ARTICLE

Development of Carbon Paste Electrode Chemically Modified with Schiff Base Complexes for Forensic Analysis of Cocaine

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In this article we have studied the electrochemical behavior of cocaine hydrochloride on the surface of a carbon paste electrode chemically modified with a Schiff base complex, namely $[\text{Fe}^{\text{III}}(\text{salen})]$, $[\text{ZrO}^{\text{II}}(\text{salen})]$, or $[\text{Ni}^{\text{II}}(\text{salen})]$, during voltammetric analyses. Among the tested complexes, $[\text{Ni}^{\text{II}}(\text{salen})]$ provided amperometric and thermal stability and it was only degraded at temperatures above 400°C . To prepare the cocaine hydrochloride was used hydrochloric acid (HCl 1 mol

L^{-1}) after we tested the electrode, the HCl did not cause electrode passivation. In this study we can see that the voltammetric analyses revealed a satisfactory result, that the peak current obtained between 0.1 and 0.2 V (vs. Ag/AgCl) varied linearly with cocaine hydrochloride concentration and the average amperometric sensitivity, the LOD, and the LOQ were $5.5 \mu\text{mol L}^{-1}$, $0.945 \mu\text{mol L}^{-1}$, and $3.16 \mu\text{mol L}^{-1}$, respectively.

Keywords: forensic chemistry, cocaine, chemically modified electrodes, voltammetry, Schiff base complexes

INTRODUCTION

About 275 million people use drugs worldwide. Among drug users, 21 million people, aged between 15 and 64, use cocaine (Figure 1, IUPAC nomenclature: methyl (1R,2R,3S,5S)-3-(benzoyloxy)-8-methyl-8-azabicyclo-[3.2.1]-octane-4-carboxylate, $\text{C}_{17}\text{H}_{21}\text{NO}_4$). Cocaine is an alkaloid that stimulates the central nervous system, causing addiction, high blood pressure, and psychiatric disorders [1-3]. It is used as a recreational drug, but it is also taken by people who live on the streets and have to deal with adverse everyday circumstances [4-7].

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Figure 1. Molecular structure of cocaine.

Cocaine can be found in *Erythroxylon* bushes, which are native to South America. Coca leaves have been found in the burial tombs of early Incas; only the royalty used cocaine at the time. Later, in the sixteenth century, Europeans gave coca leaves to slaves to take hunger and fatigue away and hence make them work harder. In 1855, the German Friedrich Gaedecke extracted the active ingredient from coca leaves and called it *Erythroxylon*. In 1859, the chemist Albert Niemann isolated an alkaloid from coca leaves and called it cocaine. This allowed cocaine to be transported to other countries because it circumvented the issue of leaf degradation and the consequent loss of its properties. Cocaine thus became an illicit drug and since then has been cause for concern [8-9].

The dire consequences of drugs of abuse to our society have encouraged research into electrochemical analyses to identify and to quantify illicit drugs in seized samples. Indeed, public agencies that are responsible for drug seizures worldwide need reliable, practical, and fast tests to help fight crime and to aid the judicial system in passing fair sentences. In this scenario, tests relying on fast and simple techniques are essential for preliminary analysis of the seized drug and for moving on to further analysis. Most preliminary tests are based on color reaction and turbidity. They are inexpensive and easy to produce, and they can be transported everywhere.

Numerous methods for cocaine analysis have been described in the literature, including voltammetry, which offers advantages such as high sensitivity in a linear concentration range, low limits of detection and quantification, and good precision. Voltammetry allows various matrixes to be analyzed within a short time (within seconds), requires only a small volume of the sample (usually in the range of microliters), and is simple to perform.

Electrodes used in voltametric analyses can be chemically modified. The modifier is of paramount importance because it will interact with the target analyte. Chemically modified electrodes have high sensitivity [10] for several target compounds, are inexpensive and easy to produce (given that their surface can be renewed), and can have the electrodynamic potential range adjusted depending on the target analyte [11-12].

Recently, Schiff base complexes have been employed to develop chemically modified electrodes for the production of voltammetric sensors for forensic purposes. Great results have been achieved for voltammetric sensors that can detect and quantify cocaine in seized samples, as described by Oliveira et al. (2013) [13,17] and Ribeiro et al. (2015) [14], who used Schiff base complexes to modify electrodes.

