Analytical Potentialities of Carbon Nanotube/Silicone Rubber Composite Electrodes: Determination of Propranolol

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Abstract
A new composite electrode based on multiwall carbon nanotubes (MWCNT) and silicone-rubber (SR) was developed and applied to the determination of propranolol in pharmaceutical formulations. The effect of using MWCNT/graphite mixtures in different proportions was also investigated. Cyclic voltammetry and electrochemical impedance spectroscopy were used for electrochemical characterization of different electrode compositions. Propranolol was determined using MWCNT/SR 70 % (m/m) electrodes with linear dynamic ranges up to 7.0 $\mu mol\,L^{-1}$ by differential pulse and up to 5.4 $\mu mol\,L^{-1}$ by square wave voltammetry, with *LOD*s of 0.12 and 0.078 $\mu mol\,L^{-1}$, respectively. Analysis of commercial samples agreed with that obtained by the official spectrophotometric method. The electrode is mechanically robust and presented reproducible results and a long useful life.

Keywords: Carbon nanotubes, Silicone rubber, Composite electrodes, Propranolol, Nanotubes

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1. Introduction

Since their discovery in 1991, by Ijima [1], carbon nanotubes (CNT) have been of considerable interest due to their unique properties [2]. CNT are nanostructures consisting of graphene sheets with hexagonal sp^2 carbon atoms, arranged in the form of cylinders, with diameters of the order of nanometres and lengths of micrometers. They combine high surface area, conductivity, chemical stability and significant mechanical strength [3].

The CNT can behave like metals or semiconductors depending on the structure [4]. Their electronic properties suggest that they present the ability to promote electron transfer in electrochemical reactions with electroactive species in solution [5–9]. Moreover, CNT have attracted considerable attention due to the reported electrocatalytic properties of carbon nanotube modified electrodes [10–15]. The advantages of CNT as electrode material or as modifier of conventional working electrodes in voltammetry has been extensively demonstrated in the large number of papers published, including in review articles that describe many advantages such as large active surface of small dimension electrodes, as well as enhanced electron transfer and electrocatalytic properties [2,8,16–20].

The development of electrochemical sensors using carbon nanotube modification can be extended to the preparation of composite electrodes in which the CNT are agglutinated by polymers such as silicone rubber, which has been used for preparation of graphite silicone rubber composite electrodes (GSR), first described by Pungor and Szepesváry [21] and recently used by us [22,23]. The main advantages of composite electrodes are the ease of preparation and surface renewal, possibility of modifier incorporation and good reproducibility and repeatability of active area.

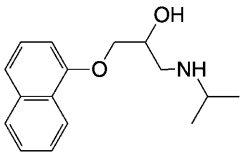
According to the definition of Tallman and Petersen [24], in which a composite electrode is a material consisting of at least one conductor phase and at least one insulator phase, the silicone rubber is the insulator phase, and the CNT is the conductor phase, with all the advantages of high conductivity and large surface area, allowing the production of highly sensitive electrodes [21–23].

Amongst the different methods to prepare and modify electrodes with CNT [4,9,25–27], Wildgoose et al. [28] describe different chemical and electrochemical modification strategies and electroanalytical and bioanalytical applications. Some of these articles report the preparation of composite electrodes based on CNT and epoxy resin with characterization by cyclic voltammetry (CV) and electrochemical impedance spectroscopy [29,30].

Propranolol (1-isopropylamino-3-(1-naphthyloxy)-2-propranolol), whose structure is presented in Scheme 1, is one of the drugs classified as β-adrenergic receptor blockers, β-adrenergic antagonists or simply β-blockers [31,32]. The β-adrenergic antagonists are widely used in the treatment of cardiovascular diseases, arterial hypertension, cardiac arrhythmias, and *angina pectoris* as well as for

Table 1. Voltammetric procedures previously proposed for electroanalytical determination of propranolol

Technique	Media	Linear range ($\mu mol\,L^{-1}$)	*LOD* ($\mu mol\,L^{-1}$)	Comments	Reference
Anodic adsorptive stripping DPV at CPE	B–R Buffer pH 2.0	0.6–50	0.2	Accumulation at open circuit, 5 min	[36]
Normal pulse voltammetry at gold electrode	0.1 $mol\,L^{-1}$ NaOH	1–20	0.5	Electrode carefully cleaned before use	[37]
DPV at GSR composite electrode	B–R Buffer pH 7.4	5–80	1.1	Direct determination without sample preparation or preconcentration	[38]
Differential pulse polarography	B–R Buffer pH 2.0	0.5–50	0.005	Indirect determination by derivatization	[39]
Adsorptive stripping SWV at Hg	B–R Buffer pH 2.0	0.017–0.67	0.006	Indirect determination by derivatization	[40]
Differential pulse polarography	B–R Buffer pH 4.0	0.2–2.7	0.03	Indirect determination by derivatization	[41]



Scheme 1. Structure of propranolol.

other types of pathologies such as anxiety or glaucoma [33–35]. There are some reports in the literature on the determination of this drug by voltammetry/polarography as can be seen in Table 1.

