Development and application of an electrochemical sensor modified with multi-walled carbon nanotubes and graphene oxide for the sensitive and selective detection of tetracycline

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ABSTRACT

In this work, an electrochemical sensor based on a carbon paste electrode modified with a combination of multi-walled carbon nanotubes functionalized with carboxyl groups (MWCNT-COOH), together with graphene oxide (GO), was developed for the sensitive and selective determination of tetracycline. Electrochemical sensors were constructed using carbon paste modified with 2.6% (w/w) of MWCNT-COOH and 3.1% (w/w) of GO. Under the optimal conditions using adsorptive stripping differential pulse voltammetry (AdSDPV), the sensor showed a linear response for tetracycline concentrations between 2.0×10^{-5} and 3.1×10^{-4} mol L^{-1}, sensitivity of 1.2×10^{4} µA L mol^{-1}, and a detection limit of 3.6×10^{-7} mol L^{-1}. The incorporation of GO and MWCNT-COOH in the carbon paste improved the sensitivity, selectivity, and stability of the device. The MWCNT-COOH-GO/CPE sensor was successfully applied for the detection of tetracycline in river water, artificial urine, and pharmaceutical samples, without any need for sample pretreatment. The relative standard deviation (RSD) of the electrochemical measurements was less than 6.0% (n = 3).

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1. Introduction

Tetracycline is one of the antibiotics most commonly used to treat bacterial diseases such as urinary tract infections, chlamydia, and acne. The extensive use of this drug in veterinary medicine has led to its accumulation in food products including meat, milk, honey, and chicken [1]. The impacts of exposure to low levels of antibiotics such as tetracycline include the development of antibiotic-resistant genes, vision problems, teeth discoloration, and allergic symptoms in humans [2,3]. Considering these concerns, it is important to develop analytical methods for the determination of low levels of tetracycline in the environment. Many analytical methods have been reported for tetracycline, such as HPLC [4], spectrophotometry [5], capillary electrophoresis [6], chemiluminescence [7], and electrochemical approaches [8]. With the exception of the electrochemical methods, these techniques require relatively expensive instrumentation, have long times of analysis, and require trained personnel.

Electrochemical sensors and biosensors are widely used in the monitoring of different substances. Carbon, platinum, gold, and silver electrodes are most common, offering the advantages of a wide potential window, low background current, chemical inertness, and low cost [9–11]. The modification of these electrodes with suitable nanostructured materials is fundamental for achieving faster electron transfer between the electrode and the analyte, a low detection limit, a wide linear response range, good stability and reproducibility, and increased sensitivity and selectivity of the electrochemical sensor [12–16]. The nanostructured materials studied in this work were multi-walled carbon nanotubes and graphene oxide.

Carbon nanotubes have attracted much attention due to their advantageous mechanical, optical, chemical, and electrical properties. Various applications of carbon nanotubes have been investigated, including their uses in field emitters, quantum wires, batteries, optoelectronic components, ultra-strength engineering fibers, and nanoelectronic devices [17–21]. Recent studies have demonstrated that modification of an electrode with carbon nanotubes can promote high electrocatalytic activity for the detection of captopril, vitamin C, hydrogen peroxide, and some important catecholamine substances such as dopamine, epinephrine, and cytochrome c, among others [18,21–23].

Graphene oxide (GO), a nanomaterial with sp^2 hybridization, has extraordinary electrical, physical, and chemical properties. Nanomaterials composed of GO have high surface areas, high specific capacitance, and exhibit electronic transport properties. These features make them attractive for use in energy conversion, field-effect transistors, and batteries. Their applications in electronic device include electrochemical sensors and biosensors for the sensitive determination of analytes including nitrogenous bases (adenine and guanine), pesticides (such as carbofuran), drugs (ascorbic acid, dopamine, and uric acid), diethylstilbestrol, and others [24–28]. Derived from graphene, GO is formed in

individual layered sheets that contain abundant C–O–C (epoxide), C–OH, and COOH functional groups located in the basal planes and at the edges [29,30]. Since they have similar compositions, GO and carbon nanotubes exhibit similar physical and chemical properties.

The aim of this work was to develop a sensitive, selective, and stable electrochemical sensor for the determination of tetracycline in pharmaceutical, river water, and artificial urine samples. For this purpose, the working electrode was modified with GO and MWCNT-COOH, and the experimental conditions were optimized in order to maximize the performance of the sensor.

2. Materials and methods

2.1. Reagents and solutions

The reagents used in this work were either analytical or HPLC grade. All aqueous solutions were prepared with deionized water (18 MΩ cm at 25 °C) obtained from a Milli-Q Direct-0.3 (Millipore) purification system. MWCNT, graphene, mineral oil (Nujol), and graphite powder (<20 μm) were acquired from Sigma-Aldrich. NaOH, $NaH_2PO_4.H_2O$, TRIS, and PIPES were obtained from Synth (Brazil).

A stock solution of 8.0×10^{-3} mol L^{-1} tetracycline was prepared by dissolving 0.04 g of the compound in 10.0 mL of deionized water. The

mixture was sonicated for 1 min to ensure complete dissolution of the tetracycline.

