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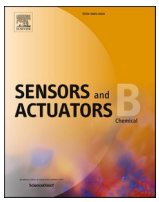

Novel colorimetric-electrochemical methods for selective identification and quantification of Scopolamine in forensic analysis using screen-printed graphite electrodes and Dragendorff reagent

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ABSTRACT

In forensic investigations, the detection of Scopolamine, popularly known as Burundanga or Devil's Breath, is of significant interest due to its potential involvement in cases of attempted murder or suicide. Currently, no efficient screening methods exist for Scopolamine detection in such forensic contexts. This study presents a novel method combining screen-printed graphite electrodes (SPGE) with square-wave voltammetry (electrochemical step) and Dragendorff reagent (colorimetric step) to detect Scopolamine in drinks (gin, tonic water, whisky, and energy drinks) and biological samples (urine, saliva, and vitreous humor). The method provides two distinct analytical responses: a visible color change (from orange to yellow) via the colorimetric reaction, and the electrochemical behavior of Scopolamine in both anodic and cathodic scans, ensuring robust and accurate identification. For the first time, the electrochemical behavior of both redox processes of Scopolamine is investigated. The proposed method demonstrated a wide linear range (0.025-0.225 mg mL^{-1} for the oxidation and 0.025–0.175 mg mL^{-1} for the reduction process) with a low limit of detection of 5.0 μg mL^{-1}, making it suitable for forensic applications. Stability of the electrochemical response was studied with SPGE showing relative standard deviations (RSD) of less than 3 % for E_p and I_p across multiple electrodes (N = 3). Interference studies confirmed the method's high selectivity for Scopolamine detection. Additionally, Scopolamine was successfully identified in both beverage and biological samples with recoveries near 100 %, indicating the absence of matrix effects. The methodology using both electrochemical with a colorimetric approach presents a promising, rapid, and selective screening method for Scopolamine detection in forensic scenarios.

1. Introduction

Scopolamine (Scopolamine) is a tropane alkaloid extracted from plants of the Solanaceae family, such as *Hyoscyamus niger*, *Datura stramonium*, and *Scopolia carniolica* [1]. It works by inhibiting the action of acetylcholine in the central and peripheral nervous systems [2,3]. Clinically, Scopolamine is used for its anticholinergic properties to prevent motion sickness, control postoperative nausea and vomiting, and serve as a premedication agent in anesthesia due to its sedative effects [3]. It is also used in ophthalmology to induce mydriasis and cycloplegia for diagnostic procedures [4]. Scopolamine is available in several formulations, including transdermal patches, oral tablets, and injectables, making it a versatile agent in medical practice [5].

However, this molecule presents toxic effects in high doses, and therefore it can be used as a poison in cases of attempted murder or suicide [6]. In excessive amounts, Scopolamine induces severe symptoms such as mental confusion, hallucinations, memory loss, paralysis, tachycardia, respiratory failure, and ultimately death [7]. There are reports of Scopolamine being used in criminal activity, often referred to as "Devil's Breath" or "Burundanga", used to incapacitate victims in

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situations such as robbery or kidnapping [6,8,9]. In forensic settings, ingestion of Scopolamine can result in fatal poisoning, making it a substance of concern in toxicological analyses due to its potential misuse in homicidal or suicidal acts [9].

Currently, there are only a few analytical methods for Scopolamine detection described in the literature, which are based on liquid chromatography [10,11], ultra-high performance liquid chromatography combined with time-of-flight mass spectrometry (UHPLC–ToF-MS) [12], optical detection [13], and capillary electrophoresis [14–16]. Although chromatographic methods are robust and commonly used for definitive identification of substances of forensic interest, they are not suitable for preliminary and on-site analysis due to their complexity, large equipment, and high cost per sample tested. However, electroanalytical methods offer an attractive alternative that can provide a cheaper, simpler, and portable platform for on-site screening of forensic samples [17,18].

Electrochemical sensors have demonstrated their prominent applicability in the detection of illicit drugs and poisons [17–27]. Among these, screen-printed graphite electrodes (SPGE) have garnered significant attention due to their simple design, disposability, portability, low mass manufacturing cost, and the minimal sample volume (microliters) required for analysis [28–40]. Additionally, the complementary application of colorimetric methods to assist the electrochemical analysis offers a cost-effective, rapid, and highly sensitive approach for both qualitative and quantitative analyses, which can effectively eliminate the need for sample pretreatment [41,42] facilitating the on-site screening of forensic compounds across diverse matrices.

Interestingly, only a few reports involving the electrochemical detection of Scopolamine have been found in the literature. Costa Oliveira et al. proposed the application of batch injection analysis – square wave voltammetry (BIA-SWV) on a boron-doped diamond (BDD) thin film deposited on a silicon wafer for the analysis of Scopolamine in beverages and urine samples [43]. Similarly, Santos et al. applied a standard BDD electrode for the voltammetric analysis of Scopolamine in pharmaceutical formulations [44]. Both methodologies required subsequent anodic and cathodic surface pre-treatments prior to use. Gañán et al. reported the intricate modification of carbon paste electrode (CPE) with synthesized mesostructured silicas derived from 2-mercaptopyrimidine and application for Scopolamine analysis in tea samples [45]. However, after each voltammetric measurement, the CPE surface required surface regeneration by performing 2 or 3 voltammetric scans in blank solution.

