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Use of voltammetric and chemometric tools to develop a sensor in forensic chemistry

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ABSTRACT

The large number of drug seizures has required the development of electrochemical sensors and new analytical techniques involving portable sensors. Here, we have studied cocaine hydrochloride oxy-reduction on the surface of carbon paste electrodes chemically modified with [$V^{II}O$(salen)], and we have evaluated these electrodes as voltammetric sensors for forensic purposes. The modified working electrode for cocaine hydrochloride analysis presented the sensitivity was 1.2 μmol.L^{-1}, and the mean limits of detection and quantification were 0.31 and 1.03 μmol.L^{-1}, respectively. As for the possible interferents, the investigated analytes exhibited similar electrochemical activity, with different sensitivities. Supervised classification of the data for the detection of analytes by the SIMCA chemometric method revealed that the voltammetric methodology predicted cocaine in real samples seized by the police more effectively than the other analytes. Thus, the developed voltammetric sensor has potential use in forensic investigations.

1. Introduction

According to the latest report by The United Nations Office on Drugs and Crime (UNODC), released in 2021, the use of illicit drugs continues to grow. Cocaine in the form of inhaled powder, chemically called cocaine hydrochloride, remains one of the most seized drugs. According to this same report, approximately 1.5 tons of cocaine has been apprehended in Colombia, the United States, Brazil, Panama, and Belgium [1–3].

The Median Lethal Dose (MLD) or LD_{50} is used to determine the acute toxicity of drugs and pesticides in the body [4,5]. According to studies, blood cocaine levels above 2 mg/L are generally associated with deaths [6]. The toxic effects caused by cocaine occur through complex mechanisms, which include central and peripheral sites of action in the human body. Cocaine in significant levels in the body can cause several damages when ingested in excess, causing respiratory, cardiovascular, psychological problems and leading to death [7,8].

The growing number of seizures has increased the use of analytical techniques geared toward combating drug trafficking [2,3]. Techniques such as high-performance liquid chromatography (HPLC) [9–14], gas chromatography (GC) [15–18], and spectroscopy have been applied more frequently in expert laboratories [19–22]. However, these techniques have drawbacks. For example, HPLC [23,24] consumes large amounts of reagents, has high operational cost, requires handling experience, employs a sensitive universal detector, and demands the use of other techniques to assist in identification. In turn, GC [25] analyses rely on columns, which have a limited number of plates, require mobile phase flow control, are relatively time-consuming, and provide low resolution, which compromises efficiency during analysis of complex samples.

Concerning spectroscopic techniques, they include Optical Spectrometry techniques like absorption spectroscopy in the ultraviolet-visible (UV–Vis) [26] and Infrared (IR) ranges [27]. Other spectroscopic techniques exist; for instance, Molecular Absorption, Molecular

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Fluorescence, and Atomic Spectrometry, but they all have disadvantages. For example, determining analytes at low concentrations is difficult during UV–Vis: the bandwidth in the UV–Vis spectrum makes the technique non-selective, and frequent calibrations are needed to maintain accuracy and precision. Therefore, other assistive techniques are desirable [26,27].

Many forensic laboratories are opting for highly efficient low-cost techniques with low detection limit, such as electroanalytical techniques [28–30]. Electrochemical techniques are becoming popular because they are inexpensive, easy to handle, and fast, not to mention that they provide low detection limits and a lot of information that helps to characterize and to describe certain systems. In the field of electroanalytics, sensors built from chemically modified electrodes have been increasingly applied—these electrodes are more selective, thereby minimizing the interference of other substances present in complex samples [31].

Schiff-base complexes constitute an important class of chemicals that can be used to modify electrodes and to form stable films during electrochemical analyses [32–34]. Oliveira et al. [35] investigated the complexes $[UO_2(3\text{-MeO salen})(H_2O)]\bullet H_2O$ and $[UO_2(5\text{-MeO salen})(H_2O)]\bullet H_2O$ as chemical modifiers of platinum electrode to determine cocaine and its interferents by voltammetric analysis and obtained good results. In another paper, Oliveira et al. [36] modified the surface of glassy carbon electrodes with the complex $[UO_2(X\text{-MeO-salen})(H_2O)]$ (where $X = 3$, 4, or 5), to detect cocaine in seized samples by voltammetry. The modified electrode proved potentially useful in the forensic area and can be applied in a more specific method for preliminary cocaine testing in drug samples.

In their study on carbon paste electrode chemically modified with N, N'-ethylene-bis-(salicylideneiminato)manganese(II) Schiff-base complex, Castro et al. [37] reported that the complex $[Mn^{II}(salen)]$ presented better amperometric sensitivity than some complexes described in the literature. Alves et al. [38] used Carbon Screen-printed Electrodes (C-SPEs) to detect 3,4-methylenedioxyamphetamine (MDMA), which helped to improve the voltammetric technique sensitivity. The authors evaluated the applicability and reproducibility of the method in intra- and inter-day tests and applied it in the analysis of seized samples. Recently, Castro et al. [39] described voltametric analyses with electrodes chemically modified with $[Fe^{II}(salen)]$, $[Ni^{II}(salen)]$, $[Cu^{II}(salen)]$, or $[Co^{II}(salen)]$, which were thermally stable during analysis of illicit drugs.

Here, we will describe the combination of electrochemical techniques based on carbon paste electrode chemically modified with $[V^{II}O(salen)]$ with other approaches like Thermogravimetric Analysis (TGA), SIMCA Chemometric Analysis, and Density Functional Theory (DFT) to confirm the oxidation–reduction mechanisms proposed in the literature.

2. Experimental

2.1. Thermogravimetry

The thermal stability of $[V^{II}O(salen)]$ was established by TGA studies on the TGA Q 5000 V3.13 build 261 instrument. The melting point of $[V^{II}O(salen)]$ was established by DSC studies on the DSC Q 1000V9.9 build 303 instrument. The analyses were conducted under synthetic air and heating ramp of 10 °C/min.

2.2. Scanning electron microscopy

The carbon paste electrode chemically modified with $[V^{II}O(salen)]$, or CPE@$V^{II}O$(salen), was analyzed by scanning electron microscopy (SEM) (Carl Zeiss AG – EVO® 50 Series) and energy dispersive spectrometry (EDS). SEM and EDS analyses were performed on the 500 Digital Processing equipment; IXRF Systems (Houston, TX, USA).

2.3. Atomic force microscopy (AFM)

The carbon paste electrode chemically modified with $[V^{II}O(salen)]$, or CPE@$V^{II}O$(salen), was analyzed by Atomic Force Microscopy (AFM) (Shimadzu - Scanning Probe Microscope – 9600). The method used was the "Phase" mode, in which the tip makes intermittent contact with the sample at room temperature and in air. All images, both topographic and phase contrast, were provided simultaneously by the equipment while scanning each selected area.

