Ionics
DOI 10.1007/s11581-016-1765-3

ORIGINAL PAPER

Carbon nanotube β-cyclodextrin-modified electrode for quantification of cocaine in seized street samples

J. M. P. J. Garrido [1,2] · F. Borges [2] · C. M. A. Brett [3] · E. M. P. J. Garrido [1,2]

Received: 29 April 2016 / Revised: 15 June 2016 / Accepted: 17 June 2016

Abstract Detection and quantification of cocaine is a key tool in fields such as police apprehensions and the fight against drug trafficking. Thus, a simple, fast and inexpensive electroanalytical methodology for the determination of cocaine in seized street samples has been developed, employing linear sweep voltammetry. The method is based on the use of a glassy carbon (GC) electrode modified by a combination of multi-walled carbon nanotubes (MWCNT) with β-cyclodextrin (β-CD) incorporated in a polyaniline film. The proposed method shows high reproducibility, repeatability and specificity. Under optimal conditions, the β-CD/MWCNT-modified GC electrode gives a detection limit of 1.02 μM cocaine. The results obtained are in good agreement with those obtained by the high-performance liquid chromatography reference method. The new methodology proposed has excellent potential as the basis of a portable analytical sensor for on-site screening of cocaine in seized street samples.

Keywords Illicit drugs · Cocaine · Voltammetric sensor · β-cyclodextrin · Carbon nanotubes

✉ J. M. P. J. Garrido
jjg@isep.ipp.pt

[1] Department of Chemical Engineering, School of Engineering (ISEP), Polytechnic of Porto, Rua Dr. António Bernardino de Almeida, 431, 4200-072 Porto, Portugal

[2] CIQ / Department of Chemistry and Biochemistry, Faculty of Sciences, University of Porto, 4169-007 Porto, Portugal

[3] Department of Chemistry, Faculty of Sciences and Technology, University of Coimbra, 3004-535 Coimbra, Portugal

Introduction

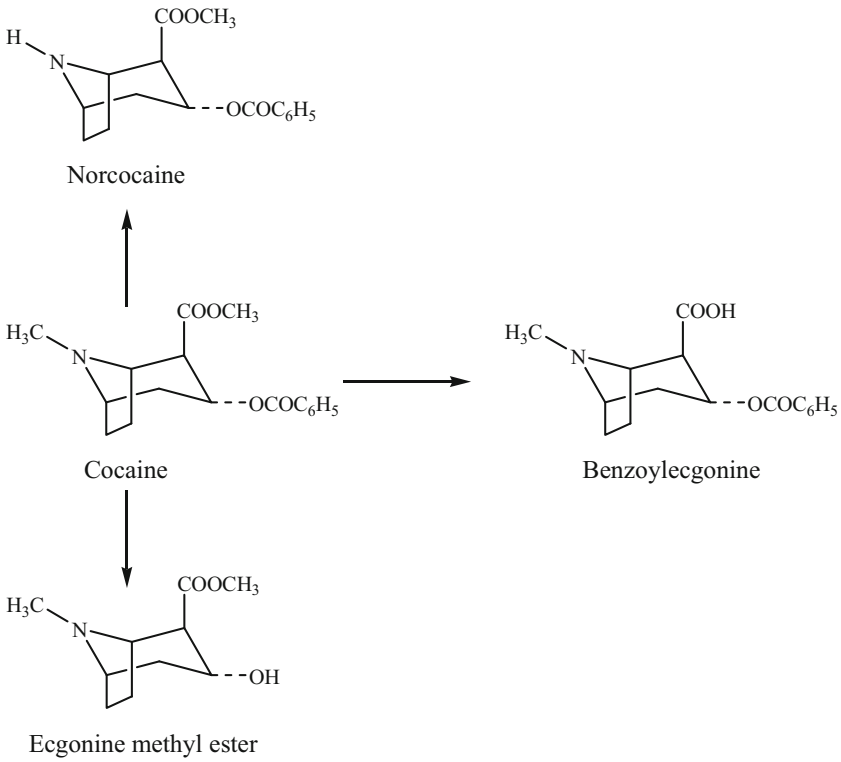
Drug abuse is a problem that affects all countries around the globe. It is estimated that almost a quarter of a billion people, or one out of 20 people between the ages of 15 and 64 years, used an illicit drug in 2013 [1]. The magnitude of the world drug problem becomes more apparent when considering that more than one out of ten drug users is a problem drug user, suffering from drug-use disorders or drug dependence [1]. This places a heavy burden on public health systems in terms of the prevention, treatment and care of drug-use disorders and their health consequences.

Cocaine remains the primary drug of concern in Latin America and the Caribbean, and its use remains high in Western and Central Europe (around 1.0 % of the global adult population aged 15–64) [1]. Based on seizure data, cocaine continues to be the third most trafficked drug in Europe [1]. Cocaine is usually trafficked northwards from the Andean countries of South America to North America and across the Atlantic to Europe via the Caribbean or Africa [1]. Portugal emerges as one of the most important European points of entry of cocaine. The huge seizures made by the authorities in Portugal are mainly linked to the rising importance of West Africa, including some of the Portuguese-speaking countries, for smuggling cocaine from the Andean region.