This article reports the preparation of an electrode based on multi-wall carbon nanotubes (MWCNT) with graphite (G) and silicone rubber (SR). These materials combine the advantages of composite materials such as easy preparation, low cost, long useful life and easy surface renewal together with the electrochemical properties of carbon nanotubes, i.e. an enhanced response due to the large surface area of CNT, and potential electrocatalytic action. The performance of composites in which the conducting phase is constituted by mixtures of MWCNT and graphite powder in different proportions was assessed by cyclic voltammetry and electrochemical impedance spectroscopy. The MWCNT/SR 70% (MWCNT, *m/m*) composite was applied to the determination of propranolol in pharmaceutical formulations.

2. Experimental

2.1. Reagents and Solutions

MWCNT (90% purity, diameter 110–170 nm and length 5–9 μm) were obtained from Sigma-Aldrich. Propranolol hydrochloride (99.8% purity) was obtained from Natural Pharma (Brazil). All other chemicals were of analytical grade.

Commercial tablets were Propranolol Ayerst (Sigma Pharma LTDA, Brazil) and Inderal (Astra Zeneca, Portugal).

All solutions were prepared using high-purity water treated in a Milli-Q system (Millipore, resistivity $>18\,M\Omega$ cm). All experiments were performed in Britton–Robinson (B–R) buffer solutions; the pH of the electrolyte solutions was adjusted using a $1.0\,mol\,L^{-1}$ NaOH solution.

A $5.0\,mmol\,L^{-1}$ propranolol stock solution was prepared daily in water, and kept at 4 °C in a refrigerator. These solutions were diluted to the desired concentration with the buffer solutions.

2.2. Pretreatment of Carbon Nanotubes

MWCNT were heated at 550 °C for 30 min in air in a furnace (ALUMINI TOP, EDG Equipamentos e Controles Ltda, Brazil), and were suspended in a mixture of concentrated nitric acid and perchloric acid in a volume ratio of 7:3. The supernatant was sonicated during 30 min (ULTRASONIC CLEAR, USC 1400, Unique, Brazil), then refluxed for 2 h at 100 °C, and finally filtered. The solid phase was washed with distilled water until neutrality, and then dried at 70 °C [42].

2.3. Electrode Preparation

As previously described [22], electrodes were prepared by mixing appropriate amounts of conductor material, in this case MWCNT, graphite or mixtures of MWCNT-graphite (MWCNT/G) – with the silicone rubber insulator phase in a glass mortar for 10 min, in order to obtain a mixture with 70% of conductor material (*m/m*). The resulting mixture was inserted in a glass tube ($\varnothing_{id}=3.0$ mm) and compressed in a hydraulic press for 24 h using a copper wire ($\varnothing=3.0$ mm). After curing, electrical contact was established by connecting a copper wire to the composite with silver epoxy (Conductive Silver Epoxy Kit, Electron Microscopy Sciences, USA).

2.4. Apparatus

The working electrodes were the MWCNT/G/SR composites, the counter electrode was a platinum wire and the

reference electrode was a saturated calomel electrode (SCE), placed in a single compartment cell of 25.0 mL total capacity. All measurements were performed at room temperature ($25 \pm 1\,^{\circ}C$).

All voltammetric experiments were carried out using a BAS CV-50W potentiostat (Bioanalytical Systems, USA) coupled to a personal computer and controlled with BAS 2.3 software.

Electrochemical impedance experiments were carried out with a Solartron 1250 Frequency Response Analyser coupled to a Solartron 1286 Electrochemical Interface with ZPlot (Scribner Associates) control software. A rms perturbation of 10 mV was applied and logarithmic frequency scans, ten frequencies per decade, were performed over the frequency range 65 kHz–0.1 Hz. Fitting of impedance spectra was performed using ZSim/CNLS impedance simulation and modelling software Version 4.1 (Scribner Associates).