In this study, we introduce a novel approach that, for the first time, applies both colorimetric and electrochemical methods for a fast on-site screening and determination of Scopolamine in beverages and biological samples of forensic interest. The colorimetric method utilizes Dragendorff reagent, a well-established solution used for the qualitative detection of alkaloids, including nitrogen-containing compounds such as scopolamine [46]. It has been successfully reported for derivatization in Scopolamine detection using chromatographic methods [47,48], prompting further interest in its use as a colorimetric reagent. Upon reaction with alkaloids present in biological samples or extracts, Dragendorff forms an orange or yellow precipitate, facilitating visual identification [46].

The simplicity and high selectivity of this reaction make it particularly advantageous for rapid analytical testing. Furthermore, this study investigates, for the first time, the utilization of both anodic and cathodic Scopolamine redox peaks for enhanced quantification of this substance in real complex samples using electrochemical techniques on a laboratory-produced screen-printed graphite electrode (SPGE). The integration of square-wave voltammetry with colorimetric testing offers a more comprehensive analytical approach, aligning with international guidelines that required confirmation of the presence of a substance by more than one analytical method [49]. This two-step approach proposed in this work will provide with a rapid, cost-effective, and direct screening method for Scopolamine detection in both beverages and biological samples relevant to forensic investigations, offering enhanced selectivity and robustness in detection.

2. Experimental

2.1. Reagents, samples and materials

Solutions were prepared using deionized water with a resistivity of no less than 18.2 MΩ cm, obtained from a Milli-Q Integral 3 system (Millipore, Watford, UK). The Scopolamine analytical standard (purity $\geq$ 98 %) and Dragendorff reagent were acquired from Sigma-Aldrich (Lancashire, UK). Stock solution (10 mg mL^{-1}) of Scopolamine was prepared by dissolving it in methanol, which was then diluted 10-fold in a supporting electrolyte prior to the electrochemical analysis. Electrochemical investigations of Scopolamine were conducted in a Britton-Robinson (BR) buffer solution (0.1 mol L^{-1}), consisting of an equimolar mixture of boric, phosphoric, and acetic acids, with the pH adjusted between 2.0 and 12.0 using 1.0 mol L^{-1} NaOH. Citrate, phosphate, and BR buffer solutions (0.1 mol L^{-1}, pH 3.0) were also tested as supporting electrolytes, and varying concentrations (0.05 and 0.1 mol L^{-1}) of BR buffer were examined to determine the effect of ionic strength on Scopolamine detection. A redox probe of 0.1 mmol L^{-1} ferrocyanide in 0.1 mol L^{-1} KCl was used to calculate the electroactive area.

Potential interferents for Scopolamine detection, including uric acid (UA), citric acid (CA), ascorbic acid (AA), caffeine (CAF), glucose (GLU), and fructose (FRU), were evaluated using the proposed method. All reagents were of analytical grade and obtained from Sigma-Aldrich (Lancashire, UK). For real sample analysis, subsequent aliquots of gin, whiskey, tonic water, and energy drink were spiked with 0.25 mg mL^{-1} of Scopolamine. Synthetic biological samples, including artificial saliva, synthetic urine, and artificial vitreous humor, were also prepared according to the methods described by Qian et al. [50], Laube et al. [51] and Thakur [52], respectively.

2.2. Instrumental and apparatus

Voltammetric experiments were conducted using a PGSTAT 204 potentiostat (Metrohm Autolab BV, Utrecht, The Netherlands), controlled by NOVA 2.1 software. The electrochemical behavior of Scopolamine was characterized with screen-printed graphite electrodes (SPGE) produced in the laboratory. These electrodes consisted of a 0.07 cm^2 graphite working electrode, a carbon auxiliary electrode, and an Ag/AgCl reference electrode. The production and characterization of these materials have been reported in our previous work [53–55]. It is worth noting that in all experiments, only the SPGE pseudo-reference electrode (*vs.* Ag/AgCl) was used.

Electrochemical studies were conducted using cyclic voltammetry on a SPGE under varying scan rates and pH conditions. Before each measurement, SPGE was electrochemically conditioned in a 0.1 mol L^{-1} BR buffer solution (pH 3.0) by performing five successive scans within the potential range of −0.4 V to + 0.6 V (*vs.* Ag/AgCl). Scopolamine detection was optimized using square-wave voltammetry on SPGE, yielding optimal parameters of 30 mV amplitude, 10 mV step potential, and 10 Hz frequency. The voltammograms obtained by square-wave voltammetry were processed using background subtraction with polynomial fitting in OriginPro 2016 software. The colorimetric analysis was carried out in standard ELISA transparent well plates by mixing 50 μL of Scopolamine stock solution or methanol (as a negative control) with 150 μL of Dragendorff reagent.

3. Results and discussion

3.1. Feasibility of colorimetric screening of Scopolamine using Dragendorff reagent

In this work, the proposed method was developed in two distinct steps: (1) a colorimetric test using Dragendorff's reagent and (2) an electrochemical step using a SPGE, where the anodic and cathodic scans were employed for the selective detection of Scopolamine. To the best of our knowledge, this is the first demonstration of using Dragendorff reagent as a colorimetric reagent for Scopolamine detection, as well as the first investigation of both electrochemical processes (oxidation and reduction) of Scopolamine for quantification purposes.

Dragendorff's reagent is widely used for the detection of alkaloids due to its ability to form precipitates or induce color changes when reacting with nitrogenous compounds [46]. Its composition includes bismuth nitrate, potassium iodide, and acetic acid, creating a sensitive and selective solution [56]. The reagent is commonly applied in forensic, pharmaceutical, and scientific analyses, enabling the identification of alkaloids in various matrices [57,58]. However, its use is limited to qualitative analyses, as the reaction intensity does not exhibit a linear correlation with the analyte concentration, restricting its application in precise quantifications [59,60]. Nonetheless, it remains valuable as an initial or complementary step in more robust analytical methods.