Cocaine (Scheme 1) is a highly addictive stimulant that occurs naturally as an alkaloid of the coca plant (*Erythroxylon coca* or *Erythroxylon novogranatense*). Due to its high potential for abuse, with its use potentially leading to severe psychological or physical dependence, coca leaf and cocaine are classified as schedule II medication under the Controlled Substances Act in the USA. The drug can be smoked, snorted and injected intravenously, subcutaneously or intramuscularly. The consequences of using cocaine vary among its users. Psychoses, violent behaviour, cardiovascular

Published online: 24 June 2016

Scheme 1 Molecular structure of cocaine and its main metabolites



and nervous system events and altered pregnancy outcomes have all been described in the literature [2]. Street forms of cocaine contain diluents and adulterants such as sugar, baking soda, anaesthetics such as lidocaine and other stimulants such as caffeine, to dilute the drug, increasing the volume and subsequent sales. Following administration, cocaine is metabolized mainly by plasma and liver esterases, to the inactive metabolites, benzoylecgonine (BE) and ecgonine methyl ester (EME) (Scheme 1) [3, 4]. These metabolites are then excreted in the urine and represent approximately 90 % of the original cocaine dose, but a small remaining percentage is excreted as the intact parent compound [4].

Quantification of cocaine is important in many areas, particularly in forensic sciences, pharmacy and therapy. Furthermore, like other illegal drugs, detection of cocaine is a key tool in fields such as police apprehensions and in the fight against drug trafficking. Traditional methods for cocaine analysis are mainly based on gas chromatography (GC) and high-performance liquid chromatography (HPLC), coupled with mass spectrometry (MS) [5–7]. These approaches are powerful and sensitive for cocaine determination, but the high cost and complicated operation limit their extensive application.

The application of electrochemical techniques in the analysis of drugs and pharmaceuticals has increased greatly over recent years. Currently, electrochemistry provides powerful analytical techniques encompassing the advantages of instrumental simplicity, moderate cost and portability. A number of strategies have been developed based on the use of nanomaterial-based electrochemical sensors [8–10]. The growing interest in the use of nanostructured conducting polymers results from the advantage of having easy synthesis control over the properties of the exposed polymeric surface such as structure, morphology and thickness. Polyaniline (PANI) is one of the most promising conducting polymers for this purpose due to its low cost, ease of preparation, chemical stability, controllable electrical conductivity and excellent environmental stability [11]. Carbon-based nanomaterials, such as carbon nanotubes (CNT), have been extensively explored due to their promising sensor applications and diverse advantages, such as a high surface-to-volume ratio, high electrical conductivity, chemical stability, biocompatibility and robust mechanical strength [12, 13]. Nanocomposites of β-cyclodextrin (β-CD) and multi-walled CNT (MWCNT) have recently been successfully used to study and quantify a variety of organic molecules owing to the synergistic effect of both materials [14–17]. The usefulness of CDs is related to their unique structures and to the fact that CDs retain their analyte-recognizing and entrapping properties under a relatively broad range of experimental conditions [18–22]. The interfacial architecture and electrochemical activity of CNT-modified electrodes after incorporating CDs and the resulting recognition effects have already been reported [14, 15].

The purpose of the present study is to establish an analytical methodology for the selective determination of cocaine using a polyaniline-β-CD/MWCNT-modified

glassy carbon electrode. The chemical recognition of cocaine by β-CD is combined with the added advantage of a faster electron transfer process due to functionalised MWCNT (fMWCNT), dispersed in a conducting PANI matrix. The new analytical methodology developed has been employed for the determination of cocaine in seized street samples by linear sweep voltammetry.

Experimental

Reagents

MWCNT were obtained from NanoLab (USA). Cocaine hydrochloride standard was kindly provided by Policia Judiciária (Lisbon, Portugal). Aniline and β-CD were supplied by Sigma–Aldrich Química (Sintra, Portugal). All other chemicals and reagents (Sigma–Aldrich Química) employed were of analytical grade and were used as received without any further purification.

All aqueous solutions were prepared using Millipore–Q water (18 MΩ cm). Phosphate buffer solutions employed for voltammetric determinations were 0.1 mol L^{-1} in the pH range 5–8.

HPLC-grade acetonitrile was supplied by Carlo Erba. The solvents were filtered through a 0.45-μm filter before use.

Apparatus

Voltammetric measurements were performed using an Autolab PGSTAT 12 potentiostat/galvanostat (Metrohm-Autolab, Netherlands) in a one-compartment glass electrochemical cell equipped with a three-electrode system arrangement consisting of a platinum wire as auxiliary electrode, a Ag/AgCl (saturated KCl) electrode as reference, and a bare or a modified glassy carbon electrode (GCE, $d = 2$ mm) as working electrode. All measurements were carried out at room temperature (25 ± 1 °C).