2.4. Electrochemical methods

The electrochemical behavior of cocaine hydrochloride and its interferents at CPE@$V^{II}O$(salen) was studied by voltammetric analyses on a potentiostat model AUTOLAB 128 N from Metrohm®. The three-electrode electrochemical cell consisted of Ag/AgCl Metrohm® as reference electrode, platinum spiral as auxiliary electrode, and CPE@$V^{II}O$(salen) as working electrode; 0.1 $mol.L^{-1}$ KCl was used as supporting electrolyte. CPE@$V^{II}O$(salen) with graphite/$[V^{II}O(salen)]$ at a 70:30 ratio was prepared by using paraffin as binding agent. Graphite, $[V^{II}O(salen)]$, and paraffin were added to a crucible, heated to 60 °C, and macerated until a homogeneous paste was obtained. The cyclic voltammetry (CV) measurements were accomplished between −1.0 and 1.8 V (*vs* Ag/AgCl); the scan rate ranged from 5 to 100 $mV.s^{-1}$. Electrochemical stability and CPE@$V^{II}O$(salen) passivation were tested, to show that $[V^{II}O(salen)]$ was stable up to 20 scan cycles, and that a maximum of 30% of the initial current value was lost. During the passivation test, whether the solvent used to prepare the cocaine hydrochloride standard solution – hydrochloric acid (1 $mol.L^{-1}$ HCl) – could degrade CPE@$V^{II}O$(salen) was investigated.

2.5. Chemometric methods

The supervised approach known as Soft Independent Modeling Classification Analogy (SIMCA) was used to model the location of the groups previously indicated in the multidimensional space through the use of Principal Component Analysis (PCA), as presented in [39].

2.6. Chromatographic methods

For validation and comparison of the voltammetric method developed herein, High Performance Liquid Chromatography (HPLC) was performed on a Shimadzu chromatograph, under isocratic flow (1.0 mL/min). The mobile phase solution contained acetonitrile and water at 95:5 (v/v) ratio. The injection volume was 20 μL. A C18 column (SGE brand, measurements 250 mm x 4.6 mm x 0.5 μm) was employed. The products were analyzed at 220 nm. Repeatability, reproducibility, etc. were evaluated [40].

2.7. Density functional theory methods

As described in a previous study [39], inputs were initially made from crystallographic structures reported in the literature [41,42]. These starting structures were used to ensure that the structures applied in the calculation were adequate. For this purpose, the Avogadro program was employed [43]. Then, all the inputs were submitted to calculation in the ORCA program [44]. DFT employing the hybrid functional B3LYP (Becke, 3-parameter, Lee–Yang–Parr) [45] and the base TZVP (Valence triple-zeta polarization) was used [46]. A continuous potential was also employed to represent the aqueous medium.

2.8. Reagents

Standards of cocaine (Cerilliant®, chromatographic purity), caffeine (Sigma-Aldrich®, 98%, solid), theobromine (Merck®, 98,5%, solid), lidocaine (Merck®, 98%, solid), and procaine (Sigma-Aldrich®, 97%,

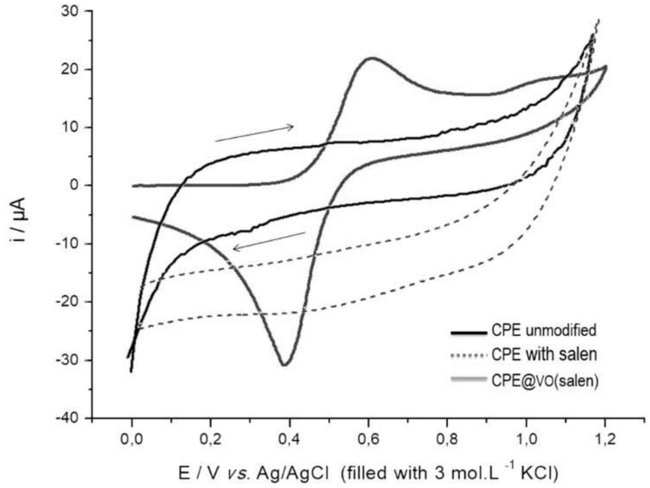

Fig. 1. . Voltammetric behavior of the CPE, CPE@salen and @V^{II}O(salen) in supporting electrolyte KCl 0.1 mol.L^{-1} and scan rate of 100 mV.s^{-1} without standards.

solid), which were all acidified (pH 3) with HCl (Merck®), were used to obtain standards in hydrochloride forms. For the voltammetric analyses, KCl (Merck®) was used to prepare the supporting electrolyte, whereas graphite (Merck®) and paraffin (Sigma Aldrich ®) were used to prepare the carbon paste electrode. For the chromatographic analyses, acetonitrile (Sigma Aldrich®, chromatographic purity) was used to prepare the mobile phase. The [VO^{II}(salen)] complex used as chemical modifier was synthesized as per literature and 98% purity was proven by spectroscopic techniques [47,48].

3. Results and discussion

3.1. *Characterization of the working electrode chemically modified with [V^{II}O(salen)]*

First, we prepared CPE@V^{II}O(salen) and characterized it. During electrode preparation, the components were heated to 60 °C for paste agglutination. Therefore, to investigate whether [V^{II}O(salen)] could be lost during heating at this temperature, we studied its combustion temperature through TG and DSC analyses.

Fig. S1 (supplementary material) illustrates the [V^{II}O(salen)] TG curve. The total mass loss was 74.05% after 500 °C was reached. The first mass loss step, corresponding to 0.3495 mg or 15.98% of the initial mass, occurred at 400 °C and was associated with loss of a water network formed during the synthesis of [V^{II}O(salen)]. The second mass loss step took place between 420 and 450 °C and corresponded to 1.270 mg or 58.07%, attributed to [V^{II}O(salen)] degradation and vanadium oxide (VO) formation. On the basis of DSC, water loss was evident from an exothermic peak at 380 °C at heat flux equal to 10 W/g. The other exothermic peak, at 460 °C and heat flux of 150 W/g, was probably due to [V^{II}O(salen)] combustion and its phase transitions. Given that [V^{II}O (salen)] was thermally stable up to 400 °C, heating at 60 °C during CPE@V^{II}O(salen) preparation should not cause [V^{II}O(salen)] to decompose.

Regarding CPE@V^{II}O(salen), we verified [V^{II}O(salen)] distribution on the CPE@V^{II}O(salen) electrode surface. According to Fig. S2, which shows the contrast micrograph (SEM), [V^{II}O(salen)] was evenly distributed on the electrode surface.

The properties and characteristics of a material are of great importance for the development of a chemically modified electrode, as the interaction between the analyte and the electrode takes place on its surface. Thus, we chose to use the Atomic Force Microscopy (AFM) technique to characterize the surface of the developed electrode. The study electrode is composed of a CPE@V^{II}O(salen).

Fig. S5 represents the AFM images of CPE@V^{II}O(salen) dimensions of 10 × 10 nm, 3D images of the CPE@V^{II}O(salen) and its phase contrast. Fig. S6 represents the AFM images of [V^{II}O(salen)] with dimensions of 10 × 10 nm, 3D images of [V^{II}O(salen)] and its phase contrast.

Observing the images one can notice a uniformly distributed surface on the surface of the CPE@V^{II}O(salen) and [V^{II}O(salen)] separately. The phase contrast images show a surface and homogeneity of CPE@V^{II}O (salen) and [V^{II}O(salen)].

