorders [1-4]. However, piroxicam has many apparent side effects, including serious gastrointestinal difficulties [5, 6], hepatotoxicity [7, 8] and nephrotoxicity [9] in clinical application. Thus, developing a rapid and convenient method for piroxicam determination in real samples is essential for its rational use and clinical evaluation.

Nowadays, several analytical procedures were proposed for determination of piroxicam, including spectrophotometry [10], HPLC [11], LC-MS/MS [12], spectrofluorimetry [13], TLC [14, 16], SFC-MS/MS [16], and electrochemical detection [17, 18]. Among of them, electrochemical method is one of the viable approaches for detection of piroxicam, and has attracted much attention because of its numerous advantages [19]. Mohammad Bagher Gholivand et al. successfully constructed a BNP-CPE electrode and applied to detect of piroxicam in serum and pharmaceutical samples. The linear range was 0.5-100.0 nM and the detection limit was 0.11 nM [20]. Jin-Wei Zhang et al. reported a AgNPs-SWCNTs-rGO/GCE sensor and used as a sensor in phosphate buffer solution (pH = 2.0) for detection of piroxicam with a wide linear range (1.5-400  $\mu$ M for LSV, 0.05-250  $\mu$ M for CA) and low detection limit (0.5  $\mu$ M for LSV, 0.5nM for CA) in tablet samples [21]. Fen-Ying Kong et al. reported Pt-N-rGO-SWCNTs/GCE sensor and applied for piroxicam determination in tablet samples, with the linear rrange was 0.06-60 $\mu$ M and the detection limit was 0.015 $\mu$ M [22].

To develop a rapid and sensitive method for piroxicam determination in pharmaceuticals or human plasma, the preparation and application of Au and Cu nanoparticle chains (Au@Cu NCs) modified electrodes (Au@Cu NCs/GCE) as an electrochemical sensor for piroxicam determination were proposed in this work. Experimental results indicated that the proposed method can be successfully applied for determination of piroxicam in liniment samples with high accuracy and precision.

## 2. EXPERIMENT

### 2.1 Reagents

The reagents of H<sub>2</sub>AuCl<sub>4</sub> and piroxicam (C<sub>15</sub>H<sub>13</sub>N<sub>3</sub>O<sub>4</sub>S) were purchased from Sinopharm Chemical Reagent Co. Ltd. (Shanghai, China) and Guizhou Dida Biological Technology Co. Ltd, respectively. CuCl<sub>2</sub>·2H<sub>2</sub>O, K<sub>3</sub>[Fe(CN)<sub>6</sub>] and trisodium citrate (C<sub>6</sub>H<sub>5</sub>Na<sub>3</sub>O<sub>7</sub>·H<sub>2</sub>O) were purchased from Tianjin Fengchuan Chemical Reagent Technology Co. Ltd. The phosphate buffer solution (PBS, NaH<sub>2</sub>PO<sub>4</sub>-Na<sub>2</sub>HPO<sub>4</sub>) was used to obtain the desired working solutions. In addition, all the other chemicals were of AR grade and used without further purification.

### 2.2 Instruments and characterizations

UV-vis spectra (UV-1800, SHIMADZU, Japan) employed to obtain UV-vis absorption spectra of Au@Cu NCs. X-ray diffraction (XRD, X'pert, Philips, Holland) was used to ascertain the phase structures of Au@Cu NCs. SEM (Nova Nano SEM 230, FEI, USA) was used to obtain the surface morphologies of Au@Cu NCs materials.

Cyclic voltammetry (CV) was performed on electrochemical workstation (CHI 660C, Shanghai). The electrochemical cell consisted of the bare glassy carbon electrode (GCE, 3.0 mm in diameter), Au@Cu NCs/GCE (working electrode) and Ag/AgCl electrode (reference electrode). PBS (NaH<sub>2</sub>PO<sub>4</sub>-Na<sub>2</sub>HPO<sub>4</sub>, pH = 5.5) was added into the electrochemical cell and all the detection solutions

were purged with N<sub>2</sub> for at least 15.0 min before measurements. All measurements were performed at 25 °C.