The colorimetric reaction occurs because alkaloids containing a tertiary amine group (R_3N) can react with acids to form ammonium salts. These salts subsequently undergo an ion-exchange reaction that occurs between the ammonium salt and potassium tetraiodobismuthate, resulting in the formation of an insoluble complex salt [46]. Similarly, the tertiary amine group in Scopolamine can react with Dragendorff's reagent, to produce an insoluble complex salt, as proposed below Scheme 1:

The ion pair formed between Scopolamine and tetraiodobismuthate modifies the orange complex of potassium tetraiodobismuthate, yielding a yellow precipitate (Scheme 1). The stability of this reaction was evaluated over periods ranging from 1 to 15 minutes, as shown in Figure S1 of the Supplementary Information. The results indicate that the color stability remains consistent even after 15 minutes of the colorimetric reaction.

It is worth noting that a further electrochemical detection after the colorimetric reaction was also explored (step 3). However, the presence of Dragendorff's reagent in the solution introduced significant noise in the electroanalytical responses, making an accurate quantification of Scopolamine voltammetric peaks difficult. This is likely due to the complex chemical composition of Dragendorff's reagent (sodium iodide, acetic acid, ethyl acetate, and sodium tetraiodobismutate), which, even after dilution in the supporting electrolyte, resulting damage to the surface of the SPGE working electrode. This can be verified in the Scanning Electron Microscopy (SEM) images of SPGE after Scopolamine analysis alone (Figure S2 A and B) and after Scopolamine analysis in the presence of Dragendorff's reagent (Figure S2 C and D). In Figure S2, it is evident that the graphite surface of the SPE undergoes "flaking" in the presence of the colorimetric reagent. Consequently, colorimetric, and electrochemical methodologies (steps 1 and 2) were investigated independently. The electrochemical performance of the electrode was evaluated through scan rate studies using the near-ideal inner-sphere redox probe $[Fe(CN)_6]^{4-}$ (1.0 mmol L^{-1} in 0.1 mol L^{-1} KCl), enabling the determination of the heterogeneous electron transfer rate constant (k_o) and the electrochemical surface area (A_e) [61]. Representative scan rate studies (5–250 mV s^{-1}) for SPGE are shown in Figure S3. A k_o value of 3.32 ($\pm$ 0.02) $\times$ 10^{-3} cm s^{-1} was calculated for SPGE, along with an electroactive surface area of 0.06 ($\pm$ 0.0026) cm^2.

Next, the colorimetric step was optimized as follows: 50 µL of Scopolamine standard solution (10 mg mL^{-1}) or methanol (as a negative control), 150 µL of Dragendorff reagent solution was added for the colorimetric reaction. Then, an orange color was observed in the absence of Scopolamine, while a clear color change to yellow (and a slight precipitate) indicated the presence of Scopolamine, as shown in Fig. 1A.

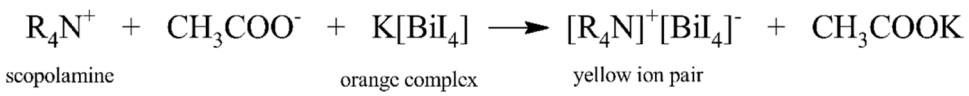
3.2. Electrochemical behavior of Scopolamine

The electrochemical behavior of Scopolamine was investigated using cyclic voltammetry in 0.1 mol L^{-1} BR buffer solution across a pH range from 2.0 to 12.0, as depicted in Fig. 1B using SPGE. Scopolamine displays two irreversible oxidation (O_1 and O_2) processes and two irreversible reduction (R_1 and R_2) processes. Notably, the oxidation process O_2 is detectable only at pH values exceeding 5.0. This behavior is likely related to the molecule's pKa (6.45) [62], as scopolamine molecules in their protonated amine form start to appear in the solution at pH $\geq$ 5.0. A pH-dependent behavior was observed only for processes O_2 and R_2, with peak potentials shifting to more negative values as the pH increased. This is shown in Figure S4 A along with the linear regression equations in Table S1. The obtained slope for R_2 of 0.048 V/pH is very close to the theoretical value of 0.0592 V/pH, indicating that equal number of electrons and protons are involved in this reduction process. This observation is further corroborated by the proposed mechanism discussed in Section 3.2. In contrast, processes O_1 and R_1 exhibited no pH dependence, indicating that protons are not involved in these reactions. A pH of 3.0 was selected for scopolamine detection using SPGE, as it provided good peak resolution and adequate peak currents (Figure S4 B). Then, three supporting electrolytes were evaluated at this pH such as citrate, phosphate, and BR, as shown in Figure S5 A, where BR displayed the best response. Next, BR buffer at two different concentration levels were evaluated to assess the effect of ionic strength on scopolamine voltammetric behavior (Figure S5 B). A BR buffer concentration of 0.1 mol L^{-1} was found to be the most effective and was chosen for further studies.