3.2. *Voltammetric analysis*

3.2.1. *CPE@V^{II}O(salen) voltammetric behavior*

Fig. 1 shows the voltammetric behavior of CPE@V^{II}O(salen) in 0.1 mol.L^{-1} KCl, as supporting electrolyte, at a scan rate of 100 mV.s^{-1}. CPE@V^{II}O(salen) presented an anodic peak at 0.6 V (*vs* Ag/AgCl) and a cathodic peak at 0.4 V (*vs* Ag/AgCl).

As demonstrated in the mechanism of interaction between analyte and the CPE@V^{II}O(salen) surface proposed by Pavlova et al. (2004) [49], Raymundo-Pereira et al. (2013) [50], and Castro et al. (2019) [37], when enough energy for interaction was reached, first diffusion-controlled electron exchange took place. When 0.6 V (*vs* Ag/AgCl) was reached, [V^{II}O(salen)] was oxidized to [V^{III}O(salen)]$^{+}$: [V^{II}O(salen)] lost one electron, while the amino group of cocaine hydrochloride lost two electrons; that is, both were oxidized. Subsequently, when 0.4 V (*v.* Ag/AgCl) was reached, [VO^{II}(salen)] was regenerated through electrochemical reduction, with concomitant reduction of cocaine hydrochloride. These two redox steps can be attributed to the electrocatalytic mechanism between CPE@V^{II}O(salen) and the cocaine hydrochloride solution.

Therefore, to achieve reduction at 0.4 V (*vs* Ag/AgCl), a positive potential value of 0.6 V (*vs* Ag/AgCl) must be applied to CPE@V^{II}O (salen) to promote [V^{II}O(salen)] electrochemical oxidation in the carbon paste, producing [V^{III}O(salen)]$^{+}$ on the electrode surface.

3.2.2. *Electronic exchange kinetics between cocaine hydrochloride and CPE@V^{II}O(salen)*

We studied electronic exchange between cocaine hydrochloride and the CPE@V^{II}O(salen) surface by analyzing current as a function of the square root of the scan rate ($v^{1/2}$). The cocaine hydrochloride concentration was 6 µmol.L^{-1} (mean concentration among those that were used), and the sweeping rate was varied from 10 to 100 mV.s^{-1}.

Fig. S3 and Eqs. (1) and 2 show that the anodic and cathodic peak currents increased linearly with ($v^{1/2}$), respectively, suggesting that cocaine hydrochloride the oxidation and reduction at CPE@V^{II}O(salen) was diffusion-controlled.

$$i_{pa} = 0.5087v^{1/2} - - 1.5848; r = 0.9989, n = 10 \tag{1}$$

$$i_{pc} = 0.3815v^{1/2} - - 1.1886; r = 0.9983, n = 10 \tag{2}$$

Addition of 10 µmol.L^{-1} cocaine hydrochloride caused loss of the amperometric signal due to CPE@V^{II}O(salen) electrode surface saturation, as shown in Fig. S4. This may limit the use of CPE@V^{II}O(salen) in the development of voltammetric sensors for cocaine hydrochloride detection and quantification.

3.2.3. *CPE@V^{II}O(salen) ampemometric stability*

According to an electrochemical stability study (not shown), there was amperometric signal loss above 30% after 90 cycles, so CPE@V^{II}O (salen) can be considered stable for quantitative analyses. As for the CPE@V^{II}O(salen) passivation test (not shown) in 1 mol.L^{-1} hydrochloric acid, there was no CPE@V^{II}O(salen) passivation.

3.2.4. *Quantitative voltammetric analyses*

Cocaine hydrochloride analyses

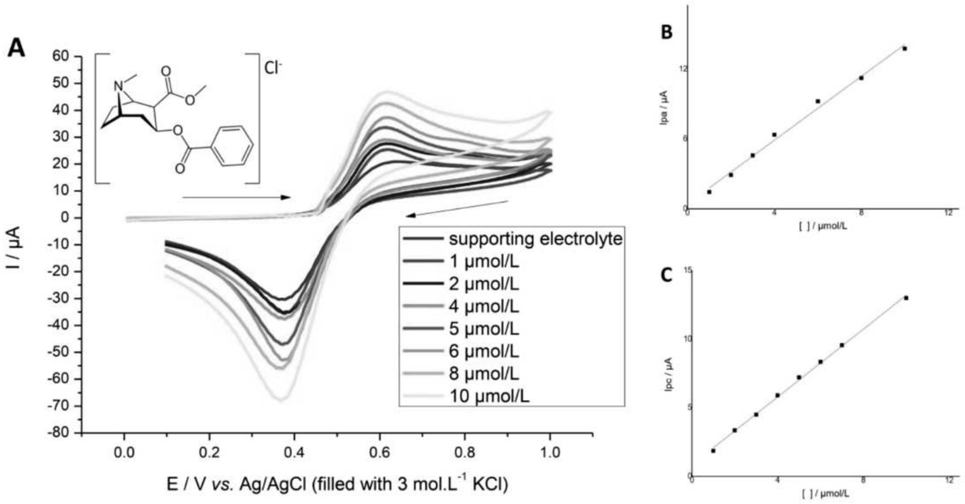

Fig. 2. . (A) cyclic voltammograms of cocaine hydrochloride standard addition using CPE@$V^{II}O$(salen) in 0.1 mol.L^{-1} KCl supporting electrolyte and scan rate of 100 mV.s^{-1} and curve analytical obtained for the concentration of cocaine hydrochloride in the linearity range of 1 to 10 μmol.L^{-1}, based on the (B) anodic (or oxidation) peak at 0.6 V (*vs.* Ag/AgCl) and (C) cathodic peak (or reduction) at 0.4 V (*vs.* Ag/AgCl).

Table 1

. Statistical data of the analysis of the oxidation of cocaine hydrochloride using the CPE@$V^{II}O$(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	1,21 (±0,002)	0,899 (±0,001)	0,0923 (±0,0023)	0,25 (±0,01)	0,76 (±0,01)	0,970 (±0,003)
Measure 2, day 1	1,26 (±0,003)	0,427 (±0,017)	0,0851 (±0,0045)	0,22 (±0,01)	0,67 (±0,02)	0,991 (±0,001)
Measure 1, day 2	1,21 (±0,004)	0,589 (±0,015)	0,0911 (±0,0027)	0,24 (±0,01)	0,75 (±0,01)	0,987 (±0,004)

Table 2

. Statistical data of the analysis of the reduction of cocaine hydrochloride using the CPE@$V^{II}O$(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	1,22 (±0,003)	0,842 (±0,003)	0,0945 (±0,0019)	0,25 (±0,01)	0,77 (±0,01)	0,997 (±0,001)
Measure 2, day 1	1,23 (±0,001)	0,851 (±0,002)	0,0862 (±0,0033)	0,23 (±0,01)	0,70 (±0,01)	0,998 (±0,002)
Measure 1, day 2	1,20 (±0,001)	0,858 (±0,004)	0,0923 (±0,0015)	0,25 (±0,01)	0,77 (±0,01)	0,997 (±0,001)

Fig. 2A shows the voltammograms of the cocaine hydrochloride standard at concentrations ranging from 1 to 10 μmol.L^{-1}; Fig. 2B and C present the analytical curves. From the analyses, performed in triplicate, we calculated the mean values of sensitivity (*s*, μmol.L^{-1}/μA), intercept (μA), standard deviation (SD, μA), limit of detection (LOD, 3SD/s, μmol.L^{-1}), and limit of quantification (LOQ, 10DP/s, μmol.L^{-1}) (see Tables 1 and 2).