### 2.3 Preparation of Au@Cu NCs

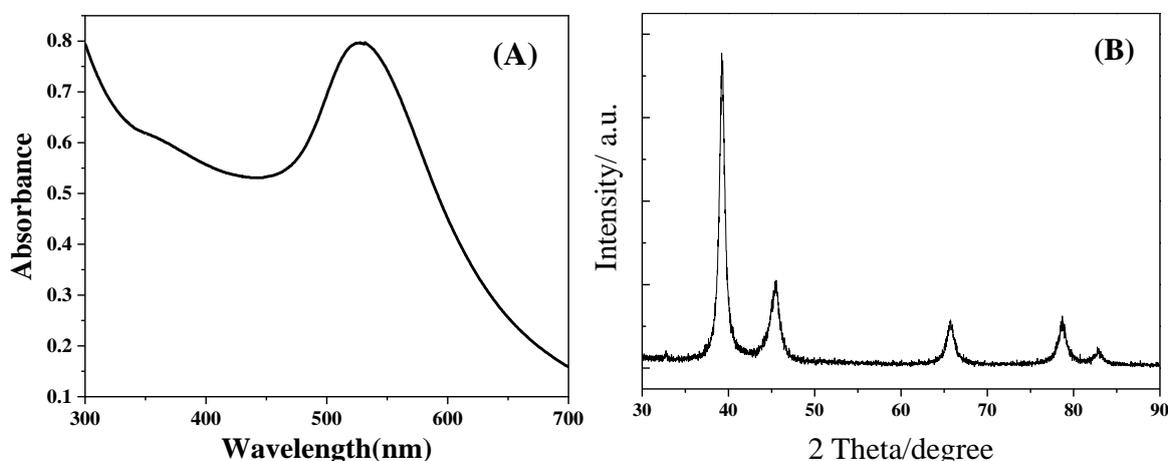
In this experiment, Au@Cu NCs was synthesized by the chemical reduction technique at low temperature. Firstly, 4.94 mL 3.175 mM HAuCl<sub>4</sub> and 4.00 mL 1.0 mM CuCl<sub>2</sub>·2H<sub>2</sub>O were mixed uniformly, and 5.0 mL 5.0 mM trisodium citrate was dropped gradually. Then, the mixtures were added 8 mL H<sub>2</sub>O and stirred for 3.0 h on a water bath (10.0 °C). The color of the light yellow solution changed to purplish red, indicating that the Au@Cu NCs formed. The UV-vis spectra, XRD and SEM of Au@Cu NCs were shown in Fig. 1.

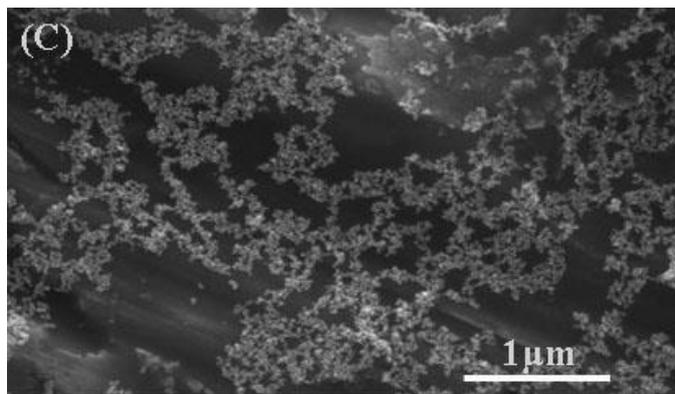
### 2.4 Preparation of electrode and analytical procedure

The fabrication procedure of polishing, ultrasonication and drying of Au@Cu NCs/GCE were as same as in our previous works [23, 24]. Then, 10.0 μL Au@Cu NCs was uniformly dropped on the surface of the GCE to obtained Au@Cu NCs/GCE electrode after drying with infrared lamp. The Au@Cu NCs/GCE electrode was regenerated after each measurement by a multi-circle potential scan in the potential range (0.0-1.0 V) in a blank PBS (pH = 5.5) until the background CV curve was invariable.