In this study, we have developed new carbon paste electrodes chemically modified with a Schiff base complex, namely [Fe^{III}(salen)], [ZrO^{II}(salen)], or [Ni^{II}(salen)]. We have studied the electrochemical activity of cocaine hydrochloride on the surface of these electrodes and assessed them as voltammetric sensors for cocaine hydrochloride detection and quantification, with a view to their application in the analysis of seized cocaine samples.

MATERIAL AND METHODS

Thermogravimetric analyses

The stability of the [Fe^{III}(salen)], [ZrO^{II}(salen)], and [Ni^{II}(salen)] complexes was evaluated by TGA studies on the TGA Q 5000 V3.13 build 261 apparatus. The melting point of these complexes was established by DSC studies on the DSC Q 1000V9.9 build 303 device.

SEM

The carbon paste electrodes chemically modified with $[\text{Fe}^{\text{III}}(\text{salen})]$, $[\text{ZrO}^{\text{II}}(\text{salen})]$, or $[\text{Ni}^{\text{II}}(\text{salen})]$ were analyzed by scanning electron microscopy (SEM) (Carl Zeiss AG - EVO® 50 Series) and dispersive energy spectrometry (DES) before and after voltammetric analysis of cocaine hydrochloride. The SEM and EDS analyses were performed on 500 Digital Processing equipment; IXRF Systems (Houston, TX, USA).

Electrochemical measurements

The electrochemical behavior of cocaine hydrochloride in carbon paste electrodes chemically modified with a Schiff base complex, electron exchange between cocaine hydrochloride and $[\text{Fe}^{\text{III}}(\text{salen})]$, $[\text{ZrO}^{\text{II}}(\text{salen})]$, or $[\text{Ni}^{\text{II}}(\text{salen})]$, and voltammetric sensors to quantify cocaine in seized samples were analyzed by voltammetry on a Metrohm® model AUTOLAB 128N potentiostat coupled to a computer. The voltammograms had the baseline corrected with the NOVA 1.8.17 software.

The seized cocaine samples were provided by the local scientific police laboratory, in a work partnership between our research group and Scientific Police of Sao Paulo State.

An electrochemical cell made up of three electrodes was employed. The reference electrode was Ag/AgCl Metrohm®; the auxiliary electrode was a platinum spiral, and the working electrode was a carbon paste electrode chemically modified with $[\text{Fe}^{\text{III}}(\text{salen})]$, $[\text{ZrO}^{\text{II}}(\text{salen})]$, or $[\text{Ni}^{\text{II}}(\text{salen})]$. The supporting electrolyte was 0.1 mol L⁻¹ KCl.

The carbon paste electrodes chemically modified with a Schiff base complex were prepared by adding graphite (conductor) and Schiff base complex (modifier), at 70:30 ratio, and paraffin, as binding agent, to a crucible. The crucible was heated to 60 °C, and the mixture was macerated until a homogeneous paste was achieved. After the paste inside the electrode solidified, voltammetric analyses were carried out. The voltammetric measurements were conducted from -0.4 to 1.8 V, at scan rates varying from 5 to 100 mV s⁻¹.

RESULTS AND DISCUSSION

Amperometric stability of the chemically modified carbon paste electrodes

We evaluated the factors that could limit cocaine hydrochloride identification and quantification. First, we verified the stability of the amperometric current of the carbon paste electrode (CPE) chemically modified with $[\text{Fe}^{\text{III}}(\text{salen})]$, $[\text{ZrO}^{\text{II}}(\text{salen})]$, or $[\text{Ni}^{\text{II}}(\text{salen})]$.

Performing these electrode stability tests before starting the analysis with the analyte of interest is extremely important, since within a laboratory where there is a high demand for forensic analysis. In this work, we look for a modified electrode that loses its amperometric signal after (at least) five voltammetric cycles, as it is suggested that any chemical analysis, whether qualitative or quantitative, be performed in at least triplicate (ours were performed in quintuplicates). Therefore, the first primary analysis was the amperometric signal stability test, in which a screening was performed: a complex that had amperometric signal loss below 10% after the 5th scan was considered stable. Higher loss of amperometric signal could jeopardize the use of the modified working electrode to identify cocaine hydrochloride.