2.2. Electrochemical measurements

All voltammetric measurements were performed using a potentiostat (Model μ-Autolab Type III, Autolab/Eco Chemie) fitted with an electrochemical cell containing three electrodes: a commercial Ag/AgCl(KCl$_{sat}$) reference electrode (Analion), a platinum wire as the counter electrode, and a modified carbon paste electrode as the working electrode (r = 1.2 mm).

2.3. Construction of the electrochemical sensor

#### 2.3.1. Preparation of the modified carbon paste electrode

The carbon paste electrode (CPE) was prepared using a mixture of 89 mg of graphite powder, 5 mg of MWCNT-COOH, 6 mg of GO, and 1 mL of 0.1 mol L^{-1} phosphate buffer solution (pH 7.0). Phosphate buffer was used to improve the conductivity of the carbon paste. The material was carefully homogenized for 20 min using a mortar and pestle, and then left to dry at room temperature. Afterwards, 85 μL (90 mg) of mineral oil was added to obtain a paste. The paste was then packed into the cavity of the Teflon working electrode (4 mm i.d., 1 mm depth), where a Pt disk was used to provide the electrical contact. The
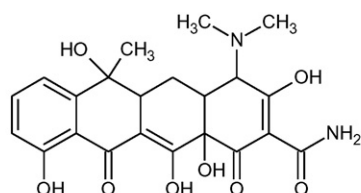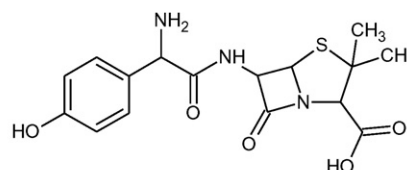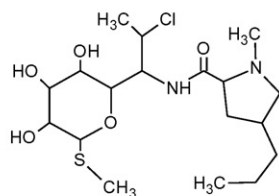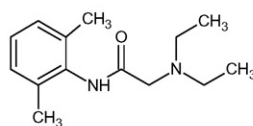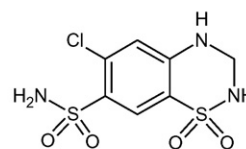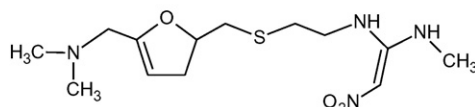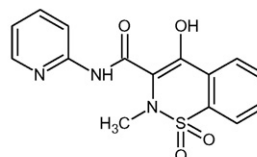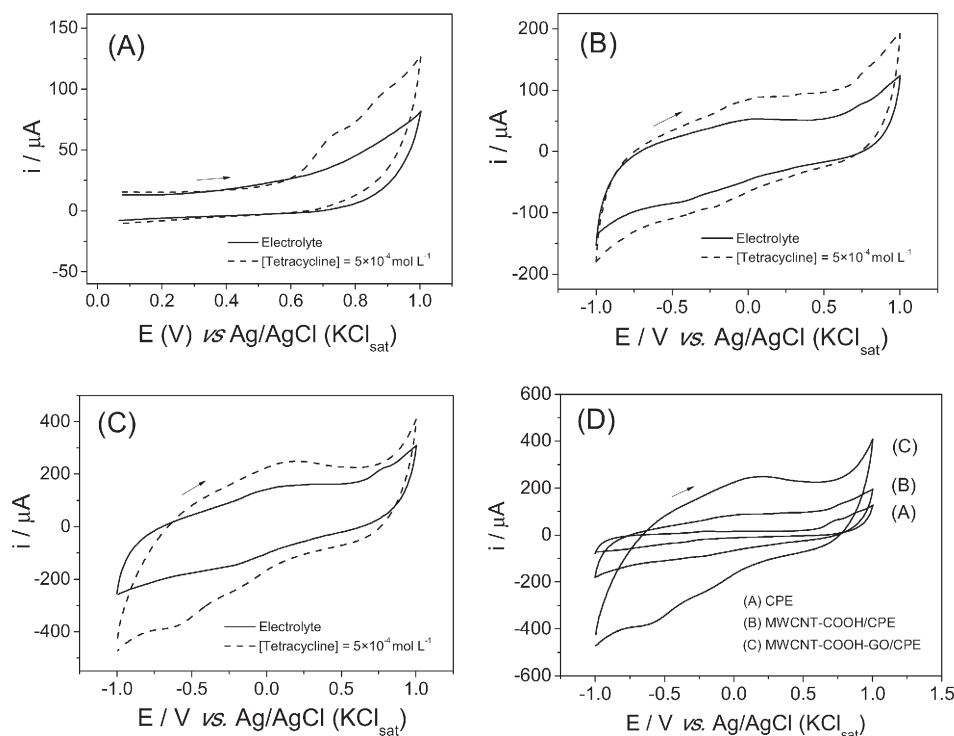

Chart 1. Chemical structures of pharmaceutical formulations analyzed in the study of selectivity.