## 3. RESULTS AND DISCUSSION

### 3.1 Characterization of Au@Cu NCs





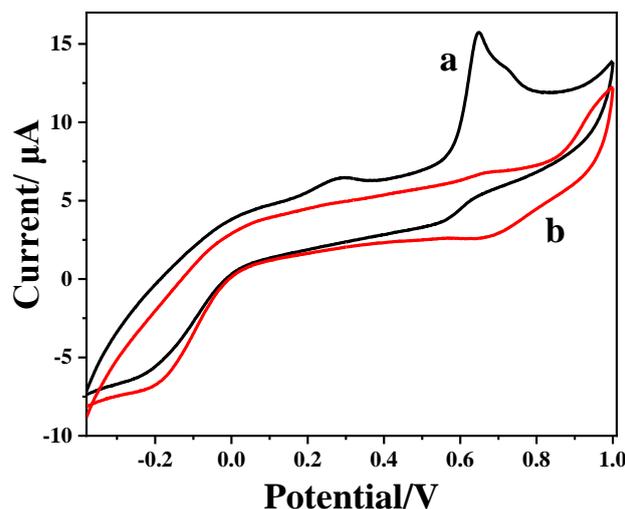
**Figure 1.** (A) UV-vis spectra of Au@Cu NCs. (B) XRD of Au@Cu NCs. (C) SEM of Au@Cu NCs

UV-vis spectra, XRD and SEM of Au@Cu NCs were shown in Fig. 1. From Fig. 1(A), a typical absorption peak at 532 nm which located at between Au and Cu nanoparticle, indicating that Au@Cu NCs has been successfully synthesized. The XRD of Au@Cu NCs was shown in Fig. 1(B). According to the literature [25], the diffraction angles ( $2\theta$ ) values of Au is  $38.3^\circ$ ,  $44.6^\circ$ ,  $64.7^\circ$ ,  $77.6^\circ$  and  $81.8^\circ$ , and the  $2\theta$  values of Cu is  $43.297^\circ$ ,  $50.433^\circ$  and  $74.130^\circ$ , respectively. In particularly, the  $2\theta$  values of Au@Cu NCs appeared at  $39.8^\circ$ ,  $45.2^\circ$ ,  $66.0^\circ$  and  $78.5^\circ$  due to the presence of Cu. XRD results demonstrated that Au@Cu NCs were composed of Au and Cu elements. Therefore, Au@Cu NCs have been successfully synthesized according to chemical reduction technique in this study. The SEM image of resultant Au@Cu NCs was shown in Fig. 1(C). There were no dispersion nanoparticles in Au@Cu NCs, and the distribution and morphology of the obtained Au@Cu NCs were uniform.

### 3.2 Electrochemical Characterization

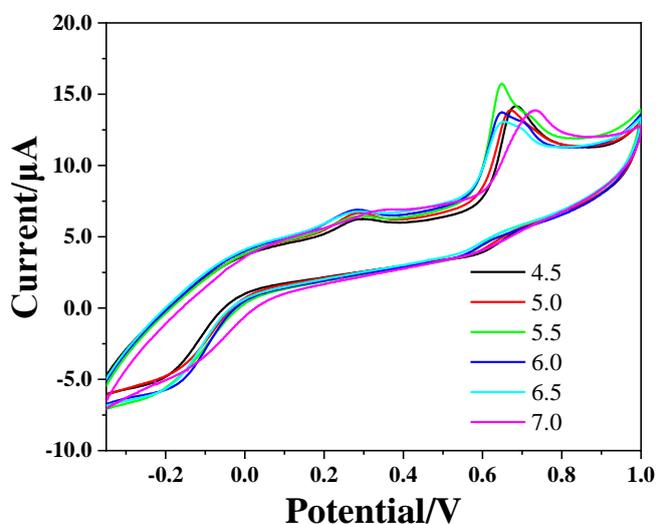
#### 3.2.1 Electrochemical behavior of piroxicam

To characterize the interfacial properties of the sensor, the voltammetric responses of Au@Cu NCs/GCE electrode and bare GCE electrode toward determination of piroxicam with CV were compared and the results were shown in Fig. 2. It was cleared that rather high currents of piroxicam were obtained on Au@Cu NCs/GCE (curve a), while poor oxidation peak was observed on GCE (curve b). The obvious catalytic performance could be attributed to the numerous reactive boundary regions of the Au@Cu NCs materials, which result in its excellent catalytic performance than the GCE electrode. These results implied that Au@Cu NCs/GCE has excellent selectivity and catalytic performance for piroxicam and can be used to determinate of piroxicam with high sensitivity.



