Derivatization of amphetamine to allow its electrochemical detection in illicit drug seizures

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Abstract

Amphetamine (AMP) is posing critical issues in our society being one of the most encountered drugs-of-abuse in the current illicit market. The continuous drug production in Europe urges the development of new tools for the rapid on-site determination of illicit drugs such as AMP. However, the direct electrochemical detection of AMP is a challenge because the molecule is non-electroactive at the potential window of conventional graphite SPEs. For this reason, a derivatization step is needed to convert the primary amine into an electroactive oxidizable group. Herein, the rapid electrochemical detection of AMP in seized samples based on the derivatization by 1,2-naphthoquinone-4-sulfonate (NQS) is presented by using square wave voltammetry (SWV) at graphite screen-printed electrodes (SPEs). First, a detailed optimization of the key parameters and the analytical performance is provided. The method showed a sensitivity of 7.9 µA mM^{-1} within a linear range from 50 to 500 µM, a limit of detection of 22.2 µM, and excellent reproducibility (RSD= 4.3%, n=5 at 500 µM). Subsequently, the effect of NQS on common cutting agents for the selective detection of AMP is addressed. The comparison of the method with drugs-of-abuse containing secondary and tertiary amines confirms the selectivity of the method. Finally, the concept is applied to quantify AMP in 20 seized samples provided

by forensic laboratories, exhibiting an accuracy of 97.3±10.5%. Overall, the fast analysis of samples with the electrochemical profiling of derivatized AMP exhibits a straightforward on-site screening aiming to facilitate the tasks of law enforcement agents in the field.

Keywords

Electrochemical profile, derivatization, amphetamine, drug seizures, screen-printed electrodes, forensics

1. Introduction

Amphetamine (AMP) is a central nervous system stimulant to psychologically enhance mood and attention used in medical treatments such as attention deficit, hyperactivity disorder and narcolepsy [1,2]. Moreover, AMP produces a transient psychotic state in healthy individuals by altering dopamine kinetics which is translated into euphoria, reward sensitivity, physical fearlessness, and impulsivity [3,4]. Unfortunately, these effects have led to an abuse of AMP in the society. AMP abuse provokes hyperthermia which can lead to fatal complications, neurotoxicity, depletion of antioxidants, increase in the oxidative stress at the cell level, among others undesired effects [5]. During prolonged used, AMP intoxications might induce severe health issues such as psychosis [6]. Hence, the consumption of AMP is a dangerous activity that has to be strictly monitored and controlled by law enforcement agencies (LEAs).

Estimates of amphetamine-type substances (ATS) use in European Union (EU) are about 2.0 million in adults (15−64) (number reported in the last year use of AMP) [7]. Synthetic drug production in clandestine laboratories appears to be driving the spread of AMP and other ATS in EU and worldwide [8]. The spreading of ATS production has led to a confiscation of 6.4 tons of AMP (in 2017) which accounts for 5% of the total EU drug seizures [8]. Hence, LEAs demands new tools and devices that can be used in a decentralized manner to tackle the ATS spreading in the streets.

AMP is the most adulterated ATS, with an average purity between 19% and 34% in Europe [7]. Caffeine is the most used adulterant found in seized samples, but also diluents such as creatine, lactose and sucrose can be encountered [7,9–11]. **Table 1** summarizes the frequency and concentration ranges of common cutting agents found

in seizures. AMP can be mainly found as a drug-of-abuse in powders but also in tablet form. Considering route of administration, 15% of users reported oral consumption of AMP, 52% reported sniffing and 17% reported injecting [7].

Table 1. Cutting agents and their proportions in seized samples.

Adulterant/ cutting agent	Frequency in seizures[a] (%)	Concentration range[a] (%)	References
Caffeine	58	0.1- 63	[9,10,12–14]
Paracetamol	3	2 - 16	[9,14]
Creatine	34	4 - 51	[14]
Sucrose	39	< 6 – 74	[9,14–16]
Lactose	65	< 9 - 79	[13,14]

Traditionally, the confiscation process starts with a fast analysis of cargos in border settings (e.g. harbors, airports), clandestine laboratories or intercepted street samples by performing presumptive color tests or portable spectroscopic analysis [17,18]. This step determines whether the material should be confiscated and send to a forensic laboratory for a confirmatory analysis. In the laboratory, AMP seized samples are traditionally analyzed by standard methods: (i.e. gas or liquid chromatography – GC/LC– coupled with mass spectrometry –MS–) due to the reliability of the method [19,20]. However, those techniques are not operational in the field due to their high cost, low portability and need for trained personnel. Therefore, there is a demand of portable devices and easy-to-use tests for the detection of AMP in the field. Today, presumptive color tests based on the Marquis reagent and Simon test are widely spread in the forensic community [21]. However, these tests might rise to false positives and true negatives depending on the composition of the sample as well as the subjective misinterpretation of the results according to the operator. Portable spectroscopic methods (i.e., Raman and infrared) are a known alternative to detect illicit drugs in the field [22,23]. These devices exhibit relevant benefits for on-site analysis of suspicious samples. For example: (i) non-invasive tests meaning that the sample remains unaltered after the analysis; (ii) easy or non-existence sample preparation; and importantly, (iii) it is a user-friendly and rapid technique. Still, these methods present some flaws: (i) data analysis needs to be performed by an expert in order to avoid errors in data interpretation, and (ii) cost-effectiveness to fulfill a complete deployment in the field.

Electrochemical sensors for the detection of illicit drugs is becoming an emerging field in forensics as they offer fast, portable, affordable and accurate qualitative and quantitative information in several applications [24–26]. The electrochemical approach is based on the characteristic electrochemical profile (EP) of each compound that reveals the electroactive moieties of the target compound [27–29]. Recently, the EP strategy coupled with electrochemical pretreatments has enhanced the effectiveness toward the selective detection of cocaine [30], and heroin [31] in mixtures with common cutting agents by the use of a graphite screen-printed electrode (SPE). Besides, the integration of data treatment improves the peak analysis as it was proven for the ketamine analysis [32]. Regarding ATS, 3,4-methylenedioxymethamphetamine (MDMA) and para-methoxyamphetamine have already been detected due to their electroactivity in the methylenedioxy group [33]. However, AMP does not contain an electroactive group in its structure in the potential window of a graphite-based SPE, thus the direct AMP detection in a SPE still remains a challenge. Therefore, an indirect detection method is needed (e.g. derivatization of AMP into an electroactive compound). Recently, our group reported a derivatization procedure that introduced formaldehyde to achieve the methylation, via an Eschweiler-Clarke mechanism, of illicit drugs containing primary and secondary amines [34]. Alternative methods such as the use of an immunosensor [35] or membranes (using a potentiometric approach) [36] have been proposed but not successfully reached on-site applications due to expensive fabrication methods and multiple electrode's modification steps.

Several papers used Folin's reagent (i.e. 1,2-naphthoquinone-4-sulphonic acