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Electrocatalytic oxidation and differential pulse voltammetric determination of sulfamethoxazole using carbon nanotube paste electrode

Majid Arvand *, Reza Ansari, Lida Heydari

Department of Chemistry, Faculty of Science, University of Guilan, Namjoo Street, P.O. Box: 1914, Rasht, Iran

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ABSTRACT

The use of a carbon-nanotube paste electrode provides an effective means for the determination of sulfamethoxazole. A decrease of ca. 110 mV in the overpotential for the oxidation of sulfamethoxazole compared to a traditional carbon paste electrode is reported along with greatly enhanced signal-to-noise characteristics. The oxidation process was found to be dependent on the pH of the supporting electrolyte. Under the optimized conditions the calibration plots are linear in the concentration range of 0.35–30 μg mL^{-1} with slope of 0.0955 μA/μg mL^{-1}, LOD 0.1 μg mL^{-1} and LOQ 0.33 μg mL^{-1}. Application of the method for the determination of the drug in the form tablet or suspension, without any interference, from the excipients, resulted in acceptable deviation from the stated concentrations.

1. Introduction

Sulfamethoxazole (SMX) is a member of the sulfonamide family of antibiotics. It has a broad spectrum of antibacterial activity against both Gram-positive and Gram-negative aerobic bacteria, also being effective against protozoa [1,2]. Sulfamethoxazole has been used successfully for the treatment of bacterial infections, including those of the respiratory and urinary tract, as well as in the treatment of opportunistic infections in transplantation and for AIDS-related complications [2]. Nevertheless, sulfamethoxazole can produce a variety of side effects that include gastro-intestinal disturbances, hypersensitivity reactions, and a number of hematological abnormalities such as thrombocytopenia, agranulocytosis, megaloblastosis, eosinophilia, and sulfhemoglobinemia [3,4]. Trimethoprim (TMP) is a dihydropteroate synthetase inhibitor that is commonly used in combination with sulfonamides for broad spectrum antimicrobial therapy. It locks the folic acid metabolism and thus, produces a synergistic antibacterial activity. In veterinary medicines, the combination of sulfonamides with trimethoprim is widely used for prevention and treatment of respiratory or gastro-intestinal tract infections in cattle, swine and poultry [5]. Determination of SMX in the presence of TMP in biological fluids by high-performance liquid chromatography has been the subject of several investigations [6–14]. In spite of structure dissimilarity between SMX and TMP, organic solvent [6,7] or solid-phase [8,9] extraction have been developed but they are time-consuming and may show variable recoveries at different concentrations [7,9]. A column-switching method [10] has the problem of the availability of the required instruments. Plasma protein precipitation [11–14] provides a simple and fast sample processing, but subsequent chromatographic separation with sufficient sensitivity is not easily achieved. Recent studies demonstrated that carbon nanotubes (CNTs) can impart strong electrocatalytic activity; and the excellent electrocatalytic activity of carbon nanotubes in redox behavior of different compounds has been reported. The unique electronic properties of these materials have been effectively exploited in electrochemistry as a means of promoting the electron transfer reaction of wide biological compounds [15–17]. The ability of CNT's modified electrodes to promote electron-transfer reactions of important biomolecules has been investigated. Palleschi and Rivas have reported on the advantages of carbon nanotubes' paste electrodes on the electrochemical behavior of some biological compounds [18,19].

This work is the first report on the electrooxidation and determination of SMX at multi-walled carbon nanotube paste electrodes (MWCNT paste electrode). The carbon nanotubes are incorporated into a paste electrode [20,21] and the attractive response is compared directly with that obtained at the traditional carbon paste electrode.

2. Experimental

2.1. Reagents and solutions

Paraffin oil, potassium chloride, sodium hydroxide, hydrochloric acid and acetic acid are from Fluka or Merck companies and were used as purchased, without further purifications. Multiwalled carbon

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* Corresponding author. Tel./fax: +98 131 3233262.
E-mail address: arvand@guilan.ac.ir (M. Arvand).

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nanotubes with a 95% purity o.d. = 5–20 nm, i.d. = 2–6 nm and 1–10 μm length were obtained from Aldrich. Sulfacetamide, sulfasalazine, cefixime and sulfamethoxazole in analytical grade were provided from Sobhan Pharmaceutical Company (Industrial city, Rasht, Iran). Since SMX generally has a low solubility in water, a stock solution of sulfamethoxazole (253 μg mL^{-1}) was prepared by dissolving appropriate amount of it in distilled water with heating. The dilute solutions were prepared daily with solutions composed of supporting electrolyte and 0.1 mol L^{-1} acetate buffer. Also co-trimoxazole tablets (Bactrim, Cotrim, Uroplus DS) and suspension (Cotrim pediatric) were purchased from a local pharmacy.

2.2. Instrumentation

Electrochemical measurements were conducted using an Autolab PGSTAT 30 electrochemical analyzer (Eco-Chemie BV, Utrecht, The Netherlands) connected to a computer with GPES (General Purpose Electrochemical System) software package. All electrochemical studies were performed at 25 ± 1 °C. A conventional three-electrode cell was employed incorporating a working modified electrode (a carbon paste or carbon-nanotube paste), a saturated Ag/AgCl reference electrode, and a platinum wire counter electrode. All potentials were measured and reported versus the Ag/AgCl reference electrode. Chromatographic measurements were carried out using a Agilent 1100 series HPLC (Germany) consisting of a gradient pump, a YMC Pack ODS-AM (5 μm, 250 mm × 4.6 mm ID) end-capped column coupled with an UV–vis detector and computer. The eluent was acetonitrile–water mixture (%50 (v/v)) in Britton-Robinson buffer (pH 2.5) at a flow rate of 1 mL min^{-1}. All separation was carried out at 25 °C. The detection was performed at 250 nm.