Fig. 1. Cyclic voltammograms obtained using different electrodes: (A) CPE, (B) MWCNT-COOH/CPE, and (C) MWCNT-COOH-GO/CPE, in the absence and presence of 5.0×10^{-4} mol L^{-1} of tetracycline; (D) electrochemical response of tetracycline for all the modifiers. Measurements performed in 0.1 mol L^{-1} phosphate buffer solution (pH 7.0), $v = 50$ mV s^{-1}.

other carbon pastes prepared were as follows: CPE (100 mg of graphite); MWCNT-COOH/CPE (95 mg of graphite and 5 mg of MWCNT-COOH); and GO/CPE (95 mg of graphite and 5 mg of GO). In all cases, the total mass of material used was therefore 100 mg. The amounts of phosphate buffer solution and mineral oil used to produce the carbon paste were the same as used for the MWCNT-COOH-GO/CPE.

Functionalization of the MWCNTs consisted of mixing 100 mg of multi-walled carbon nanotubes into a concentrated solution of 1:3 (v/v) H_2SO_4/HNO_3. This mixture was stirred for 12 h [31]. The functionalization of graphene with carboxylic acid groups was performed using a similar procedure, with agitation of 100 mg of graphene in concentrated solution of 1:1 (v/v) H_2SO_4/HNO_3 for 4 h at 25 °C. After this step, the suspension of MWCNT-COOH and GO was filtered and carefully washed with deionized water until the pH was near 7.0. The total volume of acid used in these experiments was 120 ml, following the proportions tested (1:1, 1:3, and 3:1

(v/v)). The acid ratio used for functionalization of the graphene and carbon nanotubes was based on the best electrochemical performance using $[Fe(CN)_6]^{4-}$ as a probe.

2.3.2. Selectivity experiments

The selectivity of the MWCNT-COOH-GO/CPE sensor was evaluated by analyzing six pharmaceutical formulations, using AdSDPV in the potential range from −0.2 to 1.0 V, at 50 mV s^{-1}. Electrochemical signals were obtained for pharmaceutical formulations containing clindamycin, lidocaine, hydrochlorothiazide, ranitidine, piroxicam, and amoxicillin (Chart 1). The compounds were added to the electrochemical cell to give concentrations of 8.0×10^{-5} mol L^{-1}. The following AdSDPV analytical conditions were used: modulation time = 0.1 s, modulation amplitude = 75 mV, $\Delta E_s = 4$ mV, $E_{acc} = 0.2$ V, and $t_{acc} = 30$ s.

2.3.3. Application of the MWCNT-COOH-GO/CPE sensor using river water, artificial urine, and pharmaceutical samples

The MWCNT-COOH-GO/CPE sensor was evaluated using analyses of spiked samples of artificial urine and river water from three sources. The river water samples were collected in the region of Araraquara, in the interior of São Paulo State (Brazil). Artificial urine was synthesized using the following components: 0.73 g of NaCl, 0.40 g of KCl, 0.28 g of CaCl$_2$, 0.56 g of Na$_2$SO$_4$, 0.35 g of KH$_2$PO$_4$, 0.25 g of NH$_4$Cl, and 6.25 g of urea. The components were added to a 250 mL volumetric flask and the volume was completed with deionized water [32].
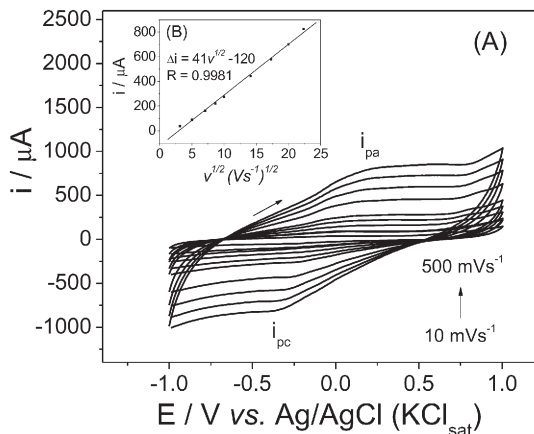
Fig. 2. (A) Typical cyclic voltammograms acquired using different scan rates (10–500 mV s^{-1}) and 0.1 mol L^{-1} phosphate buffer solution (pH 7.0); (B) i_{pa} vs. $v^{1/2}$. [Tetracycline] = 5.0×10^{-4} mol L^{-1}.

Table 1
Optimal parameters used in the differential pulse voltammetry analyses.

