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Highly sensitive amperometric detection of drugs and antioxidants on non-functionalized multi-walled carbon nanotubes: Effect of metallic impurities?

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ABSTRACT

This work demonstrates that the electrochemistry of different molecules of pharmaceutical interest, including omeprazole, ciprofloxacin, dopamine, catechol, hydroquinone, and the antioxidants tert-butylhydroquine, gallic acid, propyl gallate, and pyrogallol, is affected by the functionalization of multi-walled carbon nanotubes (MWCNTs). Voltammetric and amperometric measurements confirmed the improved analytical characteristics of the GCE modified with non-functionalized (NF) MWCNTs (as-received) in comparison with functionalized MWCNTs (F-MWCNTs). Increase in voltammetric responses (up to 10-fold), higher slope values for the amperometric detection of the analytes (up to 7-fold) and, for some molecules, widening of the linear working range, were verified. Electrochemical impedance spectroscopy measurements also revealed higher electrochemical activity of non-functionalized MWCNTs. The presence of metallic impurities on NF-MWCNTs, removed by functionalization with HNO_3/H_2SO_4, may contribute the improved performance of NF-MWCNT-modified electrodes; however, decrease in electroactive area of F-MWCNTs has to be considered. Although acid functionalization introduced oxygenated groups on the MWCNT structure, the presence of metallic impurities (Fe and Co) and higher electroactive area of NF-MWCNTs play major role on the increase in sensitivity of the electrochemical sensors. As a conclusion, we propose the use of pristine MWCNTs to produce more sensitive amperometric sensors.

1. Introduction

Carbon nanotubes (CNTs) and other carbonaceous materials have been extensively applied for the development of electrochemical sensors [1–4]. Different procedures have been described for the insertion of CNTs on electrodic substrates, mainly including as paste mixed with mineral oil (carbon paste electrodes), mixed with conductive inks to produce screen-printed electrodes and as films especially over glassy carbon electrodes. The last procedure is the most commonly applied for electroanalysis, and typically CNTs are dispersed in dimethylformamide (DMF) or solubilized in Nafion to further be added onto the glassy carbon surface by drop casting [1]. However, due to the low solubility of CNTs, their manipulation is difficult and thus their functionalization is commonly performed prior to their dispersion in solvents [1,5,6].

Functionalization of CNTs is carried out using concentrated acids (HNO_3 and H_2SO_4) under heating or sonication, and as a result of the acid treatment, defects on the CNT sp^2 structure occurs and carboxylic, ketones and alcohols groups are inserted on the CNT surface, which increases the solubility of CNTs in polar solvents [6,7]. Additionally, this acid treatment removes a series of impurities that may be present on CNTs originating from their production, such as fullerenes, amorphous carbon, and catalyst residues [1]. On the other hand, metallic impurities are only partially removed from CNTs after HNO_3 washing [7]. Residual metals present onto the CNT structure can affect the electrochemical response of hydrazine [7], hydrogen peroxide [8], organic peroxides [9], glucose [10,11], amino acids [12], sulfides [13], glutathione [14], and dopamine and adenosine [15]. Considering

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metal-free CNTs or neglected contribution of residual metals on the electrochemistry of a CNT-based sensor, the electrocatalytic activity of CNTs has been commonly attributed to the presence of edge-plane-like sites located at the ends of tubes and in the defects of their structure [1,7]. The functionalization of CNTs using acid treatment under heating or sonication typically introduces defects on the CNT structure, detected by Raman spectroscopy (I_D/I_G values) [6,16,17], which can be related with the electrocatalytic properties of CNTs.

Functionalized multi-walled carbon nanotubes (MWCNTs) have been extensively used as chemical modifier to develop electrochemical sensors applied for the determination of compounds of pharmaceutical interest, such as epinephrine [18], acetaminophen [19], norepinephrine [20], levodopa [21], carbidopa [21], dopamine [22,23], ciprofloxacin [24,25], and omeprazole [26], as well as antioxidants, such as pyrogalol [27], hydroquinone [28], catechol [29,17] and tert-butylhydroquinone [17]. No previous works have evaluated the effect of metallic impurities within non-functionalized CNTs on the detection of the before mentioned analytes, with the exception to dopamine on non-functionalized single-walled carbon nanotubes [15]. Additionally, investigation on the effect of metallic impurities within non-functionalized CNTs on the development of amperometric sensors has not been reported according to our knowledge.

This work investigates the effect of residual metals within non-functionalized MWCNTs on the electrochemistry of a series of molecules and proposes the use of non-functionalized MWCNTs (used as-received without any purification) to develop highly-sensitive amperometric sensors of drugs and antioxidants, including phenolic compounds (catechol, dopamine, hydroquinone, tert-buthydroquinone, gallic acid, propyl gallate, and pyrogallol), ciprofloxacin and omeprazole. Cyclic voltammetry, electrochemical impedance spectroscopy, determination of electroactive area, and amperometric measurements on glassy carbon electrode modified with functionalized MWCNTs were also performed for comparison and to highlight the improved performance of the sensors produced using non-functionalized MWCNTs.

2. Experimental

2.1. Materials

Pristine MWCNTs ($D \times L$ 6–9 nm × 5 μm, >95%) used in this work were obtained from Aldrich (Milwaukee, WI, USA). Catechol (<99%) from Acros (New Jersey, USA), dopamine (<99%), gallic acid (97.5%), propyl gallate (98%), pyrogallol (98%) and omeprazole from Sigma-Aldrich (St. Louis, United States), hydroquinone (<99%), sulfuric and hydrochloric acid from Vetec (Rio de Janeiro, Brazil), nitric acid from Synth (Diadema, Brazil), *tert*-butyl-hydroquinone (<98%) and ciprofloxacin from Fluka Analytical (Steinheim, Germany) were used without the need of further purification.

The solutions were prepared using deionized water obtained from a Milli Q water purification system (Millipore, Bedford, MA, USA) with a resistivity higher than 18 M′Ω cm. Perchloric acid (70% v/v) from Reagen (Rio de Janeiro, Brazil) was used to prepare one of the supporting electrolytes. Phosphoric acid (85% m/v) from Impex (São Paulo, Brazil), boric acid from QM (Cotia, Brazil), glacial acetic acid from Carlo Erba (Milan, Italy), and sodium hydroxide from Dinamica (Diadema, Brazil) were used to prepare the Britton-Robinson buffer, another supporting electrolyte used in this work. The stock solutions of the phenolic analytes were freshly prepared, just before the experiments, in 0.1 mol L^{-1} $HClO_4$. The Britton-Robinson (BR) buffer solution, composed by a mixture of 0.1 mol L^{-1} acetic acid, boric acid, and phosphoric acid, with pH adjusted with sodium hydroxide, was used to prepare stock solutions of ciprofloxacin and omeprazole.

2.2. Electrochemical measurements

All electrochemical measurements were carried out using a μ-Autolab Type III (Eco Chemie, Utrecht, Netherlands) connected to a personal computer with appropriate software for data acquisition and treatment (NOVA 1.10). The working, counter, and reference electrodes were a modified or unmodified glassy carbon disk (⌀ = 1.5 mm, BASi Inc., USA), a platinum wire, and a miniaturized Ag/AgCl/saturated KCl electrode [30], respectively.

All measurements were performed at room temperature and in the presence of dissolved oxygen. Cyclic voltammograms were carried out using a 10 mL glass electrochemical cell containing the three-electrode system. Amperometric measurements were carried out in a batch-injection analysis (BIA) cell developed and constructed in our lab [31]. An electronic micropipette (Eppendorf Multipette® stream) is responsible for the injections of analytes on the modified electrode at controlled volume and dispensing rate. These parameters were evaluated on both modified electrodes, from 25 to 200 μL and from 28 to 345 μL s^{-1}, respectively. The electrode was placed in the BIA cell containing 180 mL of the respective electrolyte, which did not require replacement during the whole experiment (due to high dilution of the standard solution after injection). The distance between the micropipette tip and the working-electrode surface was kept at around 2 mm, which was the optimized value reported in the literature [32].

All measurements ($n = 3$) of electrochemical impedance spectroscopy (EIS) were registered in a 0.1 mol L^{-1} KCl solution containing 5/5 mmol L^{-1} $K_3Fe(CN)_6/K_4Fe(CN)_6$ in the frequency range of 0.1 and 30000 Hz with an amplitude of 10 mV and 10 points per decade of frequency. The charge resistance transfer was obtained by analyzing the non-linear region of the semi-circle of the Nyquist plot ($Z_{imaginary}$ *vs* Z_{real}).

2.3. Characterization of MWCNTs

MWCNTs were characterized through Raman spectroscopy using a LabRAM HR Evolution microscope (HORIBA, Kyoto, Japan) applying a 633 nm He-Ne laser.

A Shimadzu XRD 6000 (Kyoto, Japan) X-ray diffractometer equipped with CuKα radiation ($\lambda = 1.5406$ Å) was applied in the 2θ range from 10° to 90° at 40 kV and 30 mA with 0.02° and 2 s per step to investigate the structure, crystallinity, and presence of metals in MWCNTs.

Scanning electron microscopy (SEM) measurements were performed using a Vega 3 LMU (TESCAN, Brno-Kohoutovice, Czech Republic) operated at 20 kV. The samples were dispersed in ethanol and drop-casted on silicon substrate.

Infrared (IR) spectroscopy was carried out using a Perkin Elmer (Waltham, United States) Spectrum two spectrometer using attenuate total reflectance (ATR) mode. Measurements were collected at 4000–600 cm^{-1} range with a resolution of 4 cm^{-1}.

In order to evaluate if residual metallic impurities were still present in functionalized MWCNTs, both non-functionalized and functionalized MWCNTs were wet digested in a high-pressure microwave-assisted oven and the metals determined by inductively coupled optical emission spectrometry (ICP OES, model Optima 4300 DV, Perkin Elmer, USA) and inductively coupled mass spectrometry (ICP-MS, Elan DRC II, Perkin-Elmer SCIEX, Canada) according to the literature [33]. Briefly, 25 mg of MWCNTs were transferred to digestion vessels with 6 mL concentrated HNO_3 and 0.5 mL H_2O_2 and a heating program of 65 min was executed to obtain the complete digestion of the MWCNTs.