**Figure 2.** CVs of Au@Cu NCs/GCE (a) and GCE (b) in 0.2 mM piroxicam solution, pH = 5.5, 50 mV/s.

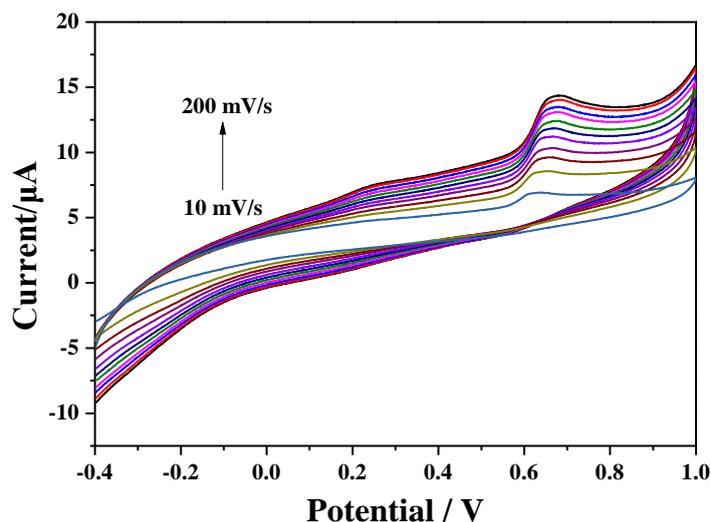
### 3.2.2 Influence of pH



**Figure 3.** CVs of Au@Cu NCs/GCE in PBS with different pH values (4.5-7.0), 0.2 mM piroxicam, 50 mV/s.

The electrochemical responses of 0.2 mM piroxicam on Au@Cu NCs/GCE with different pH values (4.5-7.0) at 50 mV/s were investigated in detail. From Fig. 3, the maximum value of the peak currents ( $I_p$ ) was obtained at pH = 5.5, and decreased slightly with further increase of pH value to 7.0. Thus, in order to determinate of piroxicam with high sensitivity, pH 5.5 was selected as the suitable pH in further experiments.

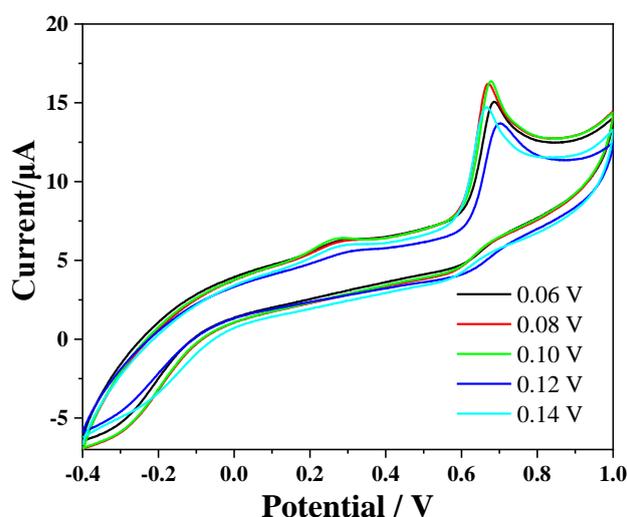
### 3.2.3 Effect of scan rate



**Figure 4.** CVs of Au@Cu NCs/GCE. 0.2 mM piroxicam, pH = 5.5, scan rate: 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200 mV/s.

The CVs of Au@Cu NCs/GCE in 5.0 mL PBS (pH = 5.5) containing 0.2 mM piroxicam at different scan rates (10-200 mV/s) were investigated and shown in Fig. 4. The  $I_p$  value increased linearly when the scan rate increased from 10 to 200 mV/s, which indicated that a surface-controlled process was ascertained [21, 22].

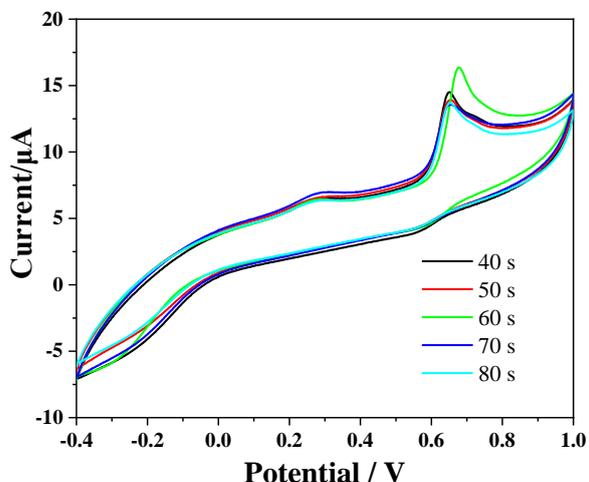
### 3.2.4 Effect of accumulation potential