Parameter	Studied range	Optimal value
Step potential (mV)	2–7	4
Modulation amplitude (mV)	25–100	75
Modulation time (s)	0.02–1.0	0.5
Accumulation time (s)	0–60	30
Accumulation potential (mV)	−400–400	200
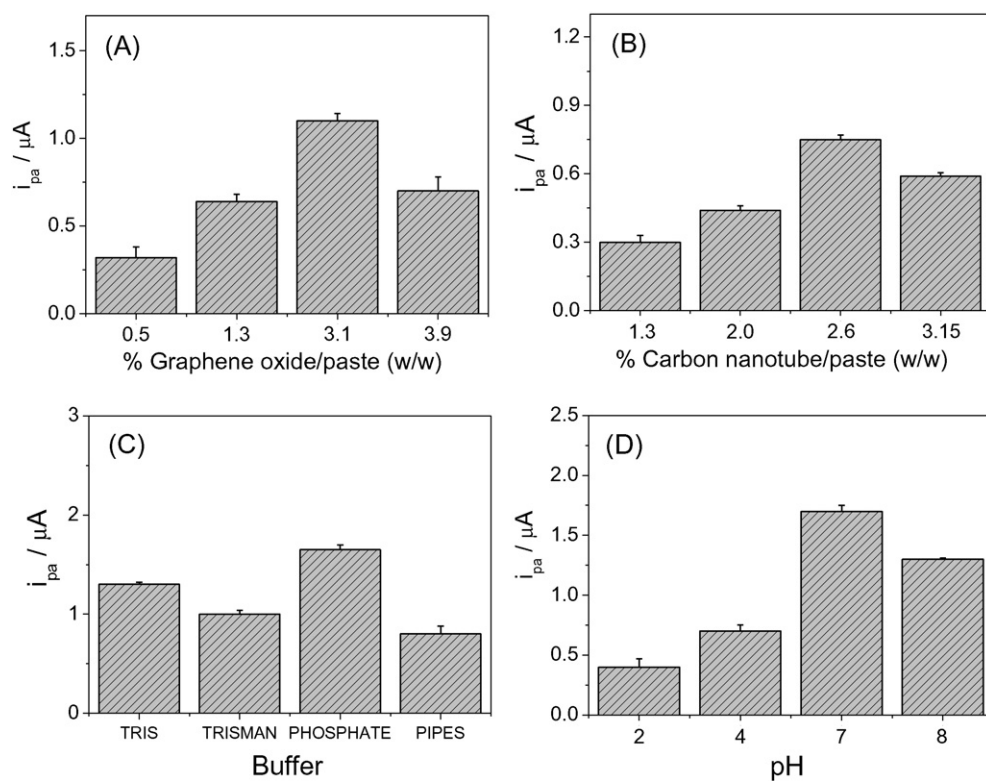
Fig. 3. Optimization of the electrochemical sensor parameters. Effects of (A) % (*w/w*) graphene oxide and (B) % (*w/w*) carbon nanotubes in the carbon paste, (C) buffer composition, and (D) pH. Measurements carried out in 0.1 mol L^{-1} phosphate buffer solution (pH 7.0) for experiments (A, B and D), modulation time = 0.5 s, modulation amplitude = 75 mV, ΔEs = 4 mV, E$_{acc}$ = 0.2 V, and t$_{acc}$ = 30 s. [Tetracycline] = 1.0×10^{-4} mol L^{-1}.
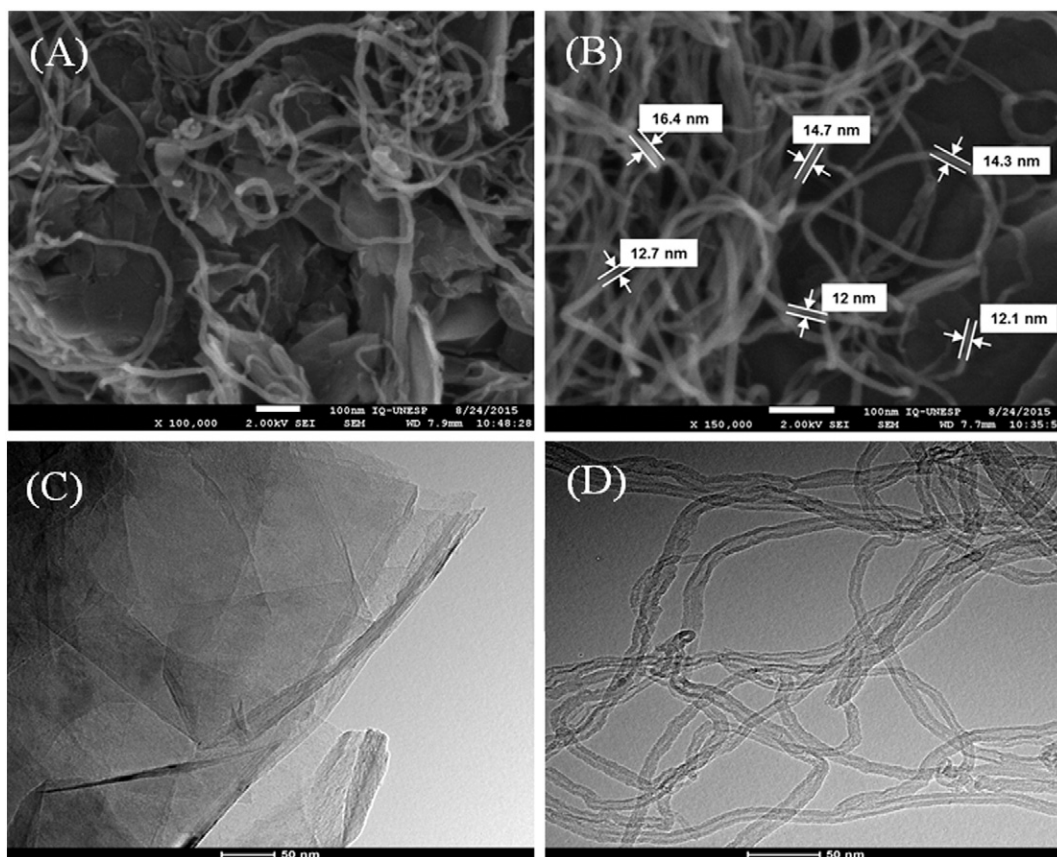
Fig. 4. SEM (A-B) and TEM (C-D) images of graphene oxide and carbon nanotubes.
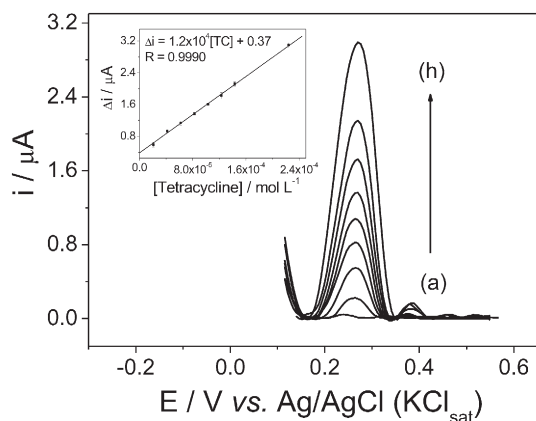
Fig. 5. Response profile using adsorptive stripping differential pulse voltammetry (AdSDPV) for different concentrations of tetracycline. Measurements carried out in 0.1 mol L^{-1} phosphate buffer solution (pH 7.0), modulation time = 0.5 s, modulation amplitude = 75 mV, ΔEs = 4 mV, E$_{acc}$ = 0.2 V, and t$_{acc}$ = 30 s. [Tetracycline] = (a) 2.0 × 10^{-5}, (b) 4.15 × 10^{-5}, (c) 6.2 × 10^{-5}, (d) 8.3 × 10^{-5}, (e) 1.03 × 10^{-4}, (f) 1.2 × 10^{-4}, (g) 1.7 × 10^{-4}, (h) 3.1 × 10^{-4} mol L^{-1}.

