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Original Article

Ultra-sensitive electrochemical sensing of acetaminophen and codeine in biological fluids using $CuO/CuFe_2O_4$ nanoparticles as a novel electrocatalyst

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ABSTRACT

Copper ferrite–copper oxide ($CuO\text{-}CuFe_2O_4$) nanoparticles as a semiconductor composite with p–n junction were synthesized by co-precipitation reaction. Then, a novel $CuO\text{-}CuFe_2O_4$ carbon paste modified electrode was fabricated which displays an effectual electrocatalytic response to the oxidation of acetaminophen (AC) and codeine (CO). A linear range of 0.01–1.5 μmol L^{-1} and 0.06–10.0 μmol L^{-1} with the detection limits of 0.007 μmol L^{-1} and 0.01 μmol L^{-1} were achieved for AC and CO, respectively. The practical usage of the proposed sensor revealed reasonable results for quantification of AC and CO in biological fluids.

1. Introduction

Nanotechnology is one of the most innovative fields in the current century [1]. Nanomaterials based sensing systems offer a novel class of fast and low cost detection. In recent years, spinel ferrites nanoparticles with general formula MFe_2O_4 (M is divalent transition metal) have revealed noticeable potentials in electrochemical sensor and biosensor [2]. Among the ferrites, $CuFe_2O_4$, the n-type semiconductor, has been focused owing to its high electronic conductivity, high thermal stability, and effective catalytic activity [3,4]. Cupric oxide (CuO) is p-type semiconductor with a fine band gap energy which widely applied in designing of superconductors, catalysts, sensors materials. Incorporation p–n junction can improve the magnetic, electrochemical and electrical properties [5]. It is reported that the addition of Fe^{3+} ion in copper oxide leads to $CuO/CuFe_2O_4$ nanocomposites. Acetaminophen (N-acetyl-p-aminophenol, AC) is an analgesic drug and a suitable alternative for aspirin as a pain reliever and fever reducer [6]. It does not exhibit any harmful side effects, but overdoses are known to cause severe liver and kidney

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damages, and its adverse effects include rashes and blood dyscrasia [7]. AC is often used in the presence of other drugs like aspirin, cetirizine, tramadol, and codeine. Combinations of AC with codeine, produce a significant increase in analgesia compared to AC alone, and it is listed as an antipyretic drug in the European and United States Pharmacopoeia [8,9]. These pharmaceutical formulations have accounted for 20% of total non-opiate analgesics during the last decade [10]. Codeine (methyl morphine), a natural opiate alkaloid prepared from poppy or from morphine by methylation, has long been used as an effective analgesic and antitussive agent [11]. Its phosphate form is usually used for the treatment of gent or moderate pains in clinical medication [12]. Ascorbic acid (AA), Vitamin C, is one of electroactive species and has important role for hydroxylation reactions for metabolic pathway in human body [13]. As some fruit and vegetables have high ascorbic acid content, it could be found with high concentration in biological fluid. To date, various methods such as high-performance liquid chromatography [14,15], spectrophotometry [16], and electrophoresis [17–19] have been developed for the simultaneous determination AC and CO. However, these methods usually have many drawbacks such as complicated sample pretreatment that is laborious and time-consuming. Electrochemical methods have also received much interest due to their higher selectivity, lower cost, and faster operation than other methods [20–23]. In this research, $CuO/CuFe_2O_4$ nanocomposite was prepared using co-precipitation reaction. The synthesized nanocomposite then used as modifier in carbon paste electrode (CPE) for the sensitive quantification of AC and CO in the biological fluids.

2. Experimental

2.1. Apparatus

Electrochemical system was the Autolab PGSTAT101 with NOVA software (Ecochemie, Utrecht, The Netherlands), and applied a conventional three-electrode cell assemblage containing an Ag/AgCl electrode (reference electrode), a platinum wire (counter electrode) and the $CuO/CuFe_2O_4$/CPE as the working electrode. The pH of the solutions was controlled with a Corning pH meter (model 146). The nature and morphology of the synthesized nanocomposite were characterized by using XRD (Holland Philips Xpert, X-ray diffractometer with Cu-K_α radiation) and FE-SEM (Hitachi S-4160). FT-IR was recorded using a JASCO FT-IR (680 plus). The analysis of chemical composition of the modified electrode was performed using an energy dispersive spectrometer (EDX).

2.2. Chemicals

Acetaminophen and codeine phosphate were purchased from Temad Co, Iran. Stock solutions of AC and CO (0.001 mol L^{-1}) were prepared daily by dissolving suitable amounts of them in doubly distilled water in a 10-mL volumetric flask.

Phosphate buffer solutions (0.10 mol L^{-1}) with different pH (3–8) values were used. Pure graphite powder (particle size <50 μm) was purchased from Sigma–Aldrich. High-viscosity paraffin (d = 0.88 kg L^{-1}) was used for the preparation of paste electrodes.

2.3. Synthesis procedure for $CuO/CuFe_2O_4$ preparation

About 0.76 g $Cu(NO_3)_2.3H_2O$ and 0.85 g $FeCl_3.6H_2O$ were dissolved together in 90 mL distilled deionized water to get a well-mixed solution. While this mixture stirring, the ammonium 25% was added dropwise until pH adjusted to 9.0. The generated precipitate was allowed to stirring about 1 h. The precipitate was washed with ethanol/distilled water several time and dried at 70 °C. Finally the powder was calcinated at 750 °C for 4 h.

2.4. Preparation of $CuO/CuFe_2O_4$ modified electrode

The modified electrode was prepared by mixing 50 mg of $CuO/CuFe_2O_4$ and 800 mg of graphite powder. Then, diethyl ether was added to achieve uniform mixture. After vaporization of diethyl ether, 200 mg paraffin oil was added and mixed with mortar and pestle to get a uniformly wetted paste. The resulting paste was pressed into the hole at the end of the electrode.

2.5. Real sample preparation

Human plasma and urine samples were originally obtained from volunteers who had taken AC/CO tablets (325/30 mg). The samples were collected 2 h after intake of tablets. Plasma samples were deproteinated using acetonitrile [24]. In order to precipitate proteins in the plasma samples, 5.0 mL of the samples was treated with 10 mL acetonitrile. Then, the mixture was vortexed for a further 30 s and after that it was centrifuged at 3000 rpm for 10 min. The supernatant was transferred to a small flask and evaporated with a stream of nitrogen. The dry residue was diluted to final volume of 20 ml with phosphate buffer solution of pH 5.0 and transferred into the voltammetric cell to be analyzed without any further pretreatment. Standard addition method was used for the determination of AC and CO in the samples.

Urine samples were stored in a refrigerator immediately after their collection. A 5.0 mL of the sample was centrifuged for 10 min at 2000 rpm. The supernatant was filtered using a 0.45 μm filter and then diluted 4-times with PBS pH 5.0 and reaching a final volume of 20 ml. The solution was transferred into the voltammetric cell to be analyzed without any further pretreatment. Standard addition method was used to determine the CO and AC content of the sample.

3. Results and discussion

3.1. Characterization of $CuO/CuFe_2O_4$

Fig. 1A shows the morphology of $CuO/CuFe_2O_4$ nanoparticles which has spherical like structure with mean diameter of 90 nm. The crystallite phases of $CuO/CuFe_2O_4$ was identified by X-ray diffraction (Fig. 1B) in 2θ range of 20–70° are in a good agreement with the standard XRD pattern of copper ferrite (tetragonal-type)/copper oxide nanoparticles [5]. Fig. 1C shows

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