Under these conditions, cyclic voltammetry studies varying the scan rate (ν), 10–600 mV s^{-1}, were conducted to evaluate the mass transport behavior of Scopolamine redox processes (O_1 and R_2) on SPGE, as shown in Figure S6 A. The peak current (I_p) for O_1 showed a stronger correlation with the square root of the scan rate (Figure S6 C) than with the scan rate itself (Figure S6 B), suggesting that the electrochemical processes are predominantly diffusion-controlled at the SPGE surface. In contrast, the R_2 process exhibited good linearity in both cases, indicating that it involves a combination of diffusion- and adsorption-controlled mass transport. The logarithmic plots of I_p *vs.* ν displayed linear relationships (Figure S6 D) in both cases, with the equations provided in Table S2. The slopes ($\leq$ 0.5 for O_1 and >0.5 for R_2) confirm that O_1 is primarily diffusion-controlled, while R_2 shows a mixed diffusion- and adsorption-controlled process. These findings likely indicate that the reduction process exhibits slower reaction kinetics.

3.3. Square-wave voltammetry of Scopolamine on SPGE and redox mechanism

After confirming the colorimetric reaction between Dragendorff and



Scheme 1. Proposed reaction between Scopolamine and Dragendorff reagent.

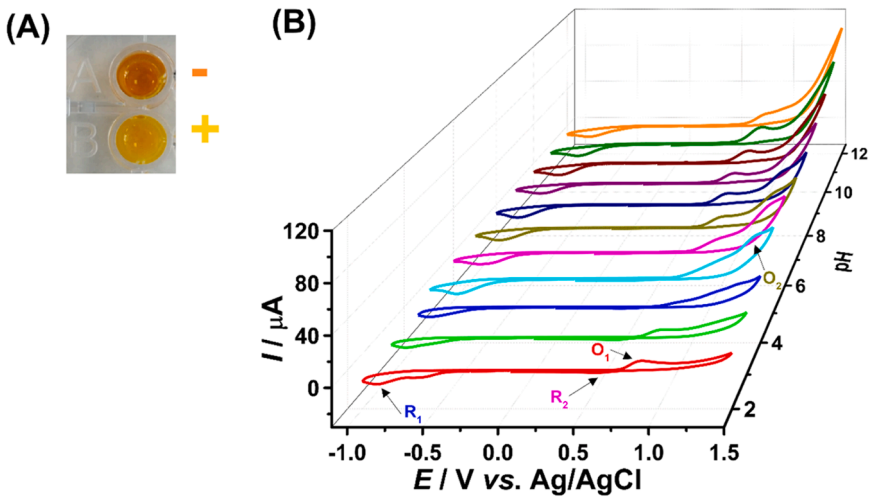


Fig. 1. (**A**) Colorimetric test result using Dragendorff reagent in the absence (orange) and in presence (yellow) of 1.0 mg mL^{-1} Scopolamine. (**B**) 3D plots of recorded cyclic voltammograms (first scan) of 0.25 mg mL^{-1} Scopolamine in 0.1 mol L^{-1} BR buffer solution with different pH values (from 2.0 to 12.0). All potential scans started at 0.0 V (*vs.* Ag/AgCl), with a scan rate of 50 mV s^{-1}.

Scopolamine and studying thoroughly Scopolamine redox processes in cyclic voltammetry, we next move to develop a square-wave voltammetric methodology for a sensitive detection of Scopolamine in forensic samples. It is important to note that the electrochemical step was performed independently of the colorimetric step, with only Scopolamine present in the solution – without the interference of Dragendorff reagent. Note that both the oxidation and reduction processes of Scopolamine were utilized for its qualitative and quantitative identification in the electrochemical step, providing a more selective electroanalytical approach, which is particularly important for screening analytes in complex samples. Under optimal conditions (50 mV amplitude, 10 mV step potential, and 10 Hz frequency), repeatability and reproducibility tests were conducted using the same (N = 3) and different (N = 3) SPGE where anodic and cathodic voltammetric peaks obtained by square-wave voltammetry are depicted in Fig. 2, while the stability of the colorimetric response with time has already been demonstrated in Figure S1 and discussed in Section 3.1.

The electrochemical step utilizes the peak potential (E_p) of Scopolamine for preliminary identification in forensic samples. The proposed method demonstrates consistent measurements across different assays using SPGE (Fig. 2). The SPGE combined with square-wave voltammetry showed good stability for the electrochemical responses of both the oxidation and reduction processes of Scopolamine, with low relative standard deviations (RSD) for E_p (< 2.5 %) and I_p (< 3 %). This stability and reliability show that an SPGE combined with square-wave voltammetry is an effective and promising screening method for Scopolamine detection; based on the square-wave voltammetric results and considering both anodic and cathodic process undertaken by Scopolamine on SPGE, we propose for the first time the following redox mechanism for Scopolamine (Scheme 2).

Scopolamine consists of a tropane structure containing an epoxide ring bonded to carbons 6 and 7. The electrooxidation course of Scopolamine has been previously proposed suggesting an oxidation of the terminal alcohol, which results in an aldehyde-derived form (Scheme 2 A) [44]. Here, we report for the first time a non-reversible reduction process (R_2) at low potential (+ 0.5 V *vs.* Ag/AgCl), which is independent of oxidation (O_1). Scheme 2 shows a proposed reduction of Scopolamine (1). The reduction of the epoxide group is characterized by a two-proton, two-electron step resulting in an enantiomeric mixture of the derived alcohols (3). The large torsional and angular strains present in the epoxy rings make them quite reactive even at low potential, as observed here.