All samples were spiked with 4.0 × 10^{-5} mol L^{-1} tetracycline. The recovery of tetracycline was determined by the standard additions method, with analysis using the MWCNT-COOH-GO/CPE sensor as well as the HPLC technique.

The study of tetracycline in pharmaceutical formulations was carried out using AdSDPV. For the preparation of each sample solution, two tablets were ground and homogenized in a mortar. A suitable amount of triturated sample was then weighed out and dissolved in deionized water, followed by a conventional filtration step to remove insoluble substances present in the solution. The standard additions procedure was used for tetracycline determination, and the results of the electrochemical analyses were compared with those obtained using the HPLC method. Prior to the HPLC analyses, the samples were filtered through 0.45 μm membranes.

2.3.4. Analysis of samples using HPLC

The chromatographic analyses were performed using a Shimadzu Model 20A liquid chromatograph fitted with a C8 column (250 mm × 4.6 m), coupled to an SPD-20A UV/Vis detector, a SIL-20A autosampler, and a DGU-20A5 degasser. The chromatography system was controlled by a microcomputer. The mobile phase was composed of 0.1 mol L^{-1} oxalic acid:methanol:acetonitrile, in a ratio of 68:20:12, at a flow rate of

1.0 mL min^{-1}. The sample injection volume was 10 μL, and the detector wavelength was 365 nm [33].

3. Results

3.1. Electrochemical characterization of the MWCNT-COOH-GO/CPE sensor

First, the behaviors of the electrochemical sensors in the presence of tetracycline were evaluated using cyclic voltammetry (Fig. 1), in order to determine the influence of MWCNT-COOH and GO on the response. Comparison of the cyclic voltammograms obtained for the carbon paste electrode (CPE) using buffer solution and the solution containing tetracycline was made using an anodic peak current of 750 mV vs. Ag/AgCl(KCl$_{sat}$) (Fig. 1A). The MWCNT-COOH/CPE voltammogram (Fig. 1B) showed the electrochemical detection of tetracycline at low redox potential, with the appearance of an anodic peak current at a potential of 270 mV vs. Ag/AgCl(KCl$_{sat}$). Inclusion of GO in the carbon paste composition (MWCNT-COOH-GO/CPE) was then used to increase the magnitude of the electrochemical signal obtained for tetracycline (Fig. 1C). Comparison of the cyclic voltammograms showed that an enhanced response, with high electronic transfer, was obtained using the MWCNT-COOH-GO/CPE electrode, with the presence of an anodic peak current at 0.27 V and a cathodic peak current at −0.5 V vs. Ag/AgCl(KCl$_{sat}$) (Fig. 1D) [21,34]. The use of