2.5. Electrochemical Procedures

Electrochemical characterization of the electrodes with different compositions, was carried out by cyclic voltammetry of $5.0\,mmol\,L^{-1}$ hexacyanoferrate (III) in $0.50\,mol\,L^{-1}$ KCl from -0.30 to $+0.60$ V. Differential pulse voltammetry (DPV) measurements for the pH study of propranolol were carried out in Britton–Robinson buffer in the pH range 5.0 to 10.0, from $+0.50$ to $+1.2$ V with an effective scan rate of $20\,mV\,s^{-1}$ (4 mV scan increment) and 50 mV pulse amplitude. Electrochemical impedance characterization experiments were carried out using $5.0\,mmol\,L^{-1}$ $K_3[Fe(CN)_6]$ in $0.50\,mol\,L^{-1}$ KCl.

Propranolol determination was carried out by DPV and square-wave voltammetry (SWV). In DPV, the pulse amplitude was optimized between 10 and 50 mV and scan rate from 5 to $25\,mV\,s^{-1}$. In SWV, the frequency was optimized between 10 and 100 Hz, the step potential from 1 to 5 mV and the pulse amplitude from 10 to 50 mV.

The standard addition method was used in the pharmaceutical formulation analysis. Solutions of commercial samples were prepared by carefully dissolving portions of powdered tablets in B–R buffer pH 7.0, in order to obtain a concentration of $2.5\,\mu mol\,L^{-1}$ according to the label. For the analysis, to this solution were successively added three aliquots of 200 µL of standard solution at a concentration of $1.0\,\mu mol\,L^{-1}$. The voltammograms were recorded for the sample and after each standard addition in triplicate, using the optimized conditions, for both DPV and SWV techniques.

2.6. Comparison Method

For comparison the official method described in The United States Pharmacopeia (USP XXI) [43] was used, a spectrophotometric procedure based on the measurement of the absorbance at 293 nm of both the standard and sample in heptane using heptane solvent as blank.

The standard solution was prepared by dissolving 10.0 mg of propranolol in 50.0 mL of water to obtain a solution with a known concentration of $0.200\,mg\,mL^{-1}$. The sample solution was prepared using a portion of 20 powdered tablets equivalent to about 100 mg of propranolol (based on the label values), that was transferred to a 500.0 mL volumetric flask and adding $0.10\,mol\,L^{-1}$ hydrochloric acid.

Aliquots of 5.0 mL of the standard and sample solutions were transferred to separation funnels. To these solutions, 1.0 mL of water, 1.0 mL of $1.0\,mol\,L^{-1}$ sodium hydroxide solution and 25.0 mL of heptane were added. The phases were separated and the absorbance of the heptane phase was measured at 293 nm.

3. Results and Discussion

3.1. Electrochemical Characterization

Previous studies on GSR composites using cyclic voltammetry and scanning electron microscopy [22] demonstrated that GSR composites containing 70% of conducting phase (*m/m*) presented the best electroanalytical response.

Composite electrodes with different proportions of the two conductor materials, MWCNT and graphite powder, in the ratios 70/0, 52.5/17.5, 35/35, 17.5/52.5 and 0/70% (MWCNT/G, *m/m*) with SR composition fixed at 30%, were evaluated using cyclic voltammetry of $5.0\,mmol\,L^{-1}$ $Fe(CN)_6^{3-}$ in $0.50\,mol\,L^{-1}$ KCl solutions. Typical results are presented in Figure 1.

It can be observed that increasing the proportion of MWCNT in the composite, there is an improvement in the electrochemical response, manifested by an increase

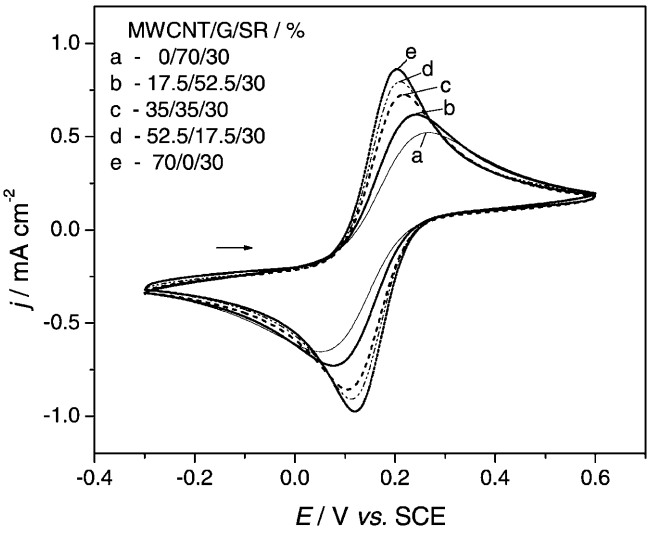


Fig. 1. Cyclic voltammograms of $5.0\,mmol\,L^{-1}$ $K_3[Fe(CN)_6]$ in $0.50\,mol\,L^{-1}$ KCl at composites containing 70% (*m/m*) of conducting phase prepared by mixing MWCNT, graphite and silicone rubber in different proportions, scan rate $50\,mV\,s^{-1}$. All the electrodes have the same geometric area ($0.0707\,cm^2$).

in the peak currents and decrease of peak potential separation, as shown in Table 2. This can be related to the increase in the active surface area due to the MWCNT and to its electrocatalytic effects, respectively [8,19].

