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Multi-walled carbon nanotubes–cobalt phthalocyanine modified electrode for electroanalytical determination of acetaminophen

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ABSTRACT

Here we described the development of a simple methodology for quantification of acetaminophen (ACOP) using square-wave voltammetry (SWV). A glassy carbon electrode modified with gold nanoparticles, functionalized multi-walled carbon nanotubes and cobalt (II) phthalocyanine was prepared and characterized with cyclic voltammetry, SWV and electrochemical impedance spectroscopy. The optimum experimental conditions, such as pH, buffer and square-wave voltammetric parameters were investigated. From the data analysis of the optimization of experimental conditions, the oxidation of ACOP was characterized as a quasi-reversible and proton-dependent process, where the reaction mechanism presents the participation of equal number of protons and electrons (two protons and two electrons) and k_s value is equal to $59.0 \pm 2.5\ s^{-1}$. Under the optimized conditions, calibration curves were linear in the concentration range of 1.49 μmol L^{-1} to 47.6 μmol L^{-1} and 47.6 μmol L^{-1} to 107.0 μmol L^{-1} with a limit of detection of 0.135 μmol L^{-1}. Other analytical parameters such as equations of the analytical curves, correlation coefficients, recovery efficiency and relative standard deviation for repeatability and reproducibility experiments were compared to results obtained by the use of UV–Vis spectrophotometry.

1. Introduction

Metal phthalocyanine complex (MPc) attached to multi-walled carbon nanotubes (MWCNT) has received considerable attention in the field of electroanalysis due to the combination of interesting properties of electrochemical devices [1–6]. The use of MWCNT is mainly due to its properties such as high surface area, mechanical strength, chemical stability and high electrical conductivity [7–10]. Furthermore, it has been shown that MPc-MWCNT provide enhanced visible-light photocatalytic activity and oxidation of organic pollutants [11,12]. Non-substituted MPc complexes are linked to MWCNT via non-covalent π–π interactions, while amino-substituted MPc complexes can be covalently linked to MWCNT via amide bond formation [13,14] and the excellent catalytic properties of phthalocyanines without losing any of the electronic properties of carbon nanotubes have been observed. The addition of gold nanoparticles (AuNPs) to provide increased surface area and conductivity facilitating the electron transfer process ensuring an increase in sensitivity and selectivity of the method [6,15]. There are no many studies in the literature describing the benefits of using electrodes modified with AuNPs-MPc-MWCNT [6,16].

Acetaminophen, {*N*-acetyl-*p*-aminophenol}, (ACOP) also known as paracetamol, is one of the most used analgesic and antipyretic drugs. It relieves fever and mild or moderate pain by inhibition of prostaglandin synthesis [17,18]. When administered in suitable doses, ACOP has an excellent safety profile, with about 90% of absorption by the organism and subsequently excreted via urine. The remaining 10% of ACOP is converted by the metabolism into *N*-acetyl-*p*-quinoneimine (NAPQI), a highly reactive electrophile and oxidant that causes injuries in liver and kidney cells and, therefore, the use of ACOP in excess leads to hepatotoxicity and nephrotoxicity cases [17–19].

An important part of analytical chemistry is the drug analysis, which plays a significant role in drug quality control in clinical and pharmaceutical chemistry. Various analytical methods such as chromatography [20,21], spectrophotometry [22,23], Fourier transform infrared spectrometry [24], colorimetry [25] and titrimetry [26,27] have been employed to ACOP determination. However, these methods are time-consuming or have high cost, pretreatment of samples and sometimes low sensitivity and selectivity. Electroanalytical methods have been established as an important tool for the determination of drugs and various environmental contaminants [25]. According to the literature there are several combinations of techniques and electrode surfaces, such as multi-walled carbon nanotubes-alumina-coated silica nanocomposite modified glassy carbon electrode (GCE) [28], graphene oxide modified GCE [29], platinum decorated multi-walled carbon nanotubes/Triton X-100 modified carbon paste electrode [30] and graphene-$CoFe_2O_4$ nancomposite modified carbon paste electrode [31] for electroanalytical studies of ACOP. Square-wave voltammetry (SWV) is consolidated as a