It is noteworthy that stability tests are performed in the absence of the analyte of interest (cocaine hydrochloride), thus, we performed the voltammetric analyses of the chemically modified carbon paste electrodes in 0.1 mol L⁻¹ KCl, as supporting electrolyte, for potential values ranging from -0.4 to 1.8 V (vs. Ag/AgCl) and scan rate of 100 mV s⁻¹. Figure 2 shows the electrochemical stability analysis of the carbon paste electrode chemically modified with $[\text{Fe}^{\text{III}}(\text{salen})]$. An anodic peak emerged at 1.3 V (vs. Ag/AgCl), but it disappeared after the first scan.

Figure 2. Cyclic voltamograms shown the amperometric stability of the carbon paste electrode chemically modified with $[\text{Fe}^{\text{III}}(\text{salen})]$, at a scan rate of 100 mV s^{-1} , in $0.1 \text{ mol L}^{-1} \text{ KCl}$.

Figure 3 depicts the electrochemical stability analysis of the carbon paste electrode chemically modified with $[\text{ZrO}^{\text{II}}(\text{salen})]$. An anodic peak (oxidation) emerged at 1.2 V (vs. Ag/AgCl), but it lost amperometric amplitude after the first scan.

As described above, the $\text{CPE}[\text{Fe}^{\text{III}}(\text{salen})]$ and $\text{CPE}[\text{ZrO}^{\text{II}}(\text{salen})]$ lose signal more than 30% of their amperometric signal before the 5th cycle. This phenomenon of instability was not interesting in the development of this study, since the demand for day-to-day analyzes is large in number of repetitions, and this could make it difficult for a professional to perform this analysis to perform the work, or generate false negatives, since as we will see later in the work, the detection of cocaine hydrochloride happens from the redox activity of the complex used as a working electrode modifier. Therefore, it is essential that the amperometric peak remains stable after consecutive sweep cycles.

Figure 3. Cyclic voltamogram of the amperometric stability of the carbon paste electrode chemically modified with $[\text{ZrO}^{\text{II}}(\text{salen})]$, at a scan rate of 100 mV s^{-1} , in $0.1 \text{ mol L}^{-1} \text{ KCl}$.

In contrast, Figure 4 presents the amperometric stability analysis of the carbon paste electrode chemically modified with $[\text{Ni}^{\text{II}}(\text{salen})]$. A cathodic peak with amperometric stability emerged at 0.2 V (vs. Ag/AgCl). After 25 scans, the amplitude of the reduction peak decreased by only 6.36%. Therefore, the complex remained stable after many scans, and the loss of signal amplitude did not affect cocaine hydrochloride analysis. In other words, as we do not have a significant loss of amperometric signal even after 25 scans, this stability results in the discarding of false negatives, thus, an analyst can carry out his analyzes with greater security to issue his report.

Figure 4. Cyclic voltammogram of the amperometric stability of the carbon paste electrode chemically modified with $[\text{Ni}^{\text{II}}(\text{salen})]$, at a scan rate of 100 mV s^{-1} , in $\text{KCl } 0.1 \text{ mol L}^{-1}$ KCl.

The second primary analysis before we begin to describe the analysis of cocaine hydrochloride is the $\text{CPE}[\text{Ni}^{\text{II}}(\text{salen})]$ passivation test, since the solvent used to prepare the standard cocaine hydrochloride solution – hydrochloric acid ($\text{HCl } 1 \text{ mol L}^{-1}$) – could degrade the $\text{CPE}[\text{Ni}^{\text{II}}(\text{salen})]$, causing it to corrode or melt, causing passivation (damage to the $[\text{Ni}^{\text{II}}(\text{salen})]$) and not making it viable for use in analysis in a forensic laboratory.