Table 2. Results obtained from cyclic voltammetry for composite electrodes with different compositions in 5.0 mmol L^{-1} $K_3[Fe(CN)_6]$ in 0.50 mol L^{-1} KCl, $\nu = 50$ mV s^{-1}. G: graphite; SR: silicone rubber. MWCNT: multiwall carbon nanotubes.

MWCNT/G/SR [a] (%)	j_{pa} (mA cm^{-2})	j_{pc} (mA cm^{-2})	ΔE_p (V)
70/0/30	1.01	−1.02	0.082
52.5/17.5/30	0.96	−0.96	0.097
35/35/30	0.88	−0.889	0.112
17.5/52.5/30	0.76	−0.77	0.167
0/70/30	0.66	−0.69	0.221

The active areas of the prepared electrodes were estimated from the Cottrell equation [44] using chronocoulometric data; the results are presented in Table 3. In conventional composite electrodes, the active area is smaller than the geometric area, due to the presence of the insulating polymeric phase occupying part of the surface. However, due to the large surface area of the carbon nanotubes, the active area obtained increases proportionally to the amount of MWCNT.

Table 3. Electroactive area determined by chronocoulometry reduction of 5.0 mmol L^{-1} $K_3[Fe(CN)_6]$ in 0.50 mol L^{-1} KCl. G: graphite; SR: silicone rubber; geometric area: 0.0707 cm^2 ($\varnothing$ = 3.0 mm).

MWCNT/G/SR [a] (%)	Electroactive area (cm^2)
70/0/30	0.108
52.5/17.5/30	0.092
35/35/30	0.083
17.5/52.5/30	0.060
0/70/30	0.039

[a] MWCNT = multiwall carbon nanotubes

Electrochemical impedance spectroscopy (EIS) was also used to examine the interfacial behaviour of the electrodes with different conducting phase composition. Figure 2 shows impedance spectra of the different composite electrodes in 5.0 mmol L^{-1} $K_3[Fe(CN)_6]$/0.50 mol L^{-1} KCl solution at a potential of +0.15 V vs. SCE. The spectra show the expected semicircle at high frequency reflecting charge transfer control and the linear portion at lower frequency corresponding to diffusion control. Modelling was done with the usual Randles circuit consisting of a cell resistance, R_Ω, in series with a combination of the double layer capacitance (using a constant phase element, CPE modelled as a non-ideal capacitance according to $CPE = -1/(Ci\omega)^\alpha$, where α reflects the surface heterogeneity,) in parallel with the charge transfer resistance, R_{ct} and Warburg diffusion impedance, Z_W.

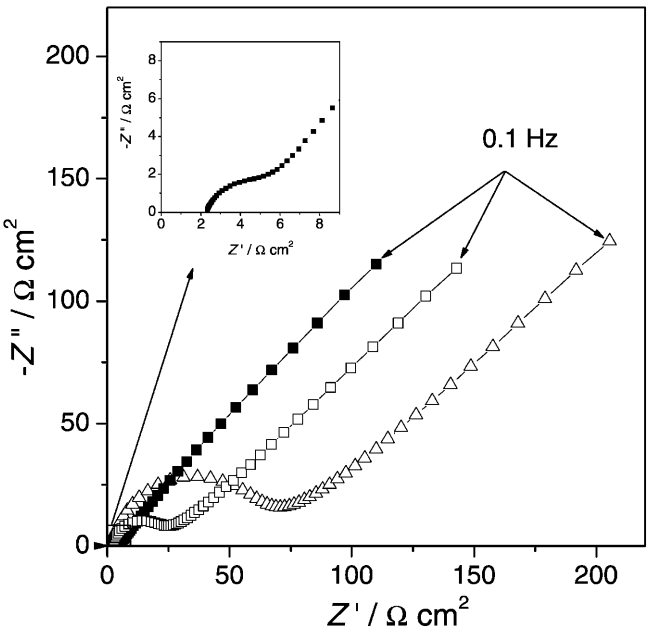


Fig. 2. Complex plane impedance spectra for 5.0 mmol L^{-1} $K_3[Fe(CN)_6]$ in 0.50 mol L^{-1} KCl at +0.15 V SCE using electrodes with composition in the ratios (■) 70/0/30, (□) 35/35/30 and (△) 0/70/30 % (MWCNT/G/SR, *m/m*). Inset: magnified image of the spectrum of (■) 70/0/30 % composition.