Fig. 6. Study of selectivity using AdSDPV in the presence of six other drugs. Measurements carried out in 0.1 mol L^{-1} phosphate buffer solu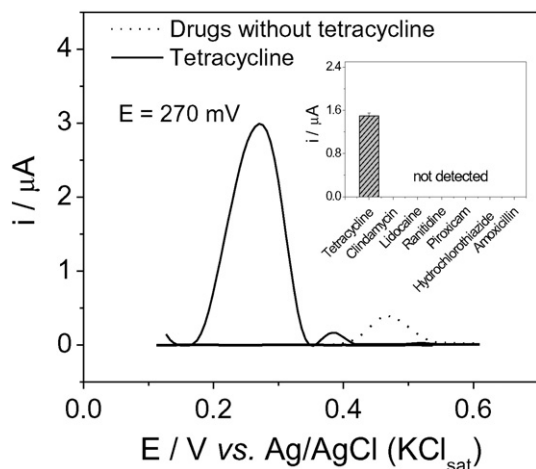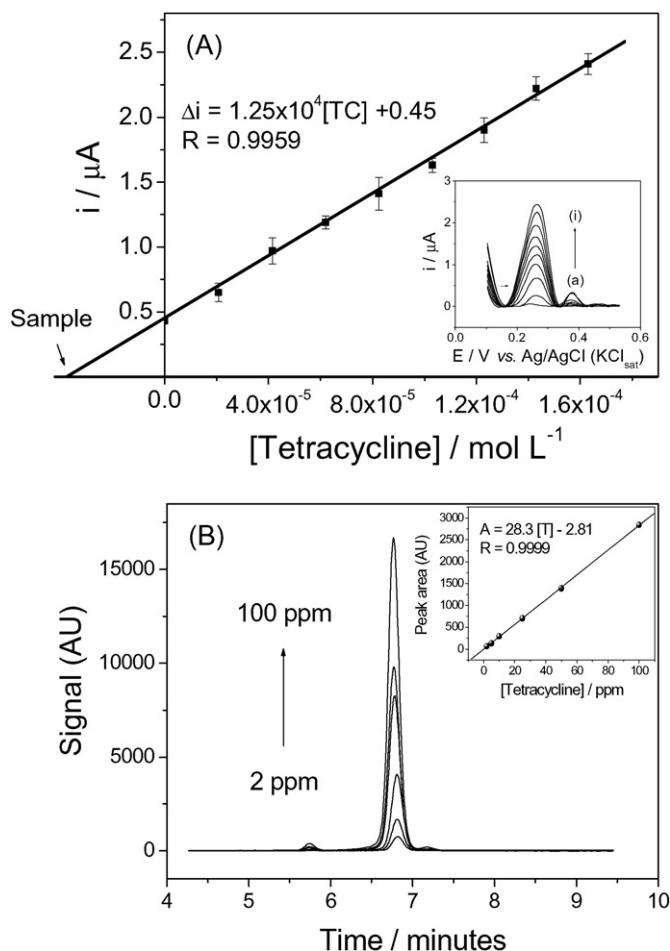tion (pH 7.0), [Tetracycline] = 8.0 × 10^{-5} mol L^{-1}, modulation time = 0.5 s, modulation amplitude = 75 mV, ΔEs = 4 mV, E$_{acc}$ = 0.2 V, and t$_{acc}$ = 30 s.

Fig. 7. (A) Typical AdSDPV profiles of the pharmaceutical samples and (insert) analytical curve. Measurements carried out in 0.1 mol L^{-1} phosphate buffer solution (pH 7.0), modulation time = 0.5 s, modulation amplitude = 75 mV, ΔEs = 4 mV, E$_{acc}$ = 0.2 V, t$_{acc}$ = 30 s, [Tetracycline] = (a) Unknown, (b) 2.1 × 10^{-5}, (c) 4.15 × 10^{-5}, (d) 6.2 × 10^{-5}, (e) 8.3 × 10^{-5}, (f) 1.03 × 10^{-4}, (g) 1.2 × 10^{-4}, (h) 1.4 × 10^{-4}, (i) 1.7 × 10^{-4} mol L^{-1}. (B) Calibration curve of tetracycline using high performance liquid chromatography (HPLC).

Table 2
Comparison of the proposed sensor with other methods described in the literature.

Electrode	Linear range (mol L^{-1})	Potential (V)	LOD (mol L^{-1})	Reference
GCE (Fe/Zn-MMT)[a]	3.0×10^{-5}–5.2×10^{-4}	1.17	1.0×10^{-5}	[39]
MIP-Pt/Ti[b]	2.0×10^{-6}–2.0×10^{-5}	0.8	5.3×10^{-8}	[40]
MWNTsGNPs[c]	2.0×10^{-7}–8.3×10^{-5}	1.1	8.3×10^{-8}	[41]
GME[d]	2.0×10^{-5}–2.0×10^{-4}	1.5	1.8×10^{-7}	[42]
GCE (IL-MWNT)[e]	1.1×10^{-7}–2.2×10^{-5}	0.54	3.0×10^{-8}	[43]
CPE (GO/MWCNT-COOH)	2.0×10^{-5}–3.1×10^{-4}	0.27	3.6×10^{-7}	**This work**

[a] Iron/zinc cation-exchanged montmorillonite (Fe/Zn-MMT) catalyst on glassy carbon electrode(GCE).
[b] Micro-nanoPt cluster deposited on titanium sheet (Pt/Ti).
[c] Molecularly imprinted polymer modified carbon nanotube-gold nanoparticles electrode.
[d] Gold modified microelectrode.
[e] Ionic liquid/carbon nanotubes on glassy carbon electrode.