The pH measurements were performed using a Crison pH-meter (Crison, Spain) equipped with a glass pH electrode.

HPLC analysis was performed using a Shimadzu LC-20AD Prominence Liquid Chromatograph (Shimadzu, Tokyo, Japan) with a diode array detector (SPD-M20A). Separation was performed on a prepacked Nucleosil 100-5 C18, analytical column (250 mm × 4.6 mm, 5 μm, Macherey–Nagel, Duren, Germany), and the mobile phase was 0.02 M phosphate buffer (pH 6.5)—acetonitrile (65:35, v/v). It was delivered isocratically at 1.0 mL min^{-1} at room temperature [23, 24]. The chromatographic data was processed using the software package LabSolutions (Shimadzu, Japan).

Preparation of PANI-β-CD/fMWCNT modified GCE sensor

The preparation and characterization of the PANI-β-CD/fMWCNT modified GCE has been previously described [15]. Briefly, two milligrams of (−COOH) fMWCNT was dispersed by using ultrasonic agitation in 1 mL aqueous β-CD solution (2 %) to give a 2 mg mL^{-1} black suspension. Before surface modification, the bare GCE was carefully polished to a mirror finish with an aqueous slurry of alumina powder (15 nm particle size; BDH Chemicals, VWR, USA) on a microcloth pad and then ultrasonically cleaned in ultrapure water and ethanol alternatively to remove traces of alumina and possible contaminants. A polyaniline film was prepared on the surface of the cleaned GC electrode by electropolymerisation in a solution of aniline monomer (0.011 mol L^{-1}) in an aqueous sulphuric acid solution (0.025 mol L^{-1}), sweeping the potential between −0.1 and 1.0 V vs. Ag/AgCl at a scan rate of 50 mV s^{-1} for 50 cycles. An aliquot of 6 μL (2 mg mL^{-1}) of the MWCNT or fMWCNT dispersion was then drop cast onto the polyaniline-coated GCE surface and dried in air at ambient temperature overnight. Finally, the surface of the PANI-β-CD/MWCNT modified GCE was gently washed with water to remove the loosely attached β-CD/MWCNT.

The PANI-β-CD/fMWCNT film coated GC sensor was activated in 0.1 mol L^{-1} phosphate buffer solution (pH 6) by cyclic voltammetric sweeps between +0.5 and +1.3 V vs Ag/AgCl until stable cyclic voltammograms were obtained.

For the cleaning of the PANI-β-CD/fMWCNT film-coated GC sensor, successive cyclic voltammetric sweeps in 0.1 mol L^{-1} phosphate buffer (pH 6) solution were performed until unchanged cyclic voltammograms were obtained (six cycles).

Analytical procedures

The electrochemical behaviour of cocaine was studied by cyclic voltammetry (CV), and the influence of the supporting electrolyte pH on its voltammetric response was assessed.

The determination of cocaine was performed using linear sweep voltammetry (LSV). The instrumental parameters were optimized before the respective analytical curve was established, using successive additions of aliquots of a cocaine stock solution (10 mM), directly in the voltammetric cell. All measurements were carried out in triplicate ($n = 3$) for each concentration. Calibration curves were obtained by plotting the peak current vs. cocaine concentration. The limit of detection (LOD) was calculated according to IUPAC recommendations, using a S/N ratio of three [25]. The precision of the proposed method was verified from repeatability studies, within day ($n = 5$) and between days ($n = 5$) for three different concentrations.

Street samples of cocaine, received as a white powder, were tested. A suitable amount of each sample was weighed and transferred to a volumetric flask and dissolved with deionized water. The solution was subjected to sonication for 10 min and then the non-dissolved solids were filtered off. An aliquot of this solution was directly added to the pH 6 0.10 mol L^{-1} phosphate buffer supporting electrolyte solution in the electrochemical cell, and the voltammogram was recorded. Quantification of the sample concentration was performed by interpolation from the analytical curve. The accuracy of the proposed method was determined by comparing the results with those obtained from a previously published HPLC method [24]. Additionally, the possible interference of some adulterants, commonly added to cocaine street samples to maximise profit, was evaluated.

Results and discussion

Electrochemical behaviour of cocaine

The electrochemical properties of cocaine on the bare GC electrode, PANI/MWCNT and PANI-β-CD/fMWCNT electrode were investigated using cyclic voltammetry. The applied potential was scanned from +0.70 to +1.3 V vs Ag/AgCl in 0.1 mol L^{-1} phosphate buffer solution (pH 6), containing 40 μM of cocaine. The CV response obtained using a scan rate of 20 mV s^{-1} at a bare GC electrode, at PANI/MWCNT and at the PANI-β-CD/fMWCNT film is shown in Fig. 1. At the bare GC electrode, a weak and broad oxidation peak is obtained for cocaine, with peak potential at 1.14 V. When the GC electrode was modified with the PANI/MWCNT film, the oxidation of cocaine occurred at a less positive potential and the peak current increased, showing the electrocatalytic effect of the CNTs. At the PANI-β-CD/fMWCNT GC electrode, the electrochemical current response increased significantly, the peak potential occurring at a less positive potential of 0.92 V. In all cases, there was no reduction peak in the reverse scan suggesting that the electrochemical reaction is an irreversible process.