The important information for understanding the effect of the proportion of MWCNT is obtained from the high frequency semicircle, see Table 4. The cell resistance is always around 2 Ω cm^2 and the CPE exponent α, is 0.90 for all compositions, a typical value for such composite electrodes, e.g. [45]. The diameter of the semicircle, equal to R_{ct}, varies according to the composition, R_{ct} is smaller the larger the amount of MWCNT in the composite, see Table 4. At the same time the capacitance becomes higher, reflecting the higher interfacial capacitances of MWCNT compared to graphite. It can be concluded that the presence of MWCNT enhances the electron transfer rate of the hexacyanoferrate redox probe.

3.2. Propranolol Analysis at a MWCNT/SR Electrode

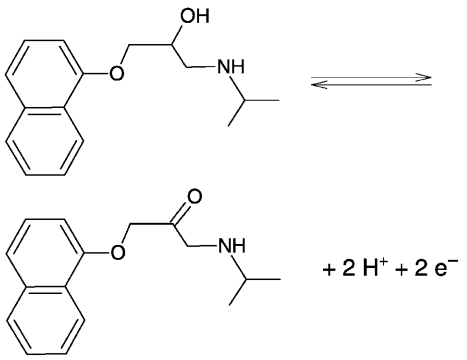
Given the significant increase in the electroanalytical signal when MWCNT are incorporated in the composite in relation to the GSR composite electrode, the capabilities of these electrodes for the determination of propra-

Table 4. Calculated equivalent circuit parameters from the impedance spectra in Figure 2 for electrodes with different compositions.

Electrode MWCNT/G/SR (%)	R_Ω (Ω cm^2)	R_{ct} (Ω cm^2)	C (μF cm^{-2} $s^{\alpha-1}$)
70/0/30	2.3	3.9	99
35/35/30	2.1	24	26
0/70/30	2.1	68	12

nolol, previously measured at GSR composite electrodes [38], were investigated.

In [38] two possible mechanisms for propranolol oxidation were considered. One by Bishop and Hussein [46] proposed that the hydroxyl group is oxidized, involving 2 protons and 2 electrons, according to:



The second by Radi et al. [36] suggests that the electrochemical oxidation takes place at the secondary amine group, involving the same number of protons and electrons. Hedge et al. [47] showed that oxidation of atenolol, another anti-hypertensive drug with a similar chemical structure, occurred at the –OH group.

In all cases the oxidation appears as an irreversible process at relatively high potentials. The presence of carbon nanotubes usually facilitates the electron transfer at the electrode surface [8,19], which could explain the better performance of the MWCNT/SR electrode compared with the G/SR electrode [38] in propranolol analysis.

DPV experiments were carried out using 5.0×10^{-5} mol L^{-1} propranolol in B–R buffer from pH 5.0 to 10.0 in order to choose the best pH value for the electroanalytical measurements. The best definition of the voltammograms was obtained at pH 7.0 with oxidation peak at 0.85 V vs. SCE as shown in Figure 3.

It is seen that the potential for propranolol oxidation depends on pH and two peaks can be observed at 0.90 and 1.0 V (vs. SCE) at pH 5.0. At pH 6 and 7 only one peak is seen and then the peak splits into two at pH 8.0, 9.0 and 10.0.

Radi et al. [36] described very similar results, at a carbon paste electrode (CPE) using cyclic voltammetry. According to those authors, propranolol exhibits two peaks at pH $\geq$ 5.0 that shift in the negative direction up to pH 9.0, above which no more peak shift was observed. This was attributed to the pK_a value of 9.4 reported in the literature for the amino group of the propranolol molecule [36].

The presence of the two peaks could be explained if one considers that the chemical oxidation of propranolol by $K_2Cr_2O_7$ also occurs in the hydroxyl group that is oxidized to its ketone form, according to studies carried out by Bishop et al. [46] and Sultan [48].