We selected a cocaine hydrochloride concentration of 6 μmol.L^{-1} (mean concentration among those tested here) to carry out the intra- ($n = 9$) and inter- ($n = 9$) day repeatability studies. For the anodic studies, the coefficients of variation were 3.85% and 4.91%, respectively. With respect to the cathodic studies, the coefficients of variation were 3.31% and 4.63%, respectively.

The relative standard deviation for nine measurements was 0.82% (anodic study) and 0.75% (cathodic study), indicating that CPE@$V^{II}O$(salen) presented good stability and repeatability, within a confidence level of 95%. The recovery test gave values of 92.72% and 94.42% in the anodic and cathodic studies, respectively.

Caffeine hydrochloride analyses

Fig. 3A shows the cyclic voltammograms of the analyses of the caffeine hydrochloride standard in the presence of CPE@$V^{II}O$(salen) in 0.1 mol.L^{-1} KCl, as supporting electrolyte, at a scan rate of 100 mV.s^{-1}. Caffeine hydrochloride has an anodic peak at 0.6 V (*vs* Ag/AgCl) and a cathodic peak at 0.4 V (*vs*.Ag/AgCl). Fig. 3B and C show the analytical curves obtained with the addition of 1 to 10 μmol.L^{-1} caffeine hydrochloride standard based on the anodic (or oxidation) peak at 0.6 V (*vs* Ag/AgCl) and cathodic (or reduction) peak at 0.4 V (*vs* Ag/AgCl). Tables 3 and 4 present the results of the analyses, performed in triplicate.

Although cocaine and caffeine hydrochlorides had similar activities, analysis of the caffeine hydrochloride standard revealed lower analytical sensitivity (s): 0.27 and 0.54 μmol.L^{-1}/μA for the anodic and cathodic activities, respectively, which were four- and twofold lower as compared to the cocaine hydrochloride standard.

We selected a caffeine hydrochloride concentration of 7 μmol.L^{-1} (mean concentration among those used here) to evaluate the intra- ($n = 9$) and inter- ($n = 9$) day repeatability studies. The anodic studies had coefficients of variation of 3.23% and 4.17%, respectively, while the cathodic studies had coefficients of variation of 2.98% and 3.79%, respectively. The relative standard deviation for nine measurements was 0.78% (anodic study) and 0.82% (cathodic study), indicating that CPE@$V^{II}O$(salen) had good stability and repeatability, within a confidence level of 95%. The recovery tests gave values of 97.43% and

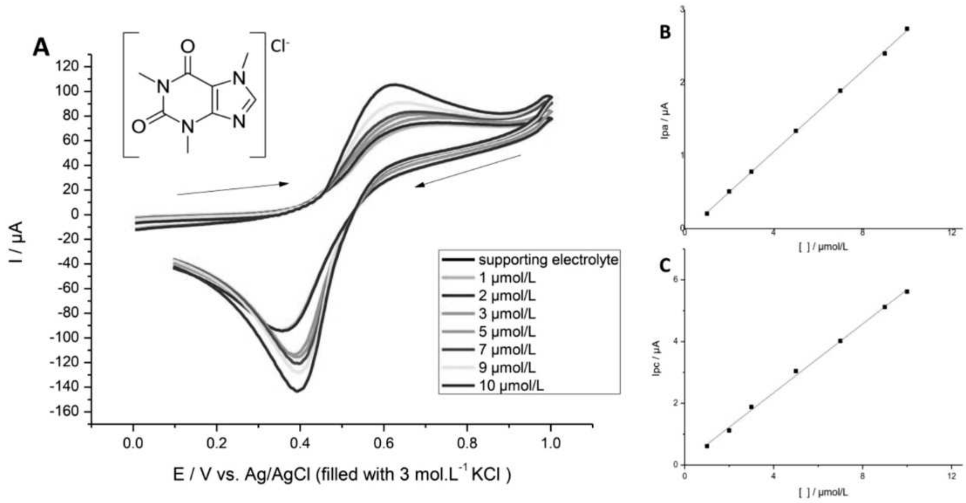

Fig. 3. . (A) cyclic voltamograms of the addition of caffeine hydrochloride standard using CPE@V^{II}O(salen) in 0.1 mol.L^{-1} KCl supporting electrolyte and scan rate 100 mV.s^{-1} and analytical curve obtained for the caffeine concentration in the linearity range of 1 to 10 μmol.L^{-1}, based on the (B) anodic (or oxidation) peak at 0.6 V (*vs.* Ag/AgCl) and (C) cathodic peak (or reduction) by 0.4 V (*vs.* Ag/AgCl).

Table 3
. Statistical data from the analysis of the oxidation of caffeine hydrochloride using the CPE@V^{II}O(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	0,277 (±0,002)	−0,547 (±0,033)	0,0264 (±0,056)	0,31 (±0,11)	0,95 (±0,08)	0,999 (±0,001)
Measure 2, day 1	0,277 (±0,003)	−0,265 (±0,017)	0,0559 (±0,031)	0,66 (±0,09)	2,01 (±0,03)	0,997 (±0,004)
Measure 1, day 2	0,270 (±0,004)	−0,287 (±0,013)	0,0410 (±0,042)	0,50 (±0,07)	1,51 (±0,11)	0,998 (±0,003)

Table 4
. Statistical data from the analysis of caffeine hydrochloride reduction using the CPE@V^{II}O(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	0,557 (±0,005)	0,112 (±0,057)	0,115 (±0,023)	0,68 (±0,19)	2,06 (±0,23)	0,999 (±0,001)
Measure 2, day 1	0,546 (±0,003)	0,196 (±0,034)	0,218 (±0,044)	1,31 (±0,02)	3,99 (±0,33)	0,997 (±0,003)
Measure 1, day 2	0,547 (±0,005)	0,257 (±0,019)	0,261 (±0,038)	1,57 (±0,03)	4,77 (±0,54)	0,998 (±0,002)

98.38% in the anodic and cathodic studies, respectively.

Lidocaine hydrochloride analyses

Fig. 4A shows the cyclic voltammograms of the lidocaine hydrochloride standard in the presence of CPE@V^{II}O(salen) in 0.1 mol.L^{-1} KCl, as supporting electrolyte, at a scan rate of 100 mV.s^{-1}. Lidocaine hydrochloride displayed an anodic peak at 0.62 V (*vs* Ag/AgCl) and a cathodic peak at 0.35 V (*vs* Ag/AgCl). Fig. 4B and C show the analytical curves obtained with addition of 1 to 10 μmol.L^{-1} lidocaine hydrochloride standard based on the anodic (or oxidation) peak at 0.62 V (*vs* Ag/AgCl) and the cathodic peak (or reduction) at 0.35 V (*vs* Ag/AgCl), respectively.

Tables 5 and 6 show the results obtained from the analysis of lidocaine hydrochloride oxidation and reduction, respectively. Lidocaine hydrochloride behaved differently from cocaine hydrochloride. In the analyses of the lidocaine hydrochloride standard, we obtained higher values of analytical sensitivity (s): 2.3 and 2.4 μmol.L^{-1}/μA for the anodic and cathodic activities, respectively, which were twofold higher as compared to the cocaine hydrochloride standard.