GO and MWCNT-COOH together resulted in a synergistic effect that increased the electrochemical signal and the stability of the sensor by combining their individual characteristics, such as high electrical conductivity and large specific surface area.

3.2. Study of the scan rate

Fig. 2 shows typical cyclic voltammograms acquired at scan rates between 10 and 500 mV s^{-1}. In this range, the change in the anodic current was a linear function of the square root of the scan rate, indicating that the oxidation of tetracycline at a potential of 270 mV was controlled by a diffusion process (Fig. 2).

3.3. Determination of electroactive surface area

The electroactive surface areas of the plain carbon paste electrode (CPE), MWCNT-COOH/CPE, and MWCNT-COOH-GO/CPE were estimated using a solution of 4.76×10^{-3} mol L^{-1} [Fe(CN)$_6$]$^{4-}$ in 0.1 mol L^{-1} KCl. The calculation employed the Randles-Sevcik equation [35]:

$$I_p = 2.69 \times 10^5 AD^{1/2}n^{3/2}v^{1/2}C,$$

Where I$_p$ is the peak current, D is the diffusion coefficient of [Fe(CN)$_6$]$^{4-}$ (6.2×10^{-6} cm^2 s^{-1}), A is the electroactive area (cm^2), n is the number of electrons, v is the scan rate (V s^{-1}), and C is the [Fe(CN)$_6$]$^{4-}$ concentration (mol cm^{-3}). The electroactive surface areas were 6.6×10^{-2}, 0.11, and 0.18 cm^2 for the carbon paste electrode, MWCNT-COOH/CPE, and MWCNT-COOH-GO/CPE, respectively. The surface area obtained with the MWCNT-COOH-GO/CPE was 2.73-fold higher than the value for the plain carbon paste electrode. The results indicated that use of both MWCNT-COOH and GO increased the electroactive area of the electrode, hence increasing the intensity of the peak current.

3.4. Optimization of AdSDPV parameters

Optimization of the AdSDPV method considered the following instrumental variables: modulation amplitude, interval time, and modulation time (Table 1). Selection of the best conditions was based on the highest anodic peak currents obtained using AdSDPV. Figs. 3A and 3B show the influence of the amounts of MWCNT-COOH and GO incorporated in the carbon paste. The effects of buffer type, buffer concentration, and pH on the anodic peak current (i$_{pa}$) of tetracycline were also studied (Figs. 3C and 3D). The best response was obtained using 3.1% (w/w) GO and 2.6% (w/w) MWCNT-COOH in the carbon paste, and 0.1 mol L^{-1} phosphate buffer solution (pH 7.0).

The morphological characteristics of the carbon paste sensor modified with MWCNT-COOH and GO were evaluated using images acquired using a JEOL JSM 7500F scanning electron microscope. As shown in Fig. 4A, the GO consisted of thin sheets of different sizes, while the MWCNT-COOH was composed of cylindrical tubes with diameters of 12–17 nm (Fig. 4B). Both materials were deposited onto graphite, which was arranged in large blocks. Figs. 4C and 4D show detailed characteristics of these materials in TEM images acquired using a TECNAI G2 microscope. GO was present in the form of transparent and wrinkled sheets, which provided a high surface area on the electrode, while the inner and outer walls of the cylindrical tubes of MWCNT-COOH had diameters similar to those obtained using SEM (Fig. 4B) [36,37].

The response profile obtained using AdSDPV (modulation time = 0.5 s, modulation amplitude = 75 mV, ΔEs = 4 mV, accumulation potential (E$_{acc}$) = 0.2 V, and accumulation time (t$_{acc}$) = 30 s) showed a linear correlation coefficient of 0.9990 for determination of tetracycline at concentrations between 2.0×10^{-5} and 3.1×10^{-4} mol L^{-1}. The sensitivity was 1.2×10^4 μA L mol^{-1}, and the detection limit was 3.6×10^{-7} mol L^{-1} (3 × SD/m, where SD is the standard deviation for the blank solution (n = 10) and m is the slope of the analytical curve) (Fig. 5) [38].

The reproducibility of the sensor response was determined from five analytical curves obtained using AdSDPV, for which the relative standard deviation (RSD) was 3.1%.

A comparison was made of these results with others reported in the literature (Table 2). It can be seen that the MWCNT-COOH-GO/CPE sensor provided a similar detection limit, with additional advantages that make this sensor more attractive than the other methods, such as lower detection potential, the ability to perform numerous analyses by renewing the electrode surface using simple

Table 3
Results obtained for the analysis of river water samples collected near the city of Araraquara.