**Figure 5.** The effect of accumulation potential on the peak current of 0.2 mM piroxicam (PBS, pH = 5.5)

The effect of accumulation potential on the determination of 0.2 mM piroxicam in PBS (pH = 5.5) has been investigated and shown in Fig. 5. The maximum value of  $I_p$  was obtained when accumulation potential was 0.10 V, which indicated that 0.10 V was the adequate saturation of piroxicam on Au@Cu NCs/GCE electrode.

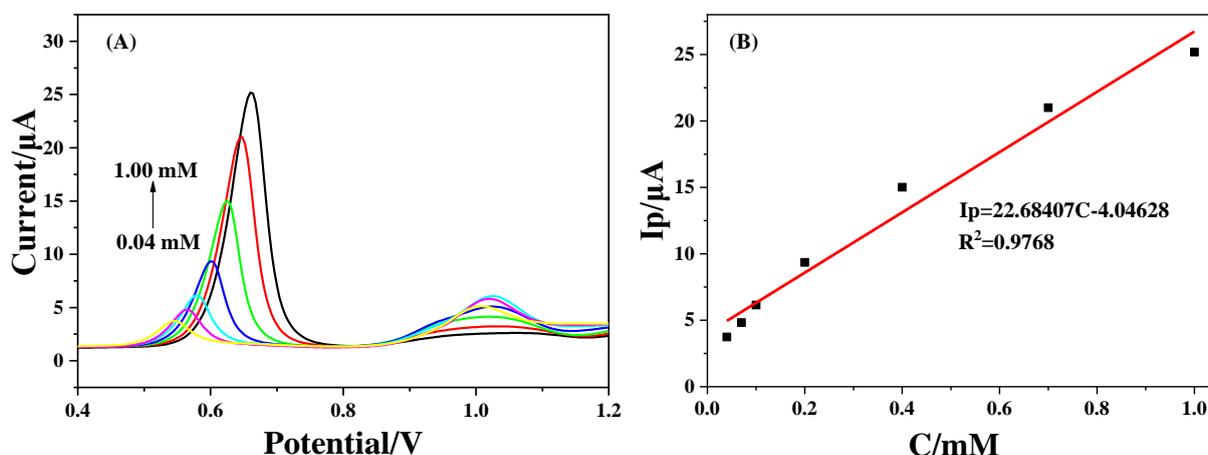
### 3.2.5 Effect of the accumulation time



**Figure 6.** The effect of accumulation time on the peak current of 0.2 mM piroxicam (PBS, pH = 5.5)

Usually, accumulation time is another important property to determinate of piroxicam in the electrochemical analysis. The effects of accumulation time on detection of piroxicam were shown in Fig. 6, from which the  $I_p$  value reached to the maximum when accumulation time was 60 s. Thus, 60 s of accumulation time was a suitable optimum and used in further experiments.

### 3.3 Determination of piroxicam on Au@Cu NCs/GCE



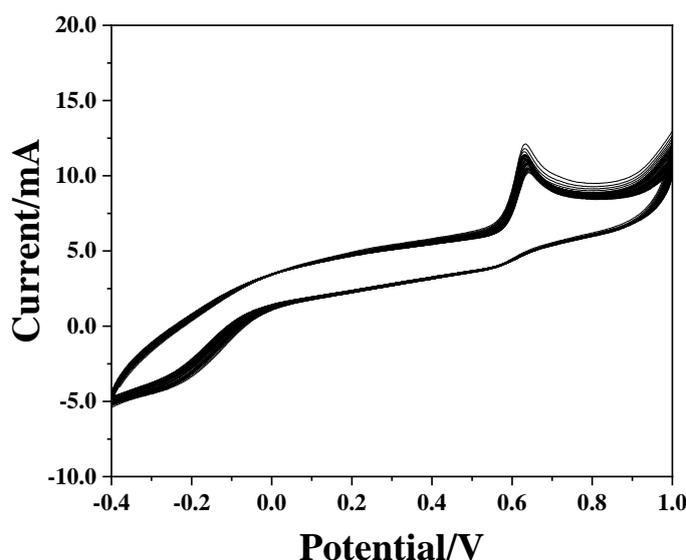
**Figure 7.** (A) DPV at Au@Cu NCs/GCE in PBS (pH = 5.5), piroxicam concentrations: 0.04-1.00 mM. (B) The relationship of  $I_p$  and piroxicam concentration.