The carbon paste electrode chemically modified with $[\text{Ni}^{\text{II}}(\text{salen})]$, designated $\text{CPE}@\text{[Ni}^{\text{II}}(\text{salen})]$ hereafter, displayed good electrochemical stability, so we submitted it to a passivation test. Our aim was to evaluate whether the solution we used to prepare the cocaine hydrochloride solution degraded $\text{CPE}@\text{[Ni}^{\text{II}}(\text{salen})]$. To this end, we added aliquots of 100, 200, 300, or 400 μL of HCl solution ($\text{pH } 3$) to the electrochemical cell containing the supporting electrolyte, 0.1 mol L^{-1} KCl , and conducted experiments at a scan rate of 100 mV s^{-1} across the potential range. On the basis of Figure 5, $\text{CPE}@\text{[Ni}^{\text{II}}(\text{salen})]$ did not undergo passivation/degradation in acidic medium. Therefore, we used $\text{CPE}@\text{[Ni}^{\text{II}}(\text{salen})]$ to detect and to quantify cocaine hydrochloride.

Figure 5. Passivation test of the carbon paste electrode chemically modified with $[\text{Ni}^{\text{II}}(\text{salen})]$ by $\text{HCl } 1 \text{ mol L}^{-1}$, at a scan rate of 100 mV s^{-1} , in 0.1 mol L^{-1} KCl .

Finally, we evaluated which scan rate provided the highest amperometric peak, and hence the best amperometric sensitivity. The scanning speed at which the amperometric signal had the greatest amplitude was sought, as this reflects the greater efficiency of qualitative and quantitative analyses. According to

Figure 6, the optimal scan rate was 100 mV s^{-1} (without the addition of cocaine hydrochloride), which gave the highest anodic peak amplitude. Thus, we accomplished qualitative and quantitative analyses of cocaine hydrochloride at a scan rate of 100 mV s^{-1} in 0.1 mol L^{-1} KCl.

Figure 6. Scan speed study of CPE[Ni^{II}(salen)] in 0.1 mol L^{-1} KCl.

Electrochemical profile of the carbon paste electrode with and without modification

Given that CPE@[Ni^{II}(salen)] was the only chemically modified carbon paste electrode that presented satisfactory amperometric stability along successive potential scans, we carried out cyclic voltammetry analysis of the carbon paste electrode without modification and modified with the [Ni^{II}(salen)] complex.

On the basis of Figure 7, the carbon paste electrode without modification was not electrochemically active in the analyzed potential range between -0.4 and 1.2 V (vs. Ag/AgCl). After chemical modification, a cathodic peak emerged at 0.2 V (vs. Ag/AgCl).

Figure 7. Voltammetric profile of the unmodified carbon paste electrode and of the carbon paste electrode chemically modified with the [Ni^{II}(salen)] complex, at a scan rate of 100 mV s^{-1} , in 0.1 mol L^{-1} KCl.

CPE@[Ni^{II}(salen)] characterization

When we prepared the chemically modified carbon paste electrode, we heated the mixture to $60 \text{ }^{\circ}\text{C}$ to promote agglutination of the paste. Therefore, we had to evaluate whether any [Ni^{II}(salen)] was lost along the process.

Figure 8 shows the TG curve of the $[\text{Ni}^{\text{II}}(\text{salen})]$ complex, which indicated total weight loss of 79.2%. The complex underwent degradation at 400 °C, when nickel oxide emerged after a major mass loss. DSC revealed an exothermic peak at 400 °C and a heat flow of 160 Wg^{-1} , associated with decomposition of the complex.

Figure 8. TGA and DSC of the $[\text{Ni}^{\text{II}}(\text{salen})]$ complex.

We also evaluated the uniformity and homogeneity of $\text{CPE}@\text{[Ni}^{\text{II}}(\text{salen})]$. SEM analysis (Figure 9) showed that the complex was uniformly and homogeneously distributed on the $\text{CPE}@\text{[Ni}^{\text{II}}(\text{salen})]$ surface.

Figure 9. Uniformity and homogeneity of the carbon paste electrode chemically modified with $[\text{Ni}^{\text{II}}(\text{salen})]$ complex as analyzed by SEM.

Analysis of cocaine hydrochloride by cyclic voltammetry

After we conducted the stability tests and optimized the scan rate, we obtained satisfactory voltammograms for the cocaine hydrochloride standard at concentrations ranging from 1 to $15 \mu\text{mol L}^{-1}$ in 0.1 mol L^{-1} KCl. Figure 10A shows the voltammograms obtained at different cocaine hydrochloride concentrations, in which an increase in the cathodic peak was observed in the range of 0.1 V – 0.2 V (vs. Ag/AgCl) as the standard of cocaine hydrochloride was added. Whereas Figure 10B shows the analytical curve profile for this analysis. The intra and inter-day repeatability studies ($n = 3$) indicated deviations of 1.68 and 3.72%. The recovery test gave 94.43% recovery.