The signal amplification observed can be attributed to the higher available surface area provided by MWCNT and also to the presence of β-CD in the PANI/fMWCNT film-modified electrode, which can promote the formation of an inclusion complex between β-CD and cocaine. The ability of β-CD to form an inclusion complex with cocaine can lead to signal enhancement due to the higher concentration of cocaine at the PANI-β-CD/fMWCNT film electrode surface. The cocaine-β-CD complex in the PANI-β-CD/fMWCNT film would then dissociate and diffuse rapidly through the porous layer of fMWCNT to the GC surface, promoting the electrochemical reaction of cocaine.

The effect of the pH of the supporting electrolyte on the cocaine oxidation peak was then investigated. Cyclic voltammograms of cocaine in different pH electrolytes were recorded at the PANI-β-CD/fMWCNT electrode. Figure 2 shows the effect of pH on the anodic peak potential, E_{pa}, of cocaine at the PANI-β-CD/fMWCNT electrode. The E_{pa} vs pH plot shows that the anodic peak potential is dependent on pH in the interval investigated, from 5.3 to 8.1, shifting negatively as the pH was increased indicating that protons participate in the electrode reaction. The slope of the dotted line, ca. 60 mV per pH unit, shows that the mechanism of this oxidation process in aqueous media involves the same number of electrons and protons. The voltammetric data suggest that the oxidation mechanism involves the tertiary amine moiety present in the

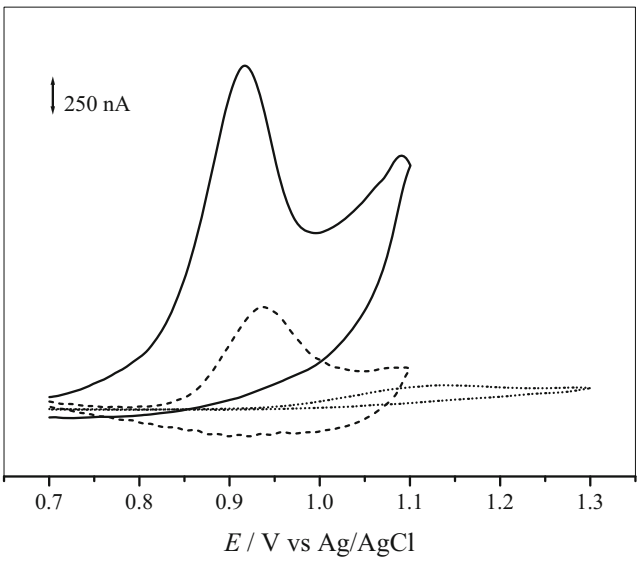


Fig. 1 Cyclic voltammograms of 40 μM solutions of cocaine at (•••) bare GC electrode, (– –) PANI/MWCNT/GCE and (—) PANI-β-CD/fMWCNT/GCE in pH 6 0.10 mol L^{-1} phosphate buffer electrolyte solution. Scan rate 20 mV s^{-1}

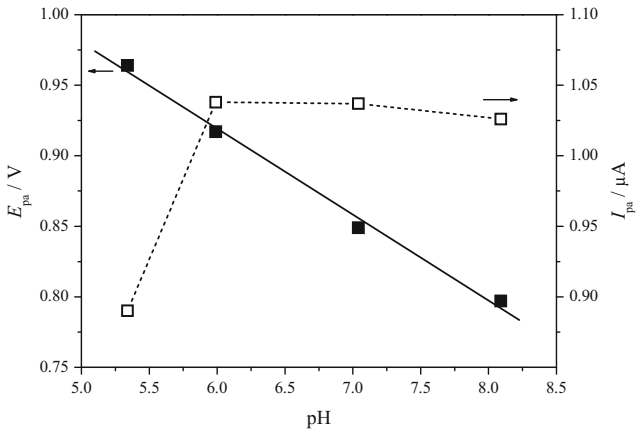


Fig. 2 Plot of anodic peak potential, E_{pa} (*filled symbols*) and anodic peak current, I_{pa} (*open symbols*) vs. pH from cyclic voltammograms of 40 μM solutions of cocaine at a PANI-β-CD/fMWCNT film electrode in different buffer electrolytes as a function of pH. Scan rate: 20 mV s^{-1}

cocaine molecular structure. The mechanism postulated for the oxidation of tertiary amines involves abstraction of an electron from the amino–nitrogen, followed by a rapid proton loss to form a neutral radical, which then loses an electron and is hydrolysed to the products. The oxidation reaction leads to a secondary amine, norcocaine (Scheme 2), and an aldehyde [26–28].

The effect of electrolyte pH on the current response of cocaine at the PANI-β-CD/fMWCNT electrode was also investigated. The results showed an increase of the anodic peak current, I_{pa}, with increase in pH until pH 6, remaining almost constant at higher pH values (Fig. 2). Thus, 0.1 mol L^{-1} phosphate buffer, pH 6, was selected for further experiments.

The effect of scan rate on the oxidation mechanism of cocaine was examined by cyclic voltammetry. Cyclic voltammograms of cocaine at different scan rates were recorded at the PANI-β-CD/fMWCNT electrode in pH 6 phosphate buffer solution. As the scan rate increases, the oxidation peak potential shifts to more positive values, confirming the irreversibility of the oxidation process. A linear relationship was observed between the peak current and the square root of scan rate in the range 10–100 mV s^{-1}, revealing that the electrode oxidation mechanism of cocaine is a diffusion-controlled process.

Analytical application

Cyclic voltammetry experiments, using the developed PANI-β-CD/fMWCNT film electrode, were carried out using the optimized experimental parameters, recording the linear sweep in the positive direction corresponding to cocaine oxidation. Linear sweep voltammograms obtained with increasing amounts of cocaine showed that the peak current increased linearly with increasing concentration (Fig. 3). A linear calibration plot, with a sensitivity of 0.0365 ± 0.0008 A M^{-1}, was obtained for cocaine concentrations ranging from 10 to 80 μM (Fig. 3, inset). A LOD of 1.02 μM was calculated using the 3S/N ratio, as recommended by IUPAC [25].

Electrochemical procedures have been already reported for the determination of cocaine. However, interferences from substances which oxidise at potentials close to that observed for cocaine make the analysis more difficult. This difficulty has sometimes been solved by the modification of the working electrode with polymers, Schiff bases, or biomolecules which increase the sensitivity and provide selectivity to the electrochemical system (Table 1) [29–37]. Comparing the analytical parameters with those previously reported in the literature (see Table 1), it is clearly seen that the use of the PANI-β-CD/fMWCNT film leads, in most cases, to comparable limits of detection. Although in a few reports the limits of detection are lower, the novel electrochemical PANI-β-CD/fMWCNT film modified electrode proposed is easy to prepare and offers a low-cost, highly reproducible and reliable sensing platform for a potential portable sensing approach to the detection of cocaine.

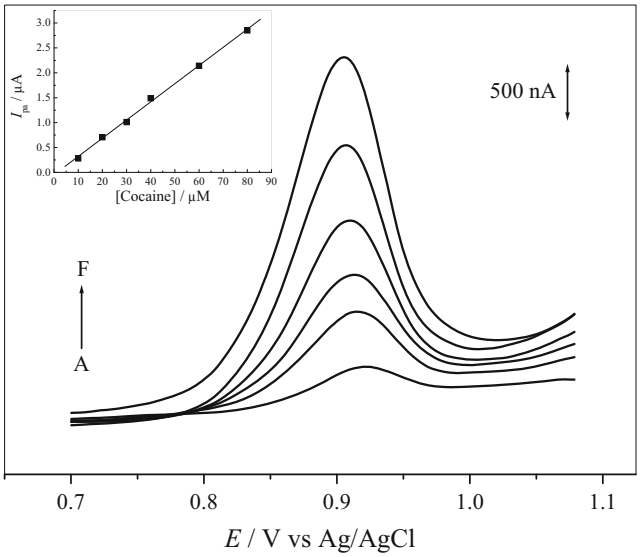
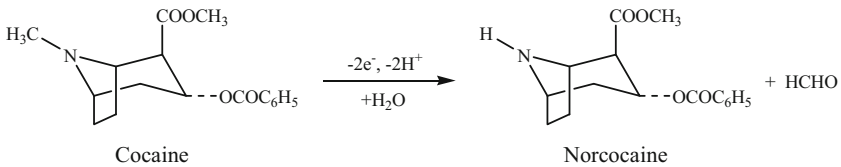


Fig. 3 Linear sweep voltammograms of cocaine standard solutions with concentrations: (A) 10, (B) 20, (C) 30, (D) 40, (E) 60 and (F) 80 μM at a PANI-β-CD/fMWCNT film electrode in pH 6 0.1 mol L^{-1} phosphate buffer electrolyte solution. *Inset*: plot of the peak current, I_{pa}, as a function of cocaine concentration. Scan rate: 20 mV s^{-1}

The intra-day and inter-day repeatability were assessed for three different concentrations of cocaine in 0.1 M phosphate buffer solution (pH 6): 10, 40 and 80 μM. The intra-day repeatability was obtained by successive simultaneous determinations (n = 5) of cocaine, resulting in a relative standard deviations (RSD) value of 1.28 %. The PANI-β-CD/fMWCNT sensor was used for at least 25 consecutive measurements without significant loss (less than 3 %) of the initial anodic peak current. The inter-day repeatability was obtained by simultaneous determinations of cocaine on five different days using freshly prepared solutions, resulting in a RSD value of 3.09 %.