We selected a lidocaine hydrochloride concentration of 6 μmol.L^{-1} (mean concentration among those used here) to evaluate the intra- ($n = 9$) and inter- ($n = 9$) day repeatability studies. The anodic studies had coefficients of variation of 3.75% and 4.63%, respectively, while the cathodic studies had coefficients of variation of 3.22% and 4.45%, respectively. The relative standard deviation for nine measurements was 0.85% (anodic study) and 0.82% (cathodic study), indicating that CPE@V^{II}O(salen) had good stability and repeatability, within a confidence level of 95%. The recovery tests gave values of 97.43% and 98.38% in the anodic and cathodic studies, respectively.

Procaine hydrochloride analysis

Fig. 5A shows the cyclic voltammograms of the procaine hydrochloride standard in the presence of CPE@V^{II}O(salen) in 0.1 mol.L^{-1} KCl, as supporting electrolyte, at a scan rate of 100 mV.s^{-1}. Procaine hydrochloride showed an anodic peak at 0.6 V (*vs* Ag/AgCl) and a cathodic peak at 0.36 V (*vs* Ag/AgCl). Fig. 5B and C show the analytical curves obtained with the addition of 1 to 10 μmol.L^{-1} procaine hydrochloride standard based on the anodic peak (or oxidation) at 0.60 V (*vs* Ag/AgCl) and cathodic peak (or reduction) at 0.36 V (*vs* Ag/AgCl), respectively.

Tables 7 and 8 list the results of the addition of the procaine hydrochloride standard. Concerning the anodic activity, the voltammetric behavior resembled the behavior of cocaine hydrochloride; that is, both analytes underwent oxidation at 0.6 V (*vs* Ag/AgCl). As for the cathodic

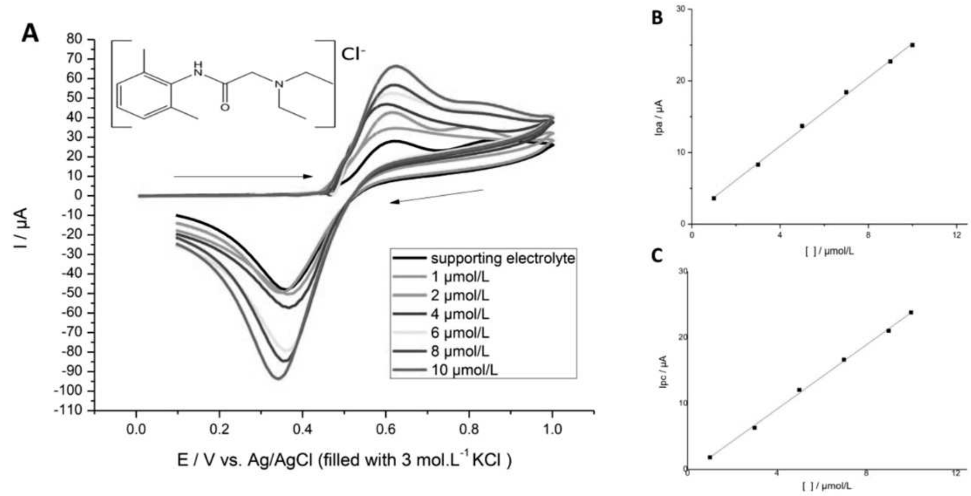

Fig. 4. . (A) cyclic voltammograms of the addition of lidocaine hydrochloride standard using CPE@V^{II}O(salen) in 0.1 mol.L^{-1} KCl supporting electrolyte and scan speed of 100 mV.s^{-1} and analytical curve obtained for the lidocaine concentration in the linearity range of 1 to 10 μmol.L^{-1}, based on the (B) anodic (or oxidation) peak at 0.62 V (*vs.* Ag/AgCl) and (C) cathodic peak (or reduction) at 0.35 V (*vs.* Ag/AgCl).

Table 5
. Statistical data from the analysis of the oxidation of lidocaine hydrochloride using the CPE@V^{II}O(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	2,42 (±0,002)	1,22 (±0,05)	0,126 (±0,038)	0,17 (±0,45)	0,52 (±0,35)	0,986 (±0,009)
Measure 2, day 1	2,38 (±0,003)	1,36 (±0,08)	0,414 (±0,023)	0,57 (±0,28)	1,73 (±0,05)	0,998 (±0,003)
Measure 1, day 2	2,35 (±0,002)	1,64 (±0,002)	0,776 (±0,003)	1,08 (±0,09)	3,30 (±0,15)	0,994 (±0,011)

Table 6
. Statistical data of the analysis of the reduction of lidocaine hydrochloride using the CPE@V^{II}O(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	2,45 (±0,005)	−0,675 (±0,02)	0,508 (±0,011)	0,68 (±0,09)	2,07 (±0,09)	0,997 (±0,013)
Measure 2, day 1	2,43 (±0,006)	−0,606 (±0,11)	0,465 (±0,016)	0,63 (±0,08)	1,91 (±0,11)	0,998 (±0,004)
Measure 1, day 2	2,42 (±0,004)	−0,581 (±0,05)	0,519 (±0,009)	0,70 (±0,07)	2,14 (±0,15)	0,997 (±0,005)

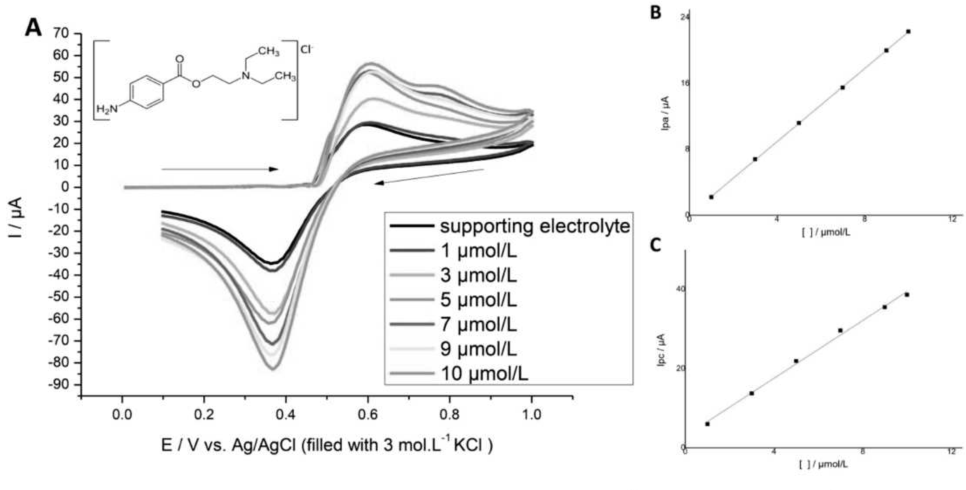

Fig. 5. . (A) cyclic voltamograms of the addition of procaine hydrochloride standard using CPE@V^{II}O(salen) in 0.1 mol.L^{-1} KCl supporting electrolyte and 100 mV. s^{-1} scan rate, and analytical curve obtained with the addition of 1 to 10 μmol.L^{-1} of the procaine hydrochloride standard based on the (B) anodic (or oxidation) peak at 0.60 V (*vs.* Ag/AgCl) and (C) cathodic (or) peak reduction) at 0.36 V (*vs.* Ag/AgCl).