River water sample	Tetracycline (mol L^{-1})			Recovery (%)
	Added (mol L^{-1})	Comparative HPLC method (RSD)	Proposed method (RSD)	
Jacaré Pepira	4.0×10^{-5}	3.94×10^{-5} (2.0)	4.16×10^{-5} (5.0)	98.5
Jacaré-Guaçu	4.0×10^{-5}	4.05×10^{-5} (1.2)	4.24×10^{-5} (4.2)	101.0
Chibarro	4.0×10^{-5}	3.76×10^{-5} (0.6)	3.68×10^{-5} (2.0)	94.0

n = triplicate, RSD = σ/μ × 100 (σ = standard deviation of 3 measured concentrations; μ = average of 3 measured concentrations).

Table 4
Results obtained for the analysis of artificial urine samples with the electrochemical sensor and HPLC.

Artificial urine sample	Tetracycline (mol L^{-1})			Recovery (%)
	Added (mol L^{-1})	Official HPLC method (RSD)	Proposed method (RSD)	
n° 1	4.0×10^{-5}	3.9×10^{-5} (1.5)	3.68×10^{-5} (5.5)	92.0
n° 2	4.0×10^{-5}	4.05×10^{-5} (1.0)	3.85×10^{-5} (5.0)	96.2

n = triplicate, RSD = σ/μ × 100 (σ = standard deviation of 3 measured concentrations; μ = average of 3 measured concentrations).

Table 5
Results obtained with the proposed sensor and the comparative method (HPLC) in the analysis of pharmaceutical formulations containing tetracycline.

Pharmaceutical formulation	Tetracycline (mg tablet^{-1})			Recovery (%)
	Nominal value	Official HPLC method (RSD)	Proposed method (RSD)	
n° 1	500	485 (2.0)	467 (1.3)	93.4
n° 2	500	505 (0.8)	510 (2.3)	102.0
n° 3	500	510 (0.6)	532 (4.2)	106.0

n = triplicate, RSD = $\sigma/\mu \times 100$ (σ = standard deviation of 3 measured values; μ = average of 3 measured values).

polishing, high repeatability, a stable analytical response for 15 days, and low cost. The sensor showed a much lower detection potential of 270 mV vs. Ag/AgCl, especially compared to the CPE method, where the electrochemical detection occurred at a potential of 750 mV. The lower potential increased the selectivity of the proposed sensor in the determination of tetracycline.

The selectivity of the MWCNT-COOH-GO/CPE sensor towards tetracycline was evaluated by observation of its response to six pharmaceutical formulations soluble in the water. Fig. 6 shows that among all the potentially electroactive compounds, only tetracycline induced an electrochemical response, with an anodic peak current (I_{pa}) at a potential of 270 mV vs. Ag/AgCl (KCl$_{sat}$). This demonstrated the high selectivity of the MWCNT-COOH-GO/CPE sensor in the detection of tetracycline. The literature reports many analytes that exhibit electrochemical activity at relatively high potentials (above 700 mV), which further supports the use of the MWCNT-COOH-GO/CPE sensor for the highly selective electrochemical determination of tetracycline [39,44–46].

3.5. Application of the MWCNT-COOH-GO/CPE sensor using river water, artificial urine, and pharmaceutical samples

The performance of the MWCNT-COOH-GO/CPE sensor was evaluated using analyses of river water and artificial urine samples fortified with tetracycline. The results showed recoveries in the range from 92 to 101%, demonstrating an absence of matrix effects. The RSD values obtained in these analyses were ≤5.5% (n = 3), indicating the high reproducibility and reliability of the MWCNT-COOH-GO/CPE sensor (Tables 3 and 4).

Table 5 shows the results obtained for the analyses of the pharmaceutical samples using the electrochemical and HPLC techniques. No significant differences were found between the two methods, from which it could be concluded that the proposed device offers an efficient and highly reliable method for the determination of tetracycline in this type of matrix. The RSD values obtained for three different concentrations, using the standard additions procedure, were lower than 4.2%, indicating good precision of the method. Fig. 7A shows the determination of tetracycline in pharmaceutical samples using the proposed sensor and the standard additions procedure. Fig. 7B shows the tetracycline calibration curve obtained using the HPLC method, which had an analyte retention time of 6.8 min and an analysis time of about 10 min per sample. In comparison, use of the proposed sensor enabled seven analytical measurements to be made in around 5 min, clearly demonstrating the advantages of this alternative methodology for the monitoring of tetracycline.

An assessment was made of possible interferences in the analytical signal caused by the presence of substances commonly found in commercial pharmaceutical formulations. The interferents studied were magnesium stearate, sodium lauryl sulfate, and talc, using interferent:tetracycline ratios of 1:1 (w/w). In all cases, only tetracycline showed a measurable electrochemical response at a potential of 270 mV.

4. Conclusions

The construction of an electrochemical sensor by modification of a carbon paste electrode with a combination of MWCNT-COOH and GO enabled the sensitive and selective determination of tetracycline. The proposed method presented a detection limit of 3.6×10^{-7} mol L^{-1} and a relative standard deviation of 3.1% (n = 5). In recovery tests using river water, artificial urine, and pharmaceutical samples, there were no matrix effects and the measured values were similar to those obtained by an HPLC method. In addition, the sensor showed advantages including simple sample preparation, rapid response, long electrode lifetime, low detection limit, low analysis potential, good repeatability, and low cost, when compared to other detection methods reported in the literature.

Acknowledgments

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