Specificity and reproducibility of the sensor

The selectivity of the proposed method was evaluated by testing some possible interferents. The adulteration of cocaine samples is a common issue in the illegal drug markets around



Scheme 2 Proposed mechanism for the electrochemical oxidation of cocaine

Table 1 Comparison of different electrochemical sensing methodologies for the determination of cocaine

Method	Sensor electrode active component	Analytical ranges	LOD	Ref.
Potentiometry	Selective membrane electrode	10^{-2}–10^{-6} M	0.4 μM	[29]
Linear sweep voltammetry	Cobalt hexacyanoferrate film	0.24–1.5 mM	0.14 mM	[30]
Alternating current voltammetry	Methylene blue-tagged engineered aptamer	1–10,000 μM	1 μM	[31]
Chronoamperometry	Cytochrome P450 biosensor	19–166 nM	23 nM	[32]
Amperometry	Nanostructured DNA	10^{-4}–1 mM	33 nM	[33]
Chronoamperometry	Cytochrome P450 2B4 biosensor	0.2–1.2 mM	0.2 mM	[34]
Cyclic voltammetry	Schiff bases of $[UO_2$(3-MeOSalen)$(H_2O)]\cdot H_2O$ and $[UO_2$(5-MeOSalen)$(H_2O)]\cdot H_2O$	0.54–9.10 μM	0.07 and 0.15 μM	[35]
Differential pulse voltammetry	Graphene/AuNP nanocomposites	1–500 nM	1 nM	[36]
Square-wave voltammetry	MWCNT-SPCE	10–155 μM	Not reported	[37]
Linear sweep voltammetry	PANI-β-CD/fMWCNT/GCE	10–80 μM	1.02 μM	This work

the globe. Usually, street samples of cocaine sold in the illegal market in Portugal contain lactose, starch, caffeine and lidocaine as common adulterants and were therefore tested. Furthermore, the possible interference of the cocaine metabolites benzoylecgonine and ecgonine methyl ester was also assessed. Apart from lidocaine (see below), using a cocaine/interferent mass ratio of 1:1, no significant interferences were observed (signal change less than 5 %) from any of these compounds (Table 2). In the specific case of lactose and starch (used as diluents to increase the bulk and consequently the profits gained) as they can be found in higher amounts than cocaine, a mass ratio of 1:10 (cocaine/interferent) was also tested; no significant changes in the current response of cocaine were observed (Table 2). Lidocaine has a considerable effect on the voltammetric signal of cocaine (data not shown). Nevertheless, since methanol is required to dissolve lidocaine, simply dissolving cocaine samples in water or aqueous buffer solution, without alcohol, serves as a simple pre-treatment. As lidocaine is insoluble, it can be filtered off, and thus, cocaine can be electroanalytically determined. The effectiveness of this pre-treatment becomes evident when applied to the sensing of cocaine street samples (Table 2).

Table 2 Effect of interferents on anodic peak current for cocaine determination at PANI-β-CD/fMWCNT film electrode, expressed as percentage change in response

Interferent	Change in current response[a] / %
Lactose	+0.2
	+0.5[b]
Starch	+0.3
	−0.6 [b]
Caffeine	−1.1
Lidocaine	+3.4
Benzoylecgonine	−1.7
Ecgonine methyl ester	+2.1

[a] $n = 3$

[b] Cocaine/interferent mass ratio of 1:10

In addition, for further evaluation of the reproducibility of the sensor, five electrodes were prepared for the detection of 10 and 80 μM cocaine. The RSD of the five measurements were 4.86 and 1.62 % for cocaine concentrations of 10 and 80 μM, respectively.

The developed PANI-β-CD/fMWCNT sensor presents as characteristics, easy preparation, good repeatability and reproducibility, appropriate stability and short time of analysis, which are clearly important for analytical purposes and for cocaine detection.

Analysis of cocaine in seized street samples

To further evaluate the analytical reliability and potential application, the PANI-β-CD/fMWCNT sensor was applied to the determination of cocaine in seized street samples. For comparison purposes, the content of cocaine was also measured using a reference HPLC method [23, 24]. Five independent measurements were carried out, for both the LSV and the HPLC methods. As shown in Table 3, the results obtained

Table 3 Results obtained for the analysis of cocaine in seized street samples using the proposed linear sweep voltammetric method and HPLC

Sample	Cocaine (% *w*/*w*)[a]			*t* test[b]	*F* test[b]
	LSV	HPLC	Relative error (%)		
A	70.1 ± 0.4	70.7 ± 0.6	−0.8	1.3	1.5
B	69.8 ± 0.8	70.3 ± 0.3	−0.7	1.1	2.7
C	71.0 ± 0.9	69.9 ± 0.5	1.6	2.1	1.8

[a] Average of five replicate measurements

[b] Tabulated *t*- and *F* values, at $P = 0.05$, are 2.31 and 6.39, respectively

using the developed sensor are in good agreement with the reference HPLC method. The *F*- and *t* test (at a confidence level of 95 %) were used to compare the results obtained by the two methods (see Table 3). Considering that the calculated *F*- and *t* values were smaller than the critical values, we can conclude that there is no difference between the results obtained by the two methods at this confidence level. Therefore, the proposed voltammetric method is highly appropriate for the determination of cocaine in seized street samples. Furthermore, the PANI-β-CD/fMWCNT film electrode proposed here enables the simple determination of cocaine in a short time and at low cost.

Conclusions

A simple electroanalytical methodology involving the use of a PANI-β-CD/fMWCNT/GC modified electrode is proposed for the determination of cocaine, employing linear sweep voltammetry. The simultaneous incorporation of β-CD and fMWCNT into the sensing film considerably enhances sensor sensitivity. The resulting signal amplification enabled a detection limit of 1.02 μM for cocaine to be reached. In addition, the PANI-β-CD/fMWCNT film presents other advantages such as high accuracy, repeatability, reproducibility, stability and specificity, which make it an interesting and useful alternative for cocaine screening purposes. The results obtained were in excellent agreement with those obtained using the reference HPLC method.

This novel sensing approach provided an inexpensive, fast and sensitive platform for the detection of cocaine in street samples.

Acknowledgments We thank V. Rahemi for her assistance in the data collection during the implementation of our procedure. The authors would like to acknowledge Polícia Judiciária (Lisbon, Portugal) and the Check-in Project (Agência Piaget para o Desenvolvimento -APDES, Porto, Portugal).

References

1. United Nations Office on Drugs and Crime (2015) World Drug Report 2015 United Nations publication, SalesNo.E.15.XI.6. https://www.unodc.org/documents/wdr2015/World_Drug_Report_2015.pdf. Accessed June 2016
2. Gordon AJ (2010) Physical illness and drugs of abuse: a review of the evidence. Cambridge University Press, Cambridge
3. Goldstein RA, DesLauriers C, Burda A, Johnson–Arbor K (2009) Cocaine: history, social implications, and toxicity: a review. Semin Diagn Pathol 26:10
4. Haile CN (2012) In: Kosten TR, Newton TF, Garza R, Haile CN (eds) Cocaine and methamphetamine dependence: advances in treatment. American Psychiatric Publishing, Arlington, pp. 13–84
5. Barroso M, Gallardo E, Queiroz JA (2009) Bioanalytical methods for the determination of cocaine and metabolites in human biological samples. Bioanalysis 1:977
6. Janicka M, Kot–Wasik A, Namieśnik J (2010) Analytical procedures for determination of cocaine and its metabolites in biological samples. Trends Anal Chem 29:209
7. Harrison R, Fu S (2014) A review of methodology for testing hair for cocaine. J Forensic Invest 2:8
8. Chen A, Chatterjee S (2013) Nanomaterials based electrochemical sensors for biomedical applications. Chem Soc Rev 42:5425
9. Tuantranont A (2013) In: Tuantranont A (ed) Applications of nanomaterials in sensors and diagnostics. Springer–Verlag, Berlin Heidelberg, pp. 1–16
10. Sanghavi BJ, Wolfbeis OS, Hirsch T, Swami NS (2015) Nanomaterial–based electrochemical sensing of neurological drugs and neurotransmitters. Microchim Acta 182:1
11. Negi YS, Adhyapak PV (2002) Development in polyaniline conducting polymers. J Macromol Sci C Polym Rev 42:35
12. Adhikari B-R, Govindhan M, Chen A (2015) Carbon nanomaterials based electrochemical sensors/biosensors for the sensitive detection of pharmaceutical and biological compounds. Sensors 15:22490
13. Barsan MM, Ghica ME, Brett CMA (2015) Electrochemical sensors and biosensors based on redox polymer/carbon nanotube modified electrodes: a review. Anal Chim Acta 881:1
14. Shen Q, Wang X (2009) Simultaneous determination of adenine, guanine and thymine based on β–cyclodextrin/MWNTs modified electrode. J Electroanal Chem 632:149
15. Rahemi V, Vandamme JJ, Garrido JMPJ, Borges F, Brett CMA, Garrido EMPJ (2012) Enhanced host–guest electrochemical recognition of herbicide MCPA using a β–cyclodextrin carbon nanotube sensor. Talanta 99:288
16. Rahemi V, Garrido JMPJ, Borges F, Brett CMA, Garrido EMPJ (2013) Electrochemical determination of the herbicide bentazone using a carbon nanotube β–cyclodextrin modified electrode. Electroanalysis 25:2360
17. Gao J, Zhang S, Liu M, Tai Y, Song X, Qian Y, Song H (2016) Synergistic combination of cyclodextrin edge-functionalized graphene and multiwall carbon nanotubes as conductive bridges toward enhanced sensing response of supramolecular recognition. Electrochim Acta 187:364
18. Szente L, Szemán J (2013) Cyclodextrins in analytical chemistry: host–guest type molecular recognition. Anal Chem 85:8024
19. Liu Z, Ma X, Zhang H, Lu W, Ma H, Hou S (2012) Simultaneous determination of nitrophenol isomers based on β–cyclodextrin functionalized reduced graphene oxide. Electroanalysis 24:1178
20. Yu X, Chen Y, Chang L, Zhou L, Tang F, Wu X (2013) β–cyclodextrin non–covalently modified ionic liquid-based carbon paste electrode as a novel voltammetric sensor for specific detection of bisphenol A. Sens Actuators B 186:648
21. Yang Y, Gao F, Cai X, Yuan X, He S, Gao F, Guo H, Wang Q (2015) β–Cyclodextrin functionalized graphene as a highly conductive and multi-site platform for DNA immobilization and ultrasensitive sensing detection. Biosens Bioelectron 74:447.
22. Zhan F, Gao F, Wang X, Xie L, Gao F, Wang Q (2016) Determination of lead(II) by adsorptive stripping voltammetry using a glassy carbon electrode modified with β–cyclodextrin and chemically reduced graphene oxide composite. Microchim Acta 183:1169
23. United Nations Office on Drugs and Crime (UNODC) (2012) Recommended methods for the identification and analysis of cocaine in seized materials. United Nations, New York
24. Brancaccio A, Maresca P, Albrizio S, Fattore M, Cozzolino M, Seccia S (2013) Development and validation of a diode array high performance liquid chromatography method to determine seized street cocaine sample purity. Anal Methods 5:2584