Table 7

. Statistical data from the analysis of the oxidation of procaine hydrochloride using the CPE@V^{II}O(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	2,22 (±0,001)	0,452 (±0,087)	0,105 (±0,098)	0,15 (±0,09)	0,47 (±0,34)	0,999 (±0,001)
Measure 2, day 1	2,21 (±0,003)	0,122 (±0,002)	0,631 (±0,034)	0,94 (±0,02)	2,85 (±0,09)	0,995 (±0,003)
Measure 1, day 2	2,31 (±0,004)	0,749 (±0,018)	0,481 (±0,046)	0,68 (±0,03)	2,08 (±0,11)	0,997 (±0,003)

Table 8

. Statistical data of the analysis of the reduction of procaine hydrochloride using the CPE@V^{II}O(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	3,90 (±0,011)	0,991 (±0,023)	0,196 (±0,011)	0,16 (±0,002)	0,50 (±0,001)	0,987 (±0,011)
Measure 2, day 1	3,64 (±0,009)	0,029 (±0,078)	0,188 (±0,009)	0,17 (±0,001)	0,51 (±0,002)	0,995 (±0,004)
Measure 1, day 2	3,87 (±0,015)	0,011 (±0,098)	0,198 (±0,012)	0,16 (±0,002)	0,51 (±0,003)	0,986 (±0,017)

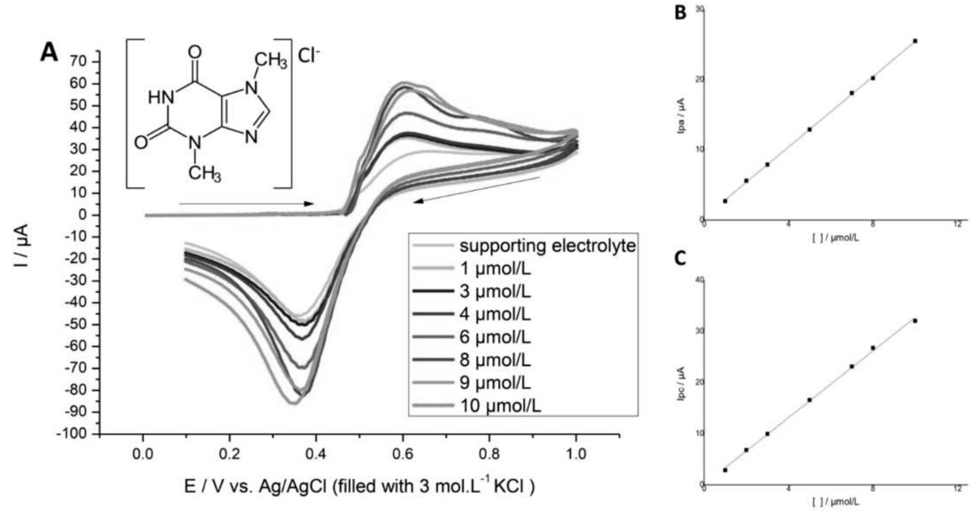

Fig. 6. . (A) cyclic voltammograms of the addition of theobromine hydrochloride standard using CPE@V^{II}O(salen) in 0.1 mol.L^{-1} KCl supporting electrolyte and scan rate of 100 mV.s^{-1}, and analytical curve obtained for theobromine concentration in the linearity range of 1 to 10 μmol.L^{-1}, based on the (B) anodic (or oxidation) peak at 0.60 V (*vs.* Ag/AgCl) and (C) cathodic peak (or reduction) by 0.34 V (*vs.* Ag/AgCl).

activity, oxidation occurred at 0.35 V (*vs* Ag/AgCl) for lidocaine hydrochloride and 0.40 V (*vs* Ag/AgCl) for caffeine hydrochloride.

We obtained higher values of analytical sensitivity (s): 2.2 and 3.8 μmol.L^{-1}/μA for the anodic and cathodic activities, respectively, which were two- and threefold higher as compared to the cocaine hydrochloride standard.

We selected a procaine hydrochloride concentration of 7 μmol.L^{-1} (mean concentration among those used here) to evaluate the intra- ($n = 9$) and inter- ($n = 9$) day repeatability studies. The anodic studies had coefficients of variation of 2.89% and 4.02%, respectively, while the cathodic studies had coefficients of variation of 3.11% and 4.19%, respectively. The relative standard deviation for nine measurements was 0.91% (anodic study) and 0.88% (cathodic study), indicating that CPE@V^{II}O(salen) had good stability and repeatability, within a confidence level of 95%. The recovery tests gave values of 95% and 102.01% in the anodic and cathodic studies, respectively.

Theobromine hydrochloride analyses

Fig. 6A shows the cyclic voltammograms of the theobromime hydrochloride standard in the presence of CPE@V^{II}O(salen) in 0.1 mol.L^{-1} KCl, as supporting electrolyte, at a scan rate of 100 mV.s^{-1}. Fig. 6B and C show the analytical curves obtained with the addition of 1 to 10 μmol.L^{-1} theobromine hydrochloride standard based on the anodic peak (or

Table 9

. Statistical data from the analysis of theobromine hydrochloride oxidation using the CPE@V^{II}O(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	2,50 (±0,002)	0,376 (±0,011)	0,222 (±0,023)	0,29 (±0,34)	0,88 (±0,45)	0,999 (±0,002)
Measure 2, day 1	2,48 (±0,003)	0,223 (±0,009)	0,625 (±0,017)	0,83 (±0,01)	2,52 (±0,02)	0,996 (±0,003)
Measure 1, day 2	2,47 (±0,001)	0,338 (±0,008)	0,358 (±0,016)	0,47 (±0,23)	1,44 (±0,11)	0,998 (±0,002)

Table 10

. Statistical data of the analysis of theobromine hydrochloride reduction using the CPE@V^{II}O(salen) through the analysis by CV.

REPETITION	Sensitivity (s) [μmol.L^{-1}/μA]	Intercept[μA]	SD[μA]	LOD[μmol.L^{-1}]	LOQ[μmol.L^{-1}]	R
Measure 1, day 1	3,25 (±0,002)	0,175 (±0,078)	0,629 (±0,009)	0,63 (±0,09)	1,93 (±0,14)	0,997 (±0,002)
Measure 2, day 1	3,26 (±0,001)	0,930 (±0,023)	0,573 (±0,014)	0,58 (±0,11)	1,75 (±0,21)	0,998 (±0,004)
Measure 1, day 2	3,24 (±0,003)	0,200 (±0,078)	0,750 (±0,011)	0,76 (±0,03)	2,31 (±0,09)	0,996 (±0,001)

Table 11

. Resizing of variables for principal components (PC).

CLASS	1	2	3	4	5
PC	2	3	5	4	4

oxidation) at 0.60 V (*vs* Ag/AgCl) and cathodic peak (or reduction) at 0.34 V (*vs* Ag/AgCl), respectively.