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highly sensitive method for the determination of drugs and environmental contaminants [13,32]. Furthermore, SWV provides information about the kinetics and mechanism of the electrochemical reactions [33]. ACOP is a compound that can be oxidized electrochemically, involving two electrons and two protons to yields N-acetyl-*p*-quinoneimine. This mechanism is described in many papers mainly from studies using cyclic voltammetry and differential pulse voltammetry [28–31,34]. However, to the best of our knowledge, there is no any proposition of studies that elucidate the ACOP oxidation mechanism by SWV. Here we construct a modified electrode based on MWCNT-CoPc/AuNPs for the detection and quantification of ACOP in commercial formulations (tablet, oral solution and suspension), to investigate the oxidation mechanism of ACOP using the diagnostic criteria of SWV and to compare the proposed electroanalytical methodology with the methodology recommended by United State Pharmacopoeia, which is the UV–Vis spectrophotometry [35].

2. Experimental

2.1. Materials

ACOP (purity higher than 99.9%), multi-walled carbon nanotubes (MWCNT) with diameter of 6–9 nm and length of 5 μm, cobalt (II) phthalocyanines (CoPc) and $HAuCl_4$ (purity of 99.99%) were purchased from Sigma-Aldrich. The stock solution of ACOP (1.0 mmol L^{-1}) was prepared by dissolving the suitable amount of the compound in ultra-pure water. All other chemicals were of analytical grade. The solutions were prepared with ultra-pure water of resistivity 18.2 MΩ cm obtained from a Millipore Milli-Q system.

2.2. Instrumentation

The electrochemical measurements were carried out using an Autolab PGSTAT 128N (EcoChemie, Netherlands) potentiostat/galvanostat controlled by NOVA 1.11 software. A conventional three-electrode system was carried out with a GCE (Metrohm) as working electrode (0.0314 cm^2), a platinum plate counter electrode (1.03 cm^2) and an Ag/AgCl/KCl (saturated) reference electrode. A Micronal B474 pH meter was used to adjust the pH values. The morphological aspects of the electrodes were performed by Scanning Electron Microscopy (SEM) measurements using an FEG Quanta 450 electron microscope equipped with energy dispersive spectroscopy (EDS) Bruker QUANTAX system coupled to the SEM microscope, using an acceleration voltage of 2 kV. A Lambda 25 (PerkinElmer Inc.) spectrophotometer was used for the UV–Vis measurements. A quartz cell with an optical path of 1 cm was employed in these measurements.

2.3. Preparation of modified electrode

A GCE was polished with 0.25 μm diamond paste and rinsed with purified water. The GCE was cleaned by ultrasonic agitation for 3 min in acetone and water, respectively. The electrochemical deposition of AuNPs onto the cleaned GCE was carried out at −0.2 V for 120 s in a solution previously deaerated with N_2 (White Martins, Brazil) for 5 min containing 1.0 mmol L^{-1} $HAuCl_4$ and 0.1 mol L^{-1} $NaNO_3$. [6,36] After, a cyclic voltammetry experiment in 0.5 mol L^{-1} H_2SO_4 was carried out in order to calculate the correspondent charge to the process of the gold oxide reduction.

The functionalization of MWCNT in acid medium was performed according to the procedure described in previous papers [13,16] for 1.0 g of MWCNT per 500 mL of a 1:3 mixture of HNO_3/H_2SO_4 for 4 h. The suspensions of 1 mg mL^{-1} functionalized MWCNT (*f*MWCNT) and 0.25 mg mL^{-1} CoPc were prepared using dimethylformamide. To assist the formation of a homogeneous suspension, the mixture was placed in an ultrasound bath for 30 min. The electrode was modified with *f*MWCNT-CoPc suspension by dropping 0.5 μL onto the AuNPs/GCE electrode surface, and dried at 24 ± 1 °C for 1 h. All modified electrodes AuNPs/GCE, *f*MWCNT/AuNPs/GCE and *f*MWCNT-CoPc/AuNPs/GCE were prepared following these steps.