To investigate the sensitivity of Au@Cu NCs/GCE for piroxicam determination, DPV has been used and the results were shown in Fig. 7(A). The peak current increased linearly when the piroxicam concentration was in the range of 0.04-1.00 mM. From Fig. 7(B), the regression equation can be obtained as:  $I_p = -22.68407C \text{ (mM)} - 4.04628$  ( $R^2 = 0.9768$ ). Experimental results demonstrated that piroxicam can be determined using Au@Cu NCs/GCE under certain conditions. The comparison of similar electrodes and Au@Cu NCs/GCE for piroxicam determination was shown in Table 1.

**Table 1.** Comparison of similar electrodes and Au@Cu NCs/GCE for piroxicam determination

Electrodes	Linear range	Samples	Reference
Glutathione-GO/ZnO/GCE	0.1-500 $\mu\text{M}$	Pharmaceutical tablets and human fluids	[17]
BNP-CPE	$0.5 \times 10^{-3}$ -0.1 $\mu\text{M}$	Serum and pharmaceutical samples	[20]
Pt-N-rGO-SWCNTs	0.06-60 $\mu\text{M}$	Piroxicam tablet samples	[22]
NHPDA/FePt/CNTs/CPE	0.5-550 $\mu\text{M}$	Tablet and urine samples	[26]
rGO-PEDOT:PSS/GCE	0.87-26 $\mu\text{M}$	River water and pharmaceutical samples	[27]
Au@Cu NCs/GCE	40-1000 $\mu\text{M}$	Piroxicam liniment	This work

### 3.4 Stability of the Au@Cu NCs/GCE



**Figure 8.** CVs of piroxicam electrocatalytic reaction at the Au@Cu NCs/GCE in PBS (pH = 5.5) containing 0.2 mM piroxicam for 45 consecutive cycles.

The Au@Cu NCs/GCE electrode was scanned continuously for 45 cycles at a scan rate of 50mV/s to investigate its stability, and the results were shown in Fig. 8. The features of the CVs curves were invariable after 45 cycles, implying that the excellent stability of Au@Cu NCs/GCE. The uniform and the well bonding between Au and Cu of Au@Cu NCs result in the improved catalytic durability. Therefore, the proposed Au@Cu NCs/GCE electrode can be employed for determination of piroxicam with high excellent and reproducibility stability.

### 3.5 Sample analysis

**Table 2.** Results of piroxicam detection in liniment samples (n=3)

Sample	Original (mM)	Added (mM)	Found (mM)	Recovery (%)	RSD (%)
Piroxicam liniment	0.32	0.10	0.39	92.86	4.69
		0.30	0.61	98.39	3.87
		0.50	0.83	101.22	2.95

To investigate the feasibility and applicability of the proposed method, piroxicam liniment was selected as real sample for determination of piroxicam in this study. A certain volume of piroxicam liniment was added into 50-mL volumetric flask and diluted with PBS (pH = 5.5) to prepare the desired the working solutions. The concentration of piroxicam in working solutions was determined by PDV method and the results were shown in Table 2. The recovery was 92.86-101.22 % and the RSD was 2.95-4.69 %, indicating that the proposed method is suitable for piroxicam determination in liniment samples.

## 4. CONCLUSIONS

In summary, Au and Cu nanoparticle chains (Au@Cu NCs) have been synthesized by a chemical reduction method. Then, the as-prepared Au@Cu NCs material was modified to a glassy carbon electrode (GCE) to prepare an electrochemical sensor (Au@Cu NCs/GCE) and used for determination of piroxicam in the liniments samples. The effects of accumulation potential, scan rate, pH and accumulation time on determination of piroxicam were investigated systematically. Significantly, the electrochemical sensor of Au@Cu NCs/GCE has an excellent response for piroxicam determination with a good linear range of 0.04-1.00 mM at desired conditions. The recovery was 92.86-101.22 % and the RSD was 2.95-4.69 %. Therefore, the proposed method is suitable for piroxicam determination in liniment samples with high accuracy and precision.

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