3.4. Electroanalytical performance of Scopolamine on SPCE-Gr

Next, the linear working range for Scopolamine determination on

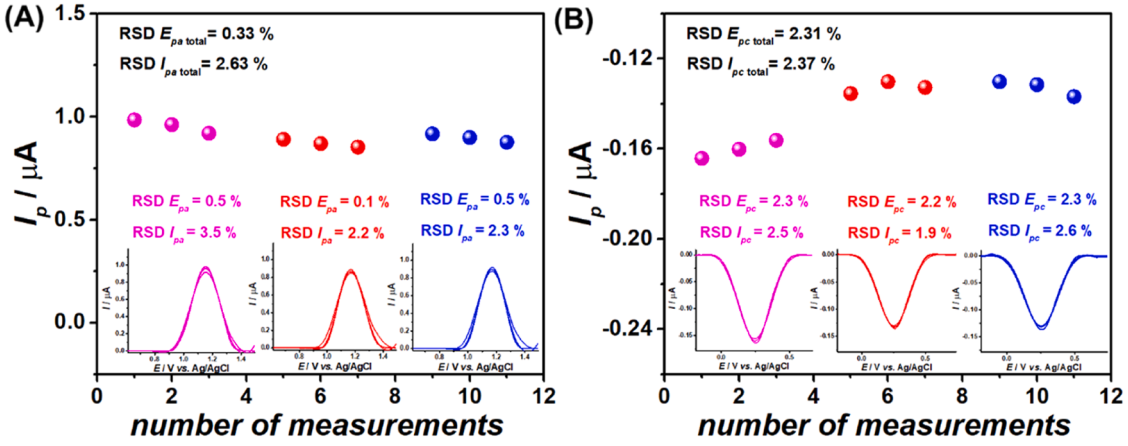
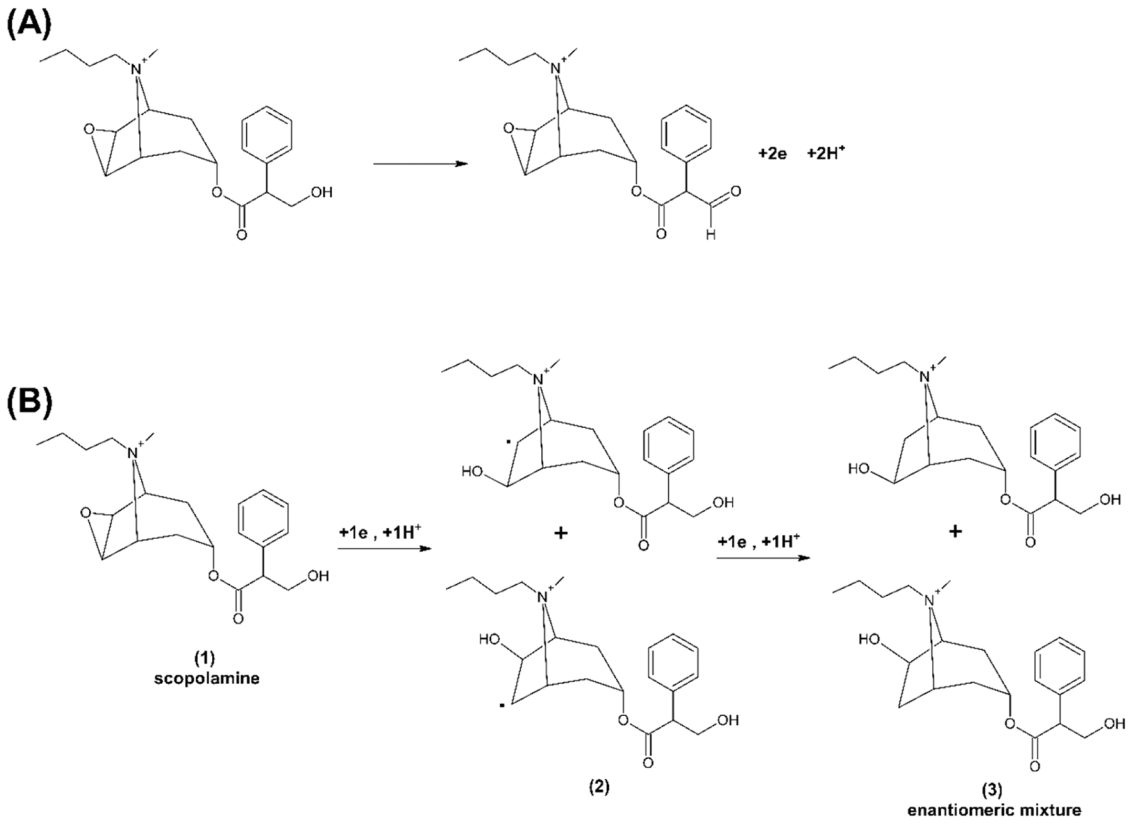


Fig. 2. Plot of I_p *vs.* number of measurements performed on three different SPGE. Insets are voltammograms recorded by SWV of 0.25 mg mL^{-1} Scopolamine in 0.1 mol L^{-1} BR buffer solution at pH 3.0. Experimental conditions: amplitude of 50 mV, step potential 10 mV, and frequency 10 Hz. Anodic (A) and cathodic (B) scans.



Scheme 2. Proposed oxidation (A) and reduction (B) mechanism of Scopolamine.

SPCE-Gr was evaluated using standard solutions of the analyte ranging from 0.025 to 0.25 mg mL^{-1}, as shown in Fig. 3, for both the oxidation and reduction peak.

As shown in Fig. 3, a linear range ($R^2 > 0.996$) between 0.025-0.225 mg mL^{-1} was obtained for Scopolamine quantification using the oxidation process, while a linear range ($R^2 = 0.995$, 0.025–0.175 mg mL^{-1}) was obtained for Scopolamine quantification via the reduction process. This demonstrates that both redox processes observed for Scopolamine can be employed for its quantification. It is worth noting that a wide range of concentrations was tested in the colorimetric assay, although Scopolamine is harmful to the human body at doses exceeding 20 mg / kg [63]. The linear regression equations are provided in Table S3 – SI.