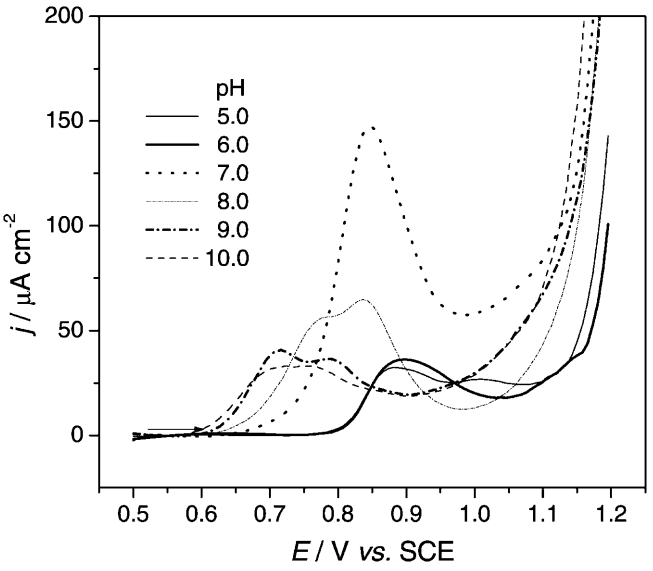


Fig. 3. DPV voltammograms of 50.0 μmol L^{-1} propranolol in B–R buffer at different values of pH. Effective scan rate 20 mV s^{-1}, pulse amplitude 50 mV.

A pH value of 7.0 was chosen for further studies, because it presented a higher current and the best peak definition.

3.3. Application to Propranolol Determination

3.3.1.-Study of Pretreatment Potential and Time

Propranolol presents an oxidation peak at +0.88 V vs. SCE at pH 7.0 in the DPV scan. In order to lower the detection limit, the possibility of preconcentration of the analyte was investigated since some adsorption of propranolol was detected. Preconcentration potentials were studied in the range of 0.0 to +0.70 V in a solution of 5.0 μmol L^{-1} propranolol. An increase in the DPV signal was observed, almost independent of the potential. The effect of the preconcentration time on the peak current was then investigated from 15 up to 180 s at +0.70 V, for concentrations of 1.0 and 5.0 μmol L^{-1} propranolol, since this potential is just before the propranolol oxidation peak and therefore reduces the experimental time. The peak current increased up to 60 s preconcentration, so this was chosen as accumulation time in further studies. Thus, the DPV measurements were performed after preconcentrating the analyte at +0.70 V (vs. SCE), during 60 s. Then a DPV run was done under the optimized conditions described below and the current was measured at the peak potential. It was also observed that accumulation is much less effective at open circuit when compared with that performed at the applied accumulation potentials mentioned above.

Figure 4 presents CV, DPV and SWV voltammograms obtained for the 50 μmol L^{-1} propranolol solution. From this figure is possible to observe that DPV and SWV are more appropriate for quantitative analysis, the latter

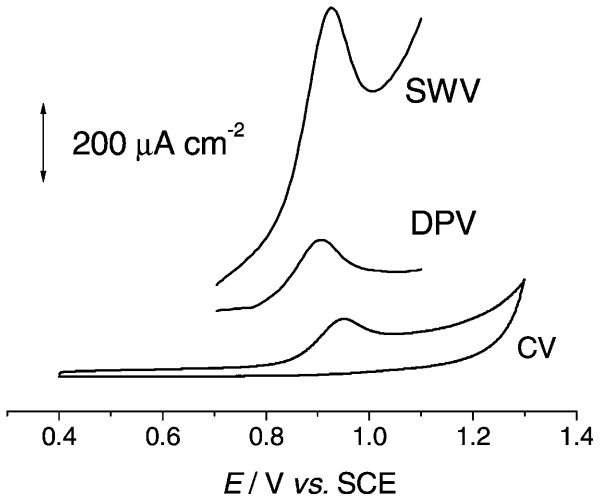


Fig. 4. Voltammograms of 50 μmol L^{-1} propranolol in B–R buffer pH 7.0 at MWCNT/SR composite electrode using the techniques SWV, DPV and CV. Conditions: SWV: pulse amplitude = 50mV, frequency = 25 Hz and step potential = 5 mV. DPV: scan rate = 25 mV s^{-1} and pulse amplitude = 50 mV. CV: scan rate = 50 mV s^{-1}.

being more sensitive. Thus the conditions for their use were optimized as described below.

3.3.2. Differential Pulse Voltammetry

Optimum conditions for propranolol determination using DPV were established in which the influence of pulse amplitude and scan rate were evaluated. The best parameters were 50 mV and 25 mV s^{-1}, for pulse amplitude and scan rate, respectively.