2.3. Preparation of paste electrodes

The constituents involved in the making of the paste electrode consisted of either carbon powder (1–2 μm, Fisher Scientific) or multi-walled carbon nanotubes and mineral oil. The constituents were mixed thoroughly, in a 60:40 carbon (nanotube or graphite) to mineral oil, weight to weight ratio. This ratio was used due to its success in previous applications [20,21]. This mixture was then forced into a plastic pipette tip (0.5 mm diameter) into which a bare copper wire was placed to produce the electrical connection. The surfaces of these paste electrodes were 'polished' (smoothed) between experiments on weighing paper (VWR Scientific Products, West Chester, PA).

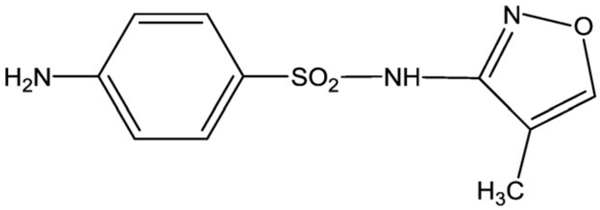
2.4. Electrochemical procedures

Cyclic voltammetry was usually conducted in the potential window from 0.5 to 1.3 V using a scan rate of 50 mV s^{-1} in solutions containing 0.1 mol L^{-1} KCl as supporting electrolyte and 0.1 mol L^{-1} acetate buffer (pH 6.0). Differential pulse voltammetric experiments were performed using the pulse amplitude of 0.05 V; pulse duration time of 0.04 s; step time of 0.4 s and a scan rate of 50 mV s^{-1} over the potential range of 0.7–1.1 V versus Ag/AgCl.

Chronoamperometric responses were recorded at both the MWCNT and carbon paste electrodes using a quiescent sulfamethoxazole solution. In these experiments, the potential was first held at 0.0 V for 20 s and then stepped to + 1.0 V for 60 s and the corresponding current transients were recorded.

3. Results and discussion

The presence of potentially oxidizable functional groups such as sulfamide suggested us to carry out study on electrooxidation of this drug on the surface of MWCNT paste electrode for the electrochemical study and also in order to develop a method for its determination (Scheme 1). To the best of our knowledge there is no any report about determination of this drug in pharmaceutical preparations using MWCNT paste electrodes.



Scheme 1. Chemical structure of sulfamethoxazole.

3.1. Electrochemical behavior of sulfamethoxazole at the MWCNT paste electrode and CPE

The cyclic voltammetric responses of a 25.3 μg mL^{-1} SMX at a MWCNT paste and carbon paste electrode in 0.1 mol L^{-1} KCl and 0.1 mol L^{-1} acetate buffer (pH 6.0) and scan rate of 50 mV s^{-1} were recorded. Fig. 1 shows the representative cyclic voltammograms. At both electrodes, an anodic current by the oxidation of sulfamethoxazole is observed, on the reverse scan, no distinct reduction wave was observed, indicating that the drug is irreversibly oxidized at the electrodes; however, no cathodic peak is found which indicate an irreversible heterogeneous charge transfer reaction in this system. This process starts by one electron oxidation of SMX to form the cation radical at the nitrogen. This followed by a rapid loss of a second electron and proton to give the iminium ion, to which the water is subsequently added [22,23].

The anodic peak potential for oxidation of SMX at a bare CPE is about + 1.0 V (curve b) while, its peak potential at a MWCNT paste electrode under identical conditions is about + 0.9 V (curve a) so, a decrease in overpotential is observed, and in comparison with the CPE the peak current was increased significantly at MWCNTs. These indicate electrocatalytic oxidation of sulfamethoxazole at the MWCNT paste electrode.

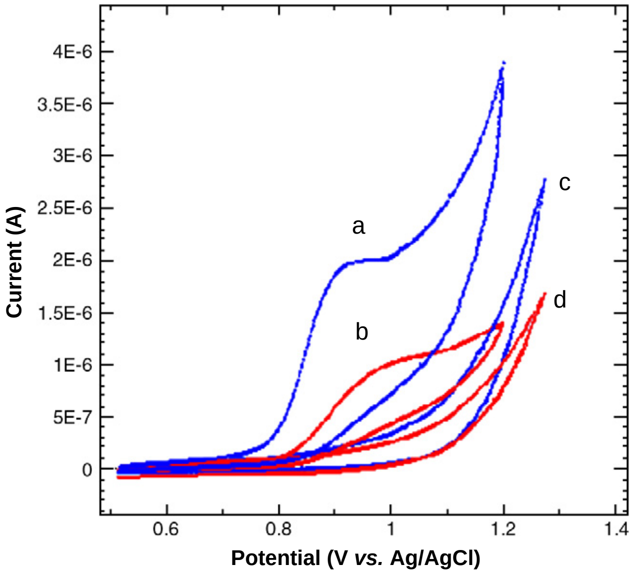


Fig. 1. Cyclic voltammograms of 25.3 μg mL^{-1} SMX in 0.1 mol L^{-1} KCl and 0.1 mol L^{-1} acetate buffer (pH 6.0) at the surface of (a) MWCNT paste electrode, (b) carbon paste electrode, (c) background current for MWCNT paste electrode, and (d) background current for carbon paste electrode; scan rate: 50 mV s^{-1}.