A calculated theoretical limit of detection (LOD) of 0.005 (O_1) and 0.008 (R_2) mg mL^{-1} was derived using the equation $3S_B/m$ [64], where S_B denotes the standard deviation (N = 10) of the background (blank) signal, and m is the slope of the calibration curve. The limit of quantification (LOQ) was found to be 0.017 (O_1) and 0.027 (R_2) mg mL^{-1} using the equation $10S_B/m$ [64]. These low detection levels for Scopolamine demonstrate the suitability of the proposed method for real forensic sample analysis. While adults have survived doses exceeding 100 mg, ingestion of as little as 10 mg has been reported to be lethal in children though precise data on fatal Scopolamine doses remain scarce [65–67]. The method shows high sensitivity for Scopolamine screening by combining two independent yet complementary techniques: a colorimetric step using Dragendorff reagent and an electrochemical step via

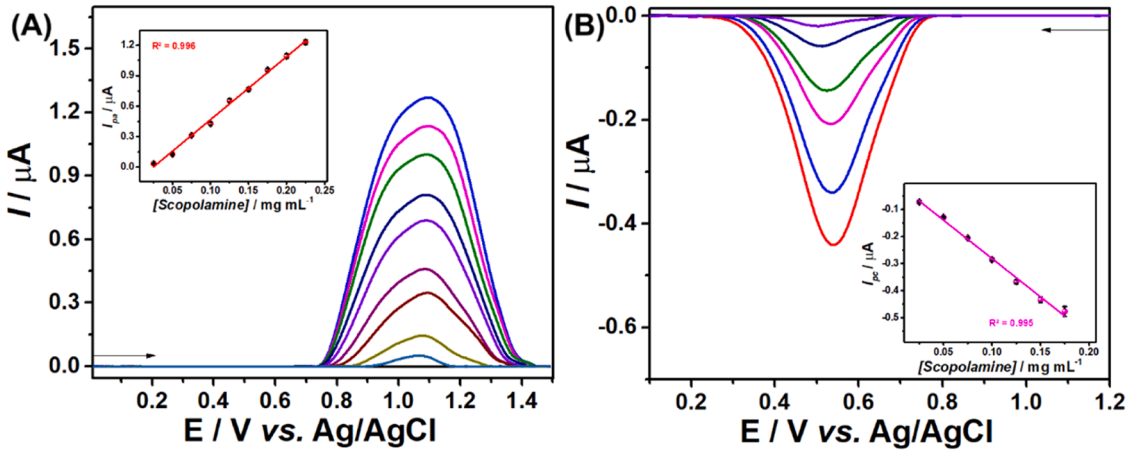


Fig. 3. Square-wave voltammograms in 0.1 mol L^{-1} BR buffer solution at pH 3.0 (blank: black line) on SPGE before and after addition of 0.025 – 0.25 mg mL^{-1} Scopolamine. The experimental conditions were the same as in Fig. 2. Inset show linear regression. All measurements were performed in triplicate and the error bars were smaller than the symbol presented in the inset. Anodic (A) and cathodic (B) scans.

SW voltammetry. While each technique operates independently, together they provide a comprehensive range of analytical information, enhancing both qualitative and quantitative identification of Scopolamine. This dual approach is particularly valuable in forensic analyses, allowing for more reliable and accurate reports on Scopolamine detection.

3.5. Interference study and determination in forensic samples

To evaluate the real-world applicability of the proposed method in beverage and biological samples, an interference study was conducted for the detection of FLU, FRU, CAF, UA, CA, and AA. The results from these interference studies are presented separately for the oxidation and reduction processes. Additionally, the outcomes of the colorimetric test, along with the negative control (methanol – orange color), are shown in Fig. 4 A. A comparison of the Scopolamine electrochemical signal is also illustrated in all graphs (red line).

As shown in Fig. 4, GLU, FRU, and CA did not exhibit redox processes under the studied conditions. In contrast, CAF, UA, and AA displayed oxidation processes at + 1.25 V, + 0.31 V and + 0.21 V (*vs.* Ag/AgCl), respectively. Fig. 4C demonstrates that none of the potential interferents or metabolites analyzed exhibited reduction processes under the studied conditions, enabling a more selective identification of Scopolamine. Additionally, the colorimetric step proved highly selective for Scopolamine, with a color change to yellow occurring only in the presence of this molecule. Although the oxidation processes of AA and UA have peak potentials sufficiently distant from that of Scopolamine for selective detection in mixtures, CAF exhibits an oxidation process at a potential close to that of Scopolamine, which may cause peak overlap at high concentrations. However, using the proposed method, a range of analytical responses provides greater reliability in confirming the presence of Scopolamine. Even if there is signal overlap in the oxidation process, the cathodic scan remains available for analysis, alongside the color change in the colorimetric step, which also contributes as a highly selective qualitative response for Scopolamine identification. Thus, the proposed method, which combines independent colorimetric and electrochemical steps while exploring both anodic and cathodic scans in the electrochemical analysis, demonstrates high selectivity for real samples containing Scopolamine. Biological samples, including artificial saliva, urine, and vitreous humor, were spiked with Scopolamine and evaluated using the proposed method (Fig. 5). Beverage samples such as tonic water, gin, whisky, and energy drink, also spiked with Scopolamine, were analyzed for Scopolamine identification. All samples were spiked with 0.125 mg mL^{-1} of Scopolamine and assessed using the proposed method, with the recovery results presented in Table 1.

