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Indirect electrochemical determination of ciprofloxacin by anodic stripping voltammetry of Cd(II) on graphene-modified electrode

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ABSTRACT

An indirect electrochemical determination method for ciprofloxacin (CIP) was developed based on the complexation of CIP with Cd^{2+}. On graphene-modified electrode, Cd^{2+} showed a strong anodic stripping peak current response, which was efficiently prohibited in the presence of CIP. Thus, the anodic stripping peak current of Cd^{2+} was employed as the indicating signal for CIP determination, which was more sensitive than the direct electrochemical oxidation response of CIP. Some influence factors such as the modified volume of graphene, solution pH, accumulation time, complexation reaction time were systematically investigated. Under optimum conditions, the anodic stripping response of Cd^{2+} on the graphene-modified electrode was inversely proportional to CIP in the concentration range from 1.0×10^{-7} to 1.0×10^{-5} mol L^{-1} with a detection limit (3S/N) of 5.9×10^{-8} mol L^{-1}. The method showed high selectivity, good reproducibility and was successfully applied to the determination of CIP in pharmaceutical formulation and human urine.

1. Introduction

Fluoroquinolones (FQs) are one of the most important groups of synthetic antibiotics used for the treatment of bacterial infections in humans and livestock. Ciprofloxacin (CIP), namely 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid (Fig. 1), is a member of the third-generation FQ family. It is a broad-spectrum antimicrobial drug with bactericidal activity against both Gram-positive and Gram-negative bacteria through its inhibition of DNA gyrase, an enzyme responsible for bacterial DNA replication [1,2]. CIP is routinely prescribed for animals to prevent veterinary diseases. However, their multiple and widespread use could be responsible for resistance by such pathogens as *Campylobacter*, *Salmomella*, and *Escherichia coli*, and residues in food of animal origin or farm wastes and present potential risks to consumers [3,4]. Therefore, it is important to determine CIP in biological fluids and pharmaceutical formulations. Various analytical techniques such as high performance liquid chromatography (HPLC) [5–7], surface enhanced Raman scattering (SERS) [8], mass spectrometry [9], enzyme-linked immunosorbent assay (ELISA) [10], electrokinetic capillary chromatography [11], spectrofluorometry [12] have been developed for CIP determination. Compared with other instrumental methods, electrochemical analysis has many advantages such as high sensitivity, low cost, fast analytical speed, simple instrumentation and portability. Various electrodes including DNA [13], multi-wall carbon nanotubes (MWCNTs) [14,15] and sodium dodecyl benzene sulfonate (SDBS) [16] modified electrodes as well as enzymatic rotating biosensor [17] have been employed for electrochemical determination of CIP.

Antibiotics can form stable complexes with some metal ions. Cesme et al. have synthesized the complexes of loracarbef and metal ions such as Cu^{2+}, Co^{2+}, Fe^{3+} and Ru^{3+} and studied their voltammetric behavior [18]. The complexation of iron ions with clarithromycin and roxithromycin [19], and bivalent metal ions with nimesulide and ibuprofen [20] has been systematically investigated. Moreover, FQs also have strong complexation with some metal ions [21,22]. For example, CIP and ofloxacin have been reported to form stable complexes with Cu^{2+}, Zn^{2+}, Cd^{2+} or Mn^{2+} [23–26].

In this work, we developed a new method for CIP determination based on the complexation of CIP with Cd^{2+}. Although CIP was electroactive and could be determined by its electrooxidation response, the sensitivity and selectivity were usually undesirable. Actually, compared with direct electroanalysis of organic compounds, anodic stripping voltammetry of heavy metals exhibits more desirable analytical figure of merit. The present work demonstrated that anodic stripping response of Cd^{2+} could be used as indicating signal for sensitive and selective determination of CIP. Graphene having large specific surface area and negative charges

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was used to modify the electrode to enhance the voltammetric response of Cd^{2+} [27]. On such a graphene-modified electrode, Cd^{2+} exhibited a well-defined anodic stripping voltammetric response which was declined in the presence of CIP due to the complexation of CIP with Cd^{2+}. The CIP concentration was inversely proportional to the signal of Cd^{2+} in the range of 0.1–10 μmol L^{-1}. The proposed method was successfully applied to the determination of CIP in real samples.

2. Experimental

2.1. Chemicals

CIP standard sample was provided by Wuhan Yuancheng Technology Development Company Ltd. (Wuhan, China). CIP Tablets were purchased from Yichang Humanwell Pharmaceutical Co., Ltd. (Yichang, China). Nafion (5% in a mixture of lower aliphatic alcohols and water) was purchased from Sigma–Aldrich. Graphite powder, 1-methyl-2-pyrrolidone, ethanol, hydrochloric acid, CH_3COONa, CH_3COOH and $CdCl_2{\cdot}2.5H_2O$ were provided by Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). All other chemicals were of analytical grade and used without further purification. Doubly distilled water was used throughout the investigation.

2.2. Synthesis of graphene

Graphene was prepared by one-pot solvent exfoliation method [28]. Briefly, 0.25 g graphite powder was put into 50.0 mL N-methyl-2-pyrrolidone (NMP), then the mixture was ultrasonicated for 48 h to obtain the stripped graphene–NMP suspension. The as-prepared graphene–NMP suspension was added with enough water. Then the precipitate was washed several times with water and ethanol to remove NMP solvent. After centrifuged and dried at 60 °C, graphene powder was ready to use.