2.4. Electrochemical investigation

The study of the experimental parameters that affect the responses of the SWV, such as the supporting electrolyte, pH of the medium, the pulse potential frequency (f), the amplitude of the pulse (a), and the potential step (ΔE_s) was performed. All parameters were properly optimized since their values exert high influence on the sensitivity of voltammetric analysis [33]. The mentioned parameters were optimized in relation to the maximum value of peak current (sensitivity) and the value of half-peak width (selectivity). The buffer solutions applied as supporting electrolytes were 0.1 mol L^{-1} McIlvaine buffer (prepared by mixture of 0.1 mol L^{-1} citric acid and 0.1 mol L^{-1} Na_2HPO_4 in suitable amounts to obtain the desired pH [37]), 0.1 mol L^{-1} Sörensen buffer (prepared by mixture of 0.1 mol L^{-1} Na_2HPO_4 and 0.1 mol L^{-1} KH_2PO_4 [37]), 0.1 mol L^{-1} potassium biphthalate (prepared by mixture of 0.1 mol L^{-1} potassium biphthalate and 0.1 mol L^{-1} NaOH [37]), and 0.04 mol L^{-1} Britton-Robinson (BR) buffer (prepared by the mixture of 0.04 mol L^{-1} H_3PO_4, H_3BO_3 and CH_3COOH [38]) and the pH was adjusted to the desired value by adding suitable amounts of 1.0 mol L^{-1} NaOH stock solution. Once the supporting electrolyte and pH have been optimized, the study of the SWV parameters was performed. To study the frequency (f), experiments were carried out between 5 and 150 s^{-1} with $a = 50$ mV and $\Delta E_s = 2$ mV. The values of amplitude were varied between 5 and 80 mV with $f = 100$ s^{-1} and $\Delta E_s = 2$ mV. The values of potential step (ΔE_s) were changed between 1 and 5 mV with $f = 100$ s^{-1} and $a = 50$ mV. The analysis of ACOP oxidation mechanism was performed using the information obtained through the diagnostic criteria of the SWV technique.

2.5. Analytical procedure and application of methodology

After the optimization of voltammetric parameters, analytical curves for ACOP were obtained by the standard addition method. The standard deviation of the intercept was used (S_b) in the determination of the detection and quantification limits (LOD and LOQ, respectively) together with the slope of the straight line of the analytical curves (s) as follows [39]:

$$\mathrm{LOD} = 3S_b/s \tag{1}$$

$$\mathrm{LOQ} = 10S_b/s. \tag{2}$$

The precision and accuracy of the method were evaluated with different standard solutions of ACOP, for which the relative standard deviations (RSD) were calculated. After calculating the analytical parameters for the determination of ACOP, studies of recovery were carried out in order to evaluate the applicability of the method. This was done by means of recovery experiments with the commercial products purchased locally. Four commercial formulations were utilized to the applications. Tylenol® 500 tablets, each tablet containing 500 mg of ACOP, purified water, starch, pregelatinized starch, sodium starch glycolate, microfine cellulose, magnesium stearate, hypromellose and Macrogol. Tylenol® DC tablets, each tablet containing 500 mg of ACOP and 65 mg of caffeine (an electroactive compound widely used in combination with ACOP), corn starch, pregelatinized starch, sodium starch glycolate, microfine cellulose, FD&C Yellow No. 6 aluminum lake, FD&C Red No. 40 aluminum lake, titanium dioxide, magnesium stearate, hypromellose and Macrogol. Tylenol® Drops oral solution containing 200 mg of ACOP in each 1 mL, citric acid, deionized water, flavors caramel, anise/mint and strawberry, sodium benzoate, sodium bisulfite, sodium cyclamate, FD&C Yellow No. 6, sodium hydroxide, Macrogol and sodium saccharin dihydrate. Tylenol® Child oral suspension containing 32 mg of ACOP in each 1 mL, anhydrous citric acid,