After optimization of the DPV experimental conditions, voltammetric measurements were carried out in pH 7.0 B–R buffer solution with different propranolol concentrations to obtain an analytical curve. The peak current was linear from 0.5 to 7 μmol L^{-1}, at +0.88 V vs. SCE obeying the equation

$$j_p = 0.237\ \text{mA cm}^{-2} + 20.35\ \text{mA cm}^{-2}\ \text{mol}^{-1}\ \text{L}\ [\text{Prop}] \quad (r = 0.9996,\ n = 9) \tag{2}$$

in which j_p is the peak current density (μA cm^{-2}) and [Prop] is the propranolol concentration (mol L^{-1}). The analytical curve was obtained measuring the peak currents for three successive DPV runs at each concentration. From these data a limit of detection (*LOD*) of 0.12 μmol L^{-1} was determined for propranolol (*LOD* = 3 × blank standard deviation/slope) [49].

At a nonmodified GSR electrode and under the same preconcentration conditions, a linear dynamic range from 0.5 to 7 μmol L^{-1} ($n = 9$) was found, obeying the equation:

$$j_p = -0.94\ \text{mA cm}^{-2} + 3.88\ \text{mA cm}^{-2}\ \text{mol}^{-1}\ \text{L}\ [\text{Prop}] \quad (r = 0.9968,\ n = 9) \tag{3}$$

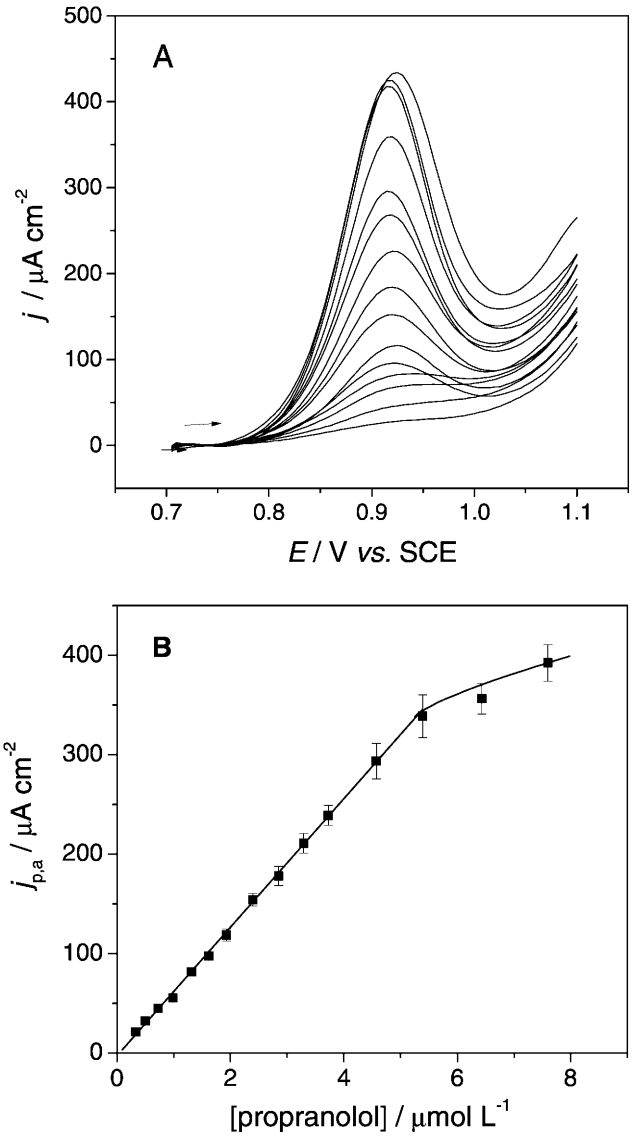


Fig. 5. (A) Square wave voltammograms in B–R buffer solution, pH 7.0, with MWCNT/SR composite electrode. Propranolol concentrations: 0.33, 0.50, 0.73, 0.99, 1.31, 1.62, 1.94, 2.39, 2.85, 3.29, 3.73, 4.57, 5.39, 6.42 and 7.59 μmol L^{-1}. (B) Analytical curve.

with *LOD* = 0.6 μmol L^{-1}. As can be seen, the sensitivity is lower by a factor of 5 and the detection limit is a factor of 5 higher, when compared to the electrode modified with MWCNT.