Figure 10. (A) cyclic voltammograms obtained with addition of the cocaine hydrochloride standard by using CPE@[Ni^{II}(salen)] in 0.1 mol L⁻¹ KCl and (B) analytical curve obtained for the addition of cocaine hydrochloride concentrations ranging from 1 to 15 $\mu\text{mol L}^{-1}$, where a reduction activity in the range of 0.1 V – 0.2 V (vs. Ag/AgCl) is observed.

The chemical modification of CPE using Ni^{II}(salen) presented an increase in voltammetric response for cocaine species. In fact, Figure 11 exhibits the voltammetric response for cocaine in a CPE without chemical modification, being possible to observe an unsatisfactory and less specific response for cocaine.

Figure 11. Cyclic voltammograms obtained with addition of the cocaine hydrochloride standard in $1.0 \mu\text{mol L}^{-1}$ by using CPE in 0.1 mol L⁻¹ KCl.

Table I shows the linear correlation coefficient (r), standard deviations, amperometric sensitivities (s), limits of detection (LOD, $3\text{DP}/s$), and limits of quantification (LOQ, $10\text{DP}/s$) for nine replicates on three different days.

Table I. Statistical data from the analyses of cocaine hydrochloride standard by using CPE@[Ni^{III}(salen)], performed on different days

	Sensitivity [μmol L ⁻¹] / [μA]	Intercept [μA]	Number of points	Standard deviation [μA]	LOD [μmol L ⁻¹]	LOQ [μmol L ⁻¹]	r
Measurement 1, day 1	5.60	-4.91	15	1.16	0.62	2.07	0.992
Measurement 2, day 1	5.24	-3.14	15	3.77	2.15	7.19	0.991
Measurement 3, day 1	5.57	-3.97	15	0.94	0.50	1.68	0.996
Measurement 1, day 2	5.46	-4.12	15	1.58	0.87	2.89	0.993
Measurement 2, day 2	5.32	-4.87	15	2.55	1.44	4.79	0.992
Measurement 3, day 2	5.24	-3.78	15	4.45	2.55	8.49	0.995
Measurement 1, day 3	5.57	-3.87	15	0.95	0.51	1.70	0.995
Measurement 2, day 3	5.13	-3.99	15	1.01	0.59	1.96	0.993
Measurement 3, day 3	5.25	-4.15	15	0.89	0.51	1.69	0.998

As we can see in Table II, the new electrode developed on this article shows itself superior when compared on the literature, with another methods and another working electrodes. Table II shows various methods and their respective working electrodes and their value of LOD. The best value of LOD is from the electrode developed on this study, showing its efficiency.

Table II. Comparison of different electrochemical results for quantification and determination of cocaine

Method	Working Electrode	LOD [μmol L ⁻¹]	Ref.
Cyclic voltammetry	GCE@[U ^{III} O(salen)]	0.50	[1]
Cyclic voltammetry	PtE@[U ^{III} O(salen)]	0.29	[1]
Cyclic voltammetry	CP@[UO ₂ (5-MeOSalen)(H ₂ O)]	0.15	[13]
Potentiometry	Selective membrane electrode	0.4	[15]
Linear sweep voltammetry	PANI-β-CD/fMWCNT/GCE	1.02	[16]
Cyclic voltammetry	CP@[U ^{III} O(salen)]	0.326	[17]
Cyclic voltammetry	CP@[Mn(salen)]	0.9320	[18]
Cyclic voltammetry	CP@[Ni ^{III} (salen)]	2.55	This work

CP: Carbon Paste Electrode; PtE: Platinum Electrode; GCE: Glassy Carbon Electrode; β-CD: Beta-Cyclodextrin.

Kinetics and mechanism of cocaine hydrochloride electroreduction on the CPE@[Ni^{II}(salen)] surface

Komorsky-Lovric et al. (1999) [19] and Pavlova et al. (2004) [20] reported that electron exchange between cocaine and the electrode surface occurs by diffusion. We evaluated this process by analyzing 8 $\mu\text{mol L}^{-1}$ cocaine hydrochloride at scan rates of 10, 20, 30, 40, 50, 60, 70, 80, 90, and 100 mV s^{-1} . In Figure 12, we present the curve i_{pc} vs. $v^{1/2}$. The curve suggested that the exchange of two electrons during cocaine hydrochloride oxidation at CPE@[Ni^{II}(salen)] was controlled by diffusion, as suggested in the literature (Equation 1).

$$i_{\text{pc}} = 0.37899 v^{1/2} - 1.3380 \quad r = 0,9907 \quad n = 10 \quad \text{Equation 1}$$

Figure 12. Study of cocaine mass transport for 8 $\mu\text{mol L}^{-1}$ cocaine hydrochloride by using CPE@[Ni^{II}(salen)] in 0.1 mol L^{-1} KCl.

To understand the mechanism of electrochemical cocaine hydrochloride reduction on the CPE@[Ni^{II}(salen)] surface, it is necessary to revisit the description of the fragmentation of cocaine during cocaine hydrochloride reduction on the surface of graphite electrodes reported by Komorsky-Lovric et al. (1999) and Pavlova et al. (2004). These authors found that the diffusion-controlled cathodic reaction occurred in the ester group; that is, the oxygen-containing groups were the electroactive centers of the cocaine molecule when the analyte was in close contact with the graphite surface [19-20].

Through the mechanism proposed by Castro et al. (2019) [18], we can assume that the exchange of electrons between the cocaine molecule and the complex [Ni^{II}(salen)] occurs in two concomitant steps: in the first step, when the oxidation potential is applied to the working electrode, the complex [Ni^{II}(salen)] is electrochemically oxidized, producing [Ni^{IV}(salen)]²⁺ on the electrode surface (this step was not observed in the worked potential range). In the second step (as noted), in scanning the cathode potential, the complex [Ni^{II}(salen)] is electrochemically regenerated; that is, the complex in the reduced form reacts with the reduced cocaine, consequently oxidizing the [Ni^{II}(salen)] complex to [Ni^{IV}(salen)]²⁺, which is electrochemically reduced, thus, as seen in Figure 7B, only the increase in the magnitude of the peak cathodic current obtained between 0.1 and 0.2 V (vs. Ag/AgCl) was proportional to the concentration of cocaine hydrochloride in solution.

CONCLUSIONS

TGA and DSC analyses proved that the $[\text{Ni}^{\text{II}}(\text{salen})]$ complex that we used to modify a carbon paste electrode was thermally stable up to 400 °C, which was five times higher than the temperature that we used for the carbon paste agglutination. During voltammetric analyses, the cathodic peak current obtained between 0.1 and 0.2 V (vs. Ag/AgCl) increased linearly with the cocaine hydrochloride concentration. The prototype of the chemically modified carbon paste electrode developed in this work presented good and specific electrochemical activity for cocaine hydrochloride, and we can see that the complex reacts with cocaine, this behavior can be explained in two steps when we do the voltammetric analyses.

The first step occurs when the oxidation potential is applied, the complex $[\text{Ni}^{\text{II}}(\text{salen})]$ is electrochemically oxidized, producing $[\text{Ni}^{\text{IV}}(\text{salen})]^{2+}$, this product can be found on the surface of the working electrode. The second step occurs in the cathode potential, when the complex $[\text{Ni}^{\text{II}}(\text{salen})]$ is electrochemically regenerated, thus the complex in the reduced form reacts with reduced cocaine, oxidizing the $[\text{Ni}^{\text{II}}(\text{salen})]$ in to $[\text{Ni}^{\text{IV}}(\text{salen})]^{2+}$, this process increases the magnitude of the peak cathodic current obtained between 0.1 and 0.2 V (vs. Ag/AgCl), that was proportional to the concentration of the cocaine hydrochloride in the solution.

The linear correlation coefficient was 0.9760, the average amperometric sensitivity was 5.5 $\mu\text{mol L}^{-1}$, and the LOD and LOQ were 0.945 $\mu\text{mol L}^{-1}$ and 3.16 $\mu\text{mol L}^{-1}$, respectively.

Conflicts of interest

The authors have no financial conflicts of interest or lack thereof.

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