25. Mocak J, Bond AM, Mitchell S, Scollary G (1997) A statistical overview of standard (IUPAC and ACS) and new procedures for determining the limits of detection and quantification: application to voltammetric and stripping techniques. Pure Appl Chem 69:297
26. Masui M, Sayo H (1971) Anodic oxidation of amines. Part II. Electrochemical dealkylation of aliphatic tertiary amines. J Chem Soc B 1593. doi:10.1039/J29710001593
27. Garrido JMPJ, Marques MPM, Silva AMS, Macedo TRA, Oliveira–Brett AM, Borges F (2007) Spectroscopic and electrochemical studies of cocaine–opioid interactions. Anal Bioanal Chem 388:1799
28. Garrido JMPJ, Quezada E, Fajín JLC, Cordeiro MNDS, Garrido EMPJ, Borges F (2013) Electrochemical oxidation of tamoxifen revisited. Int J Electrochem Sci 8:5710
29. Watanabe K, Okada K, Oda H, Furuno K, Gomita Y, Katsu T (1995) New cocaine-selective membrane electrode. Anal Chim Acta 316:371
30. Oiye EN, Figueiredo NB, Andrade JF, Tristão HM, Oliveira MF (2009) Voltammetric determination of cocaine in confiscated samples using a cobalt hexacyanoferrate film-modified electrode. Forensic Sci Int 192:94
31. Zuo XL, Xiao Y, Plaxco KW (2009) High specificity, electrochemical sandwich assays based on single aptamer sequences and suitable for the direct detection of small-molecule targets in blood and other complex matrices. J Am Chem Soc 131: 6944
32. Asturias–Arribas L, Alonso–Lomillo MA, Domínguez–Renedo O, Arcos–Martínez MJ (2011) CYP450 biosensors based on screen–printed carbon electrodes for the determination of cocaine. Anal Chim Acta 685:15
33. Wen YL, Pei H, Wan Y, Su Y, Huang Q, Song SP, Fan CH (2011) DNA nanostructure-decorated surfaces for enhanced aptamer-target binding and electrochemical cocaine sensors. Anal Chem 83:7418
34. Asturias–Arribas L, Alonso–Lomillo MA, Domínguez–Renedo O, Arcos–Martínez MJ (2013) Electrochemical determination of cocaine using screen-printed cytochrome P450 2B4 based biosensors. Talanta 105:131
35. Oliveira LS, Balbino MA, Menezes MMT, Dockal ER, Oliveira MF (2013) Voltammetric analysis of cocaine using platinum and glassy carbon electrodes chemically modified with uranyl Schiff base films. Microchem J 110:374
36. Jiang B, Wang M, Chen Y, Xie J, Xiang Y (2012) Highly sensitive electrochemical detection of cocaine on graphene/AuNP modified electrode via catalytic redox-recycling amplification. Biosens Bioelectron 32:305
37. Asturias-Arribas L, Alonso-Lomillo MA, Domínguez-Renedo O, Arcos-Martínez MJ (2014) Sensitive and selective cocaine electrochemical detection using disposable sensors. Anal Chim Acta 834:30