2.3. Preparation of graphene-modified electrode

Two milligrams of graphene powder was dispersed in 1.0 mL of 0.3% Nafion solution to give a 2.0 mg mL^{-1} graphene suspension with the aid of at least 1-h ultrasonic agitation. Prior to modification, the glassy carbon electrode (GCE) surface was polished to a mirror-like smoothness with an aqueous slurry of 0.05 μm alumina powder on a damp silk cloth, and then cleaned with ethanol and water. After being dried with nitrogen gas, the GCE surface was coated with 6 μL of 2.0 mg mL^{-1} graphene suspension and dried under infrared lamp for 10 min to obtain graphene-modified GCE.

2.4. Apparatus and procedure

All electrochemical experiments were performed on an EC550 electrochemical workstation (Wuhan Gaoss Union Instrument Company, China) in a conventional three-electrode system. A modified GCE, a saturated calomel electrode (SCE) and a platinum electrode were used as working, reference and auxiliary electrodes, respectively.

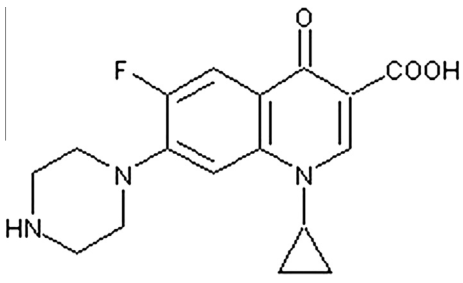

Fig. 1. Structure of ciprofloxacin.

The high performance liquid chromatography (HPLC) measurements were performed on an Agilent (USA) 1100 module system with C_{18} column according to the reference procedure [29]. The mobile phase consisted of 0.4 mol L^{-1} citric acid, acetonitrile and methanol (78:7:15, v:v:v). All CIP samples were finally filtered by 0.45 μm membrane filters and degassed prior to use. The UV detection wave-length was set at 287.5 nm. The flow rate was 1.2 mL min^{-1} and the injection volume was 20 μL. All measurements were performed at normal pressure and room temperature.

3. Results and discussion

3.1. Anodic stripping voltammetry of Cd^{2+}

The electrochemical responses of Cd^{2+} on bare and graphene-modified GCE were compared in 0.1 mol L^{-1} acetate buffer solution (ABS) (pH 3.6) using anodic stripping voltammetry. It can be seen that Cd^{2+} shows an anodic peak at −0.71 V on bare GCE (curve *a* in Fig. 2A), owing to the stripping of Cd during the anodic process.

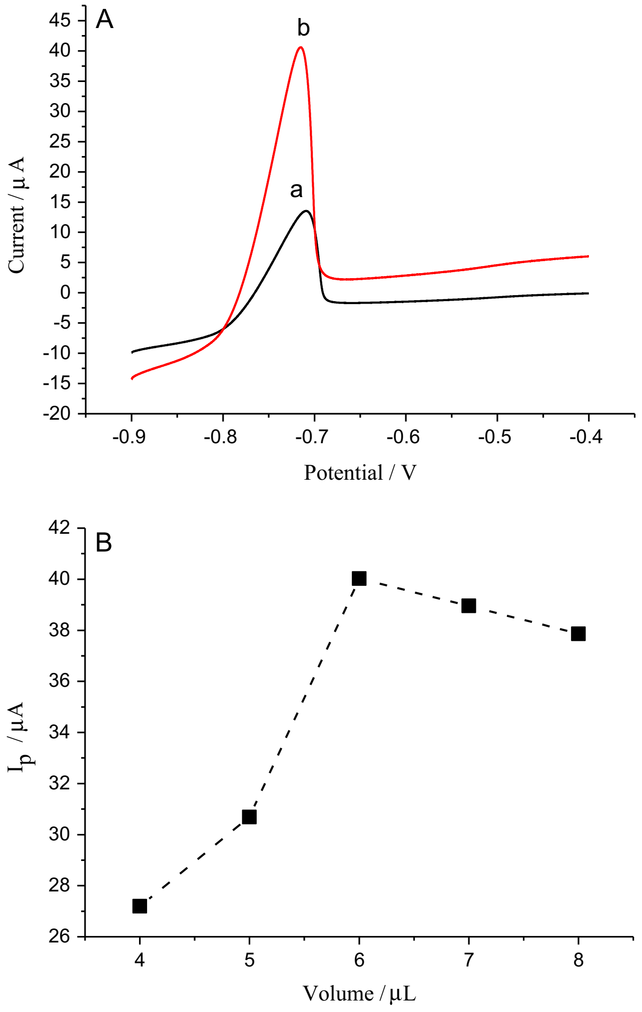

Fig. 2. (A) Anodic stripping voltammetric curves of 1.0×10^{-4} mol L^{-1} Cd^{2+} in 0.1 mol L^{-1} ABS (pH 3.6) at (a) bare GCE and (b) graphene-modified GCE. (B) Influence of *G* amount on the peak current. Accumulation time: 10 s. Scan rate: 100 mV s^{-1}.