Fig. 5 shows that the electrochemical behavior of Scopolamine in biological samples was consistent with the standard behavior of this substance. Therefore, the proposed method is effective for the identification of Scopolamine in saliva, urine, and vitreous humor (VH) samples, both through the colorimetric result (a color change to light yellow) and the redox processes of Scopolamine. It is worth noting that in the VH matrix, the colorimetric test exhibited a lighter color, likely due to the sample's pH. As indicated in Table 1, Scopolamine can be quantified across all studied matrices (beverages and biological samples) with good recovery values using both oxidation and reduction processes, with recoveries ranging from 99 (± 2) to 145 (± 5)% for oxidation process and 89 (± 2) to 120 (± 4)% for reduction process. This demonstrates that the proposed method is not significantly affected by matrix effects and can be reliably used in real analyses of beverage and biological samples. Table 2 presents a comparison of the main analytical parameters for scopolamine determination using electroanalytical methods reported to date.

As shown in Table 2, the proposed method provides a linear range and a higher LOD compared to other reported electroanalytical methods. However, it is important to note that for forensic applications involving attempted homicide or suicide using scopolamine, the concentrations typically found in beverages and biological samples are high [65–67]. Therefore, the linear ranges and LOD achieved by this method are adequate for practical application. Furthermore, the proposed sensor, which utilizes both the oxidation and reduction of scopolamine, offers a highly selective method that requires a minimal sample volume (45 µL) and eliminates the need for complex electrochemical cells requiring assembly and disassembly. The detection of scopolamine in forensic samples is achieved through a straightforward two-step process — colorimetric and electrochemical —providing significant advantages for forensic analysis by delivering a selective and reliable method

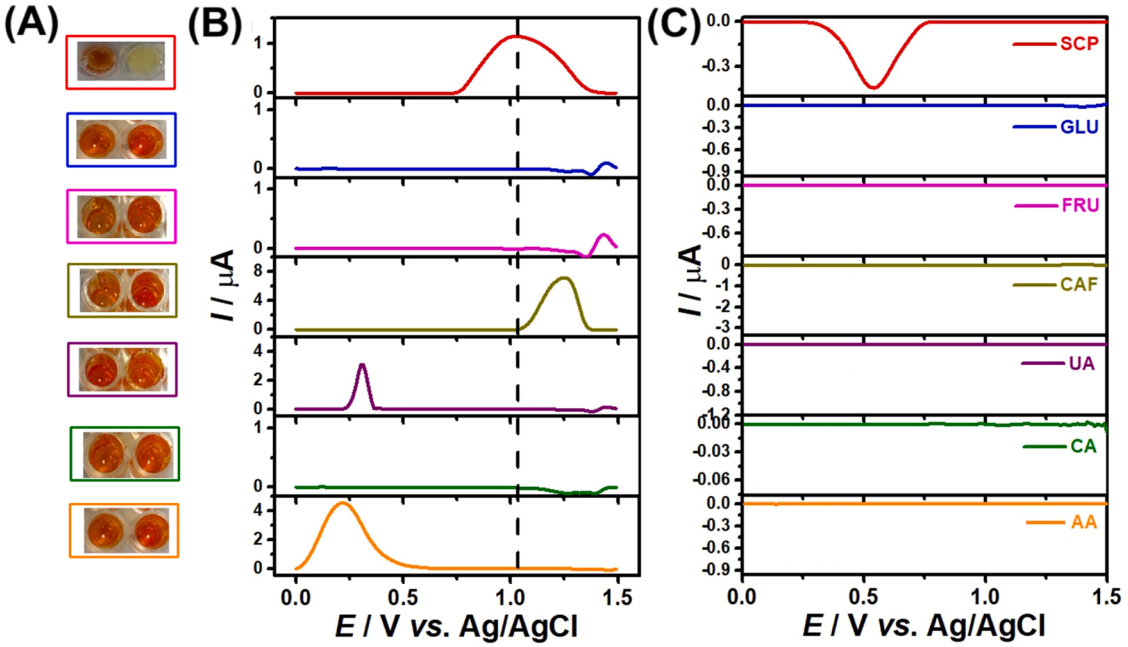


Fig. 4. (**A**) Results of the colorimetric step, all at 2.5 mg mL^{-1}. SWVs voltammograms anodic (**B**) and cathodic (**C**) scans on SPGE. Scopolamine (red line), GLU (blue line), FRU (magenta line), CAF (dark yellow line), UA (purple line), CA (olive line) and AA (orange line). All compounds were at a concentration of 0.25 mg mL^{-1} in 0.1 mol L^{-1} BR buffer solution pH 3.0. The experimental conditions were the same as in Fig. 2.