Tables 9 and 10 list the results of the addition of the procaine hydrochloride standard. Concerning the anodic activity, the voltammetric behavior resembled the behavior of cocaine hydrochloride; that is, both analytes underwent oxidation at 0.6 V (*vs* Ag/AgCl). As for the cathodic activity, oxidation occurred at 0.34 V (*vs* Ag/AgCl) for theobromine hydrochloride and 0.40 V (*vs* Ag/AgCl) for caffeine hydrochloride.

We obtained higher values of analytical sensitivity (s): 2.4 and 3.2 μmol.L^{-1}/μA for the anodic and cathodic activities, respectively, which were two- and threefold higher as compared to the cocaine hydrochloride standard.

We selected a theobromine hydrochloride concentration of 6 μmol. L^{-1} (mean concentration among those used here) to evaluate the intra- ($n = 9$) and inter- ($n = 9$) day repeatability studies. The anodic studies had coefficients of variation of 3.23% and 4.65%, respectively, while the cathodic studies had coefficients of variation of 3.01% and 4.43%, respectively. The relative standard deviation for nine measurements was 0.87% (anodic study) and 0.79% (cathodic study), indicating that CPE@V^{II}O(salen) had good stability and repeatability, within a confidence level of 95%. The recovery tests gave values of 99.87% and 100.98%in the anodic and cathodic studies, respectively.

Finally, Chart 1 shows data, such as oxidation potential (E_{ox}), reduction potential (E_{red}), and sensitivity (s), for each of the five studied analytes. All the analytes had similar electrochemical activity, including anodic activity at 0.6 V (*vs* Ag/AgCl) and cathodic activity around 0.40 V (*vs* Ag/AgCl), albeit with different sensitivities.

Caffeine hydrochloride was the only interferent with lower sensitivity than cocaine hydrochloride, whereas the other interferents (lidocaine, procaine, and theobromine hydrochlorides) showed two- to threefold higher sensitivity than cocaine hydrochloride. As demonstrated, we could say that CPE@V^{II}O(salen) is an excellent sensor for these analytes that are widely used in food and related industries.

3.2.5. Chemometric analysis

To investigate the potential use of CPE@VO^{II}(salen) as sensor for cocaine detection and quantification through chemometric tools, we identified, classified, and separated redox peak of cocaine hydrochloride from the redox peaks of the possible interfering agents.

We performed supervised classification of the results obtained by using CPE@V^{II}O(salen) as the working electrode in two stages: **(1)** training, in which we divided different samples into five classes of analytes (cocaine, caffeine, lidocaine, procaine, and theobromine) and **(2)** external validation with 3 real samples and 15 simulated samples. Thus, through the SIMCA training model, we structured the analyzed samples of analytes into five classes, namely Class 1 (caffeine hydrochloride), Class 2 (cocaine hydrochloride), Class 3 (lidocaine hydrochloride), Class 4 (procaine hydrochloride), and Class 5 (theobromine hydrochloride).

Table 12

. Analysis result using SIMCA for sample prediction.

MISCLASSIFICATIONS	C1 (Pred.)	C2 (Pred.)	C3 (Pred.)	C4 (Pred.)	C5 (Pred.)
C1 (Orig.)	24	0	0	0	0
C2 (Orig.)	0	24	0	0	0
C3 (Orig.)	0	0	21	0	0
C4 (Orig.)	0	0	0	21	0
C5 (Orig.)	0	0	0	0	24
INTERCLASS RESIDUES	Class 1	Class 2	Class 3	Class 4	Class 5
Class 1	0,06	0,74	2,67	1,09	3,03
Class 2	6,97	0,50	1,51	1,64	1,34
Class 3	11,62	2,27	0,43	2,47	1,39
Class 4	8,90	1,54	1,90	0,40	1,41
Class 5	10,68	1,46	1,14	1,97	0,56
INTERCLASS DISTANCES	Class 1	Class 2	Class 3	Class 4	Class 5
Class 1	0	12,76	26,20	20,67	18,56
Class 2	12,76	0	3,11	2,48	1,63
Class 3	26,20	3,11	0	4,25	1,54
Class 4	20,67	2,48	4,25	0	2,48
Class 5	18,56	1,63	1,54	2,48	0

Table 13

. Prediction result for real samples using the SIMCA model.

SAMPLE	PREDICITON CLASSES	COCAINE PROPORTION
SAMPLE 1	2	–
SAMPLE 2	0	–
SAMPLE 3	2	–
SAMPLE 1	2	20 μmol.L^{-1}
SAMPLE 2	2	25 μmol.L^{-1}
SAMPLE 3	2	30 μmol.L^{-1}
SAMPLE 4	5	20 μmol.L^{-1}
SAMPLE 5	3	25 μmol.L^{-1}
SAMPLE 6	3	30 μmol.L^{-1}
SAMPLE 7	5	20 μmol.L^{-1}
SAMPLE 8	5	25 μmol.L^{-1}
SAMPLE 9	0	30 μmol.L^{-1}
SAMPLE 10	0	20 μmol.L^{-1}
SAMPLE 11	0	25 μmol.L^{-1}
SAMPLE 12	0	30 μmol.L^{-1}
SAMPLE 13	2	60 μmol.L^{-1}
SAMPLE 14	2	50 μmol.L^{-1}
SAMPLE 15	2	50 μmol.L^{-1}

The variables were the scanning potentials applied in cyclic voltammetry, which ranged cyclically from 0 to 1.2 V. We did not detect the presence of anomalous samples (outlier) in the training set. As a result of the modeling, we entered the variables rewritten as principal components, summarized in Table 11.

Table 12 presents the result of the predictions. To verify the result, we used three indicators: misclassification, interclass residual, and interclass distance. In the first case, there was no misclassification. The values of the interclass residual were higher in the different classes than in the class used as comparison. In tur, the values of the interclass distances were greater than the class used as a comparison.

Table 14
. Quantification data of seized cocaine samples by CV using CPE@V^{II}O(salen).

WORKING ELECTRODE	IDENTIFICATION	Ip (μA)	PURITY (%)•
CPE@$V^{II}O(salen)_{oxi}$	A*	7789	59,60
	B#	6686	50,38
	C#	6100	45,76
CPE@$V^{II}O(salen)_{red}$	A*	7150	57,93
	B#	6174	48,72
	C#	5523	42,88

[*] crack;.
[#] cocaine power.

With the created model and its delimited parameters, we forecasted real and simulated samples (Table 13). By using CPE@V^{II}O(salen) in this prediction, identified two samples (1 and 3) as belonging to Class 2, which corresponded to cocaine, as well as a sample that was not predicted in any of the five classes present in the model. We were able to demonstrate that the developed SIMCA model was able to identify and to predict in which of the samples the illicit substance was present by using the same modeling properties.

For the simulated samples, we could observe some trends within the set of responses, which would not be possible with real samples because the simulated samples are controlled samples and may not contain all the studied adulterants. These observations were that: **(i)** in proportions greater than 50% of cocaine, cocaine is correctly identified (Samples 13–15); **(ii)** the SIMCA model, in this case, correctly predicted lidocaine proportions lower than 45% correctly; and **(iii)** caffeine, procaine, and theobromine may be difficult to predict in samples. However, in a forensic context, the latter analytes would not represent a technical-legal problem because they are not illicit substances. Thus, within this dataset, we observed a trend for more effective prediction of cocaine compared to the other analytes.