3.3.3. Square Wave Voltammetry

The oxidation peak of propranolol is at +0.930 V vs. SCE using square wave voltammetry. In this case, the best determination conditions, after preconcentration under the same conditions as used in DPV studies, were found to be frequency 25 Hz, 5 mV step potential and 50 mV pulse amplitude. Typical results are shown in Figure 5. The

linear range was from 0.30 to 5.4 μmol L^{-1} ($n=12$) (see Figure 5B) according to:

$$j_p = -2.54\ \text{mA cm}^{-2} + 64.0\ \text{mA cm}^{-2}\ \text{mol}^{-1}\ \text{L} \times [\text{Prop}] \quad (r = 0.9995,\ n = 12) \tag{4}$$

in which j_p is the peak current density (μA cm^{-2}) and [Prop] is the propranolol concentration (mol L^{-1}). The analytical curve in Figure 5B was obtained from peak currents for three successive SWV runs at each concentration. A *LOD* of 0.078 μmol L^{-1} was obtained (*LOD* = 3 × blank standard deviation/slope) [49]. In relation to the DPV voltammetric procedure, this represents an increase in sensitivity by a factor of 3 and a decrease in detection limit by 30 %.

3.4. Analysis of Commercial Samples

In order to evaluate the applicability of the proposed procedures, propranolol was analysed in the pharmaceutical formulations Inderal and Propranolol Ayerst by DPV and SWV techniques using the standard addition method, as described in Section 2.5, in order to eliminate matrix effects. The results were compared with those obtained by the official method and are presented in Table 5.

The results obtained for both DPV and SWV techniques agree with those from the spectrophotometric procedure at the 95 % confidence level. Recovery tests of propranolol using from 1.0 to 4.0 μmol L^{-1} resulted in a mean recovery of 96.4 to 103 % by DPV and of 98.4 to 102 % by SWV. Thus, the standard addition method was sufficiently good to determine propranolol without interference from other components of the pharmaceutical formulations tested in this study.

3.5. Comparison with Other Methods

The performance of the MWCNT/SR electrode proposed to determine propranolol was found to be good, the main advantage being that it is possible to perform direct determinations without any need for sample preparation. In relation to other electroanalytical studies described in the literature (Table 1), the *LOD* is comparable with that found using a CPE [36], with the advantage of being faster, since for CPE the optimum preconcentration time was 5 min rather than 60 s. In other reports, lower *LOD*s of the order of 10^{-9} mol L^{-1} were found, but the authors used indirect methods, that required preliminary nitration [39,40] or nitrosation [41] procedures to transform the drug to an electroactive form that could react at mercury electrodes. The only disadvantage of the present procedure, as well as that at a CPE, is that renewal of the electrode surface by mechanical polishing was required after each experiment (approximately 1 min) due to irreversible adsorption of the analyte; however, no electrochemical conditioning of the surface was needed.

Compared to a nonmodified GSR electrode, the present material is more sensitive with detection limits below 0.1 μmol L^{-1} by both DPV and SWV, while the GSR electrode reached only down to 1.0 μmol L^{-1}. Thus, the use of MWCNT with preconcentration significantly improved the performance of the GSR-based composite electrode for propranolol determination.

4. Conclusions

A new composite electrode has been developed and its use in the determination of propranolol demonstrated. The results obtained showed that the presence of MWCNT in the conductive material provides an improvement in the response of the electrochemical sensor, verified by hexacyanoferrate(III)/(II) as electrochemical probe using cyclic voltammetry and electrochemical impedance spectroscopy.

The MWCNT/SR 70 % (MWCNT, *m/m*) composite electrode and the DPV and SWV methods with adsorptive preconcentration developed here were successfully applied to the determination of propranolol in pharmaceutical formulations, providing results that were comparable with those obtained from the official spectrophotometric method. The optimised SWV procedure at MWCNT/SR led to a sensitivity 3 times that of the DPV procedure and higher than that at the GSR electrode with an excellent detection limit of 78 nM. Application to the analysis of commercial samples was demonstrated. Although renewal of the electrode surface is required due to adsorption of the analyte, excellent repeatability and reproducibility were obtained. The electrodes are mechanically robust and with a long useful life - all the present work was performed with the same electrode material during more than 6 months.

Table 5. Analysis of propranolol (mg/tablet) in commercial samples (declared amount of 40 mg per tablet).

	Propranolol (mg/tablet)			Relative error (%)	
	DPV	SWV	UV-vis [a]	E_1 [b]	E_2 [c]
Propranolol Ayerst	42 ± 2	41 ± 2	42 ± 0.4	0	−2
Inderal	41 ± 1	41 ± 1	41 ± 0.5	0	0

[a] Official/comparison method according to the USP-21 [43]; [b] $E_1 = [(\text{DPV} - \text{UV-vis})/\text{UV-vis}] \times 100$; [c] $E_2 = [(\text{SWV} - \text{UV-vis})/\text{UV-vis}] \times 100$.

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