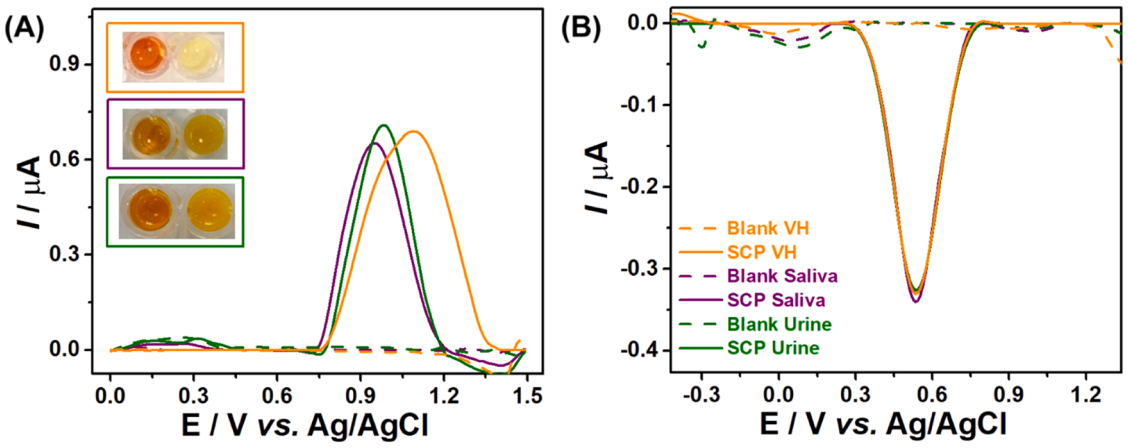


Fig. 5. Square-wave voltammograms anodic (A) and cathodic (B) scans on SPGE. VH (orange line), saliva (purple line), and urine (olive line), in absence (dash) and in the presence of 0.125 mg mL^{-1} Scopolamine (solid), in 0.1 mol L^{-1} BR buffer solution pH 3.0. The experimental conditions were the same as in Fig. 1. Inserted the results of the colorimetric test.

Table 1
Recovery (± RSD) for I_p of 0.125 mg mL^{-1} Scopolamine in 0.1 mol L^{-1} BR buffer solution (pH 3.0) for drink and biological samples.

	Recovery % (I_p)		
Drink		**O_1**	**R_2**
	Gin	144.7 (± 3.2)	120.2 (± 3.5)
	Whisky	102.2 (± 2.4)	92.8 (± 2.4)
	Tonic water	145.2 (± 5.1)	116.9 (± 2.9)
	Energy drink	112.7 (± 2.7)	90.3 (± 2.3)
Biological	**Artificial Saliva**	99.4 (± 1.9)	92.8 (± 1.8)
	Synthetic Urine	108.1 (± 3.2)	88.7 (± 2.3)
	Artificial VH	105.1 (± 3.7)	90.1 (± 2.3)

Table 2
Electroanalytical methods for Scopolamine determination.

Technique	Working electrode	Linear range (µmol L^{-1})	LOD (µmol L^{-1})	Sample	Ref.
SWV	BDD	1 – 110	0.84	Pharmaceutical formulations	[44]
DPV	CPE-HMS-MPY	0.9 – 200	0.30	Tea	[45]
BIA-SWV	BDD	1 – 14	0.14	Drinks	[43]
DPV	Pt	1.6 – 1000	0.20	Pharmaceutical formulations	[68]
SWV	SPGE	82 – 742 and 82 – 577	16.5 and 26.4	Drinks and biological samples	This work

SWV: square-wave voltammetry; DPV: differential pulse voltammetry; BIA: batch injection analysis; BDD: boron-doped diamond; CPE-HMS-MPY: carbon paste electrodes modified with mesostructured silicas; Pt: platinum; SPGE: graphite screen-printed electrode.

capable of producing accurate expert reports. Unlike previous studies (Table 2), this work includes an extensive interference study, underscoring the robustness of the method in selectively identifying scopolamine. This robustness is largely attributed to the novel application of the reduction process, which significantly reduces the risk of signal overlapping with other substances that may be present in forensic samples. Additionally, the colorimetric step uniquely changes color only in the presence of scopolamine, further enhancing specificity. To our knowledge, this is the first time the reduction process and the Dragendorff reagent have been applied in tandem for the detection of Scopolamine.

4. Conclusions

This work introduces a novel colorimetric-electrochemical method that forms a strong analytical foundation for generating accurate forensic reports in cases involving Scopolamine-related poisoning or attempted murder. By combining the advantages of both colorimetric and electrochemical techniques, the method offers a highly sensitive, efficient, and reproducible approach for the detection and quantification of Scopolamine in forensic samples. Using square-wave voltammetry using SPGE, Scopolamine was rapidly and sensitively detected in both biological and beverage samples, achieving a LOD of 5.0 µg mL^{-1}. The method relies on both anodic and cathodic electrochemical responses of Scopolamine, alongside a colorimetric test based on Dragendorff reagent, which enables a visible color change in the presence of Scopolamine. The proposed method exhibited excellent reliability in forensic applications, showing good stability across different SPGE (RSD < 0.3 % for E_{pa}, <2.3 % for E_{pc}, < 2.6 % for I_{pa}, and < 2.4 % for I_{pc}). Moreover, with a minimal sample requirement (40 µL), the method is well-suited for portable and on-site analysis, simplifying the process while ensuring accurate results. Therefore, this approach offers a promising, fast, and straightforward alternative for the forensic analysis of Scopolamine in various matrices.

CRediT authorship contribution statement

Larissa M.A. Melo: Conceptualization, Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Elena Bernalte:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Ana C.M. Oliveira:** Formal analysis, Investigation, Methodology. **Robert D. Crapnell:** Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Rodrigo M. Verly:** Writing – original draft, Writing – review & editing, Funding acquisition. **Rodrigo A.A. Munoz:** Writing – original draft, Writing – review & editing, Funding acquisition. **Wallans T.P. dos Santos:** Conceptualization, Writing – original draft, Writing – review & editing, Funding acquisition, Supervision. **Craig E. Banks:** Conceptualization, Formal analysis, Funding acquisition, Project administration, Resources, Supervision, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.snb.2024.137131.

Data availability

Data will be made available on request.

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