3.2.6. Chromatographic analysis

When a sensor to detect and to quantify any substance of forensic interest is developed, it is necessary to validate it by comparison with another methodology. Thus, we chose to use high performance liquid chromatography (HPLC) for this purpose. Through voltammetric and chromatographic analyses, we compared parameters such as analytical sensitivity, limit of detection, limit of quantification, repeatability, reproducibility, and recovery test.

The results of the HPLC analyses of the cocaine standard at concentrations ranging from 10 to 150 μmol.L^{-1} afforded standard deviation (SD) of 2376.49 mAU, limit of detection (LOD) of 6.58 μmol.L^{-1}, and limit of quantification (LOQ) of 21.93 μmol.L^{-1}. The intra- and inter-day repeatability studies (n = 9) showed deviations of 3.99 and 5.78%, respectively, and the recovery test indicated a value of 110.26%.

In the end of the HPLC analyses, the three seized samples presented purity of 58.37% (sample A), 49.28% (sample 2) and 41.6% (sample C). Bernardo et al. verified the presence of adulterants in seized samples. In their study, carried out with 209 seized samples, they detected caffeine (50.2%), lidocaine (65%), and procaine (11%) in addition to pharmacologically inactive adulterants such as starch, carbonates/bicarbonates, and sugars [51]. The authors also showed that the cocaine content ranged from 2.8 to 63.3% in the analyzed samples. The low purity of these samples was worrying because the adulterants therein could modify or intensify the signs and symptoms of intoxication, which could be acute or even fatal [51].

Maldaner et al. described the gas chromatography chemical profile (purity, level of oxidation, and cutting agents) of the main components in 642 cocaine samples seized in five different Brazilian states between 2011 and 2014. This study revealed that cocaine corresponded to 49.8% of the seized samples [52]. The study presented very detailed data, showing that the free base samples had an average cocaine content of 66.0%, while the cocaine hydrochloride samples had a cocaine content of 44.5%. Regarding adulterants, the study showed that approximately 34% of all the analyzed samples contained none of the analyzed adulterants. Cocaine base samples were even less adulterated, with phenacetin present in 53% (average 15%) of them. Caffeine and lidocaine were the major adulterants used in hydrochloride samples [52].

Table 15
. Comparison of different electrochemical methods for determining cocaine.

WORKINGELECTRODE	Sensitivity (s) (μmol.L^{-1}/μA)	LOD (μmol. L^{-1})	LOQ (μmol. L^{-1})	Ref.
CPE@[U^{II}O(salen)]	0,06	0,326	1,10	[35]
CPE@[Mn^{II}(salen)]	0,33	0,96	3,21	–
CPE@[Co^{II}(salen)]	0,086	0,35	1,18	–
CPE@[V^{II}O(salen)]	1,36	0,86	2,88	This Wok.
CPE@[V^{II}O(salen)]	1,20	0,31	1,03	This Wok.

SPEs: Screen-Printed Electrode**; PtE:** Platinum electrode**; GCE:** Glassy Carbon electrode**; CPE:** Carbon Paste Electrode**.**

Table 16
. DFT evaluations of the oxidation–reduction mechanisms proposed in the literature.

HYPOTHESIS	REAGENTS	PRODUCTS
1	[V^{II}O(salen)] + 1 mol cocaine hydrochloride	$[VO^{IV}(salen)]^{2+}$ + 1 mol reduced cocaine
2	[V^{II}O(salen)] + 1 mol cocaine hydrochloride	$[VO^{IV}(salen)]^{2+}$ +1 mol oxidized cocaine + 1 mol formaldehyde

Table 17
. Energy values for each of the calculation hypotheses.

HYPOTHESIS	ΔEE (10^5kcal/ mol)	ΔH (10^5kcal/ mol)	ΔS (kcal/ mol)	ΔG (10^5kcal/ mol)	ΔG (KeV)
1	−2,41	−2,41	0,50	−2,41	−10,46
2	−2,88	−2,88	11,92	−2,88	−12,49

Chart 1
. Summary of the average of the data resulting from the analysis by cyclic voltammetry of cocaine, caffeine, lidocaine, procaine and theobromine hydrochloride using CPE@V^{II}O(salen) as working electrode in 0.1 mol.L^{-1} KCl supporting electrolyte .

COCAINE HYDROCHLORIDE MOLECULAR STRUCTURE	E_{OXI}	E_{RED}	SENSITIVITY (s)[μmol.L^{-1}/μA]
	0,60 V	0,40 V	1,22 (I_{pa}) 1,21 (I_{pc})
CAFFEINE HYDROCHLORIDE			
	0,60 V	0,40 V	0,27 (I_{pa}) 0,54 (I_{pc})
LIDOCAINE HYDROCHLORIDE			
	0,62 V	0,35 V	2,38 (I_{pa}) 2,43 (I_{pc})
PROCAINE HYDROCHLORIDE			
	0,60 V	0,36 V	2,24 (I_{pa}) 3,80 (I_{pc})
THEOBROMINE HYDROCHLORIDE			
	0,60 V	0,34 V	2,48 (I_{pa}) 3,25 (I_{pc})

We quantified the same three samples by voltammetry using CPE@VO^{II}(salen) as the working electrode. Table 14 shows the results of the seized samples. On the basis of cyclic voltammetry, we found mean purities of 59.68 (± 1.26), 50.08 (± 0.99),and 43.30 (± 1.20) for samples A, B, and C, respectively, which was in accordance with the purity presented by Bernardo et al. (2003) and Maldaner et al. [51,52]. Finally, in Table 15, we compare the amperometric sensitivity of

CPE@VO^{II}(salen).

3.2.7. Computational analysis

To verify the interactions between the cocaine molecule and [$V^{II}O$ (salen)] and to confirm the mechanisms proposed in the literature [49, 51,52], we made calculations by the DFT method for the molecules alone and for the possible products according to the reduction and oxidation mechanisms. Table 16 presents all the evaluations we made to verify the most probable mechanisms through simulation of the reactants and products; we considered the stoichiometric coefficients. Table 17 provides the energy values found for each of the calculation hypotheses. In all cases, we obtained a favorable free energy value for the process. In this way, the DFT calculations conformed the reported experimental behaviors.

4. Conclusion

A voltammetric sensor is based on the use of a working electrode that has good sensitivity, selectivity, and specificity. Thus, we were able to develop a voltammetric sensor for detection of cocaine hydrochloride based on a carbon paste electrode chemically modified with [$V^{II}O$ (salen)], evaluated by two methodologies, namely cyclic voltammetry and SIMCA. We showed that the developed sensor effectively detects cocaine hydrochloride, with parameters such as sensitivity, selectivity, and specificity as good as HPLC parameters, widely used in forensics nowadays. The proof of redox mechanisms obtained by the DFT method revealed the scientific nature of the oxidation reaction and answered questions related to the functioning of the sensor.

Declaration of Competing Interest

The corresponding author, in the name of all authors, declares that there is no conflict of interests in the proposed article.

Best Regards,

Marcelo Firmino de Oliveira

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.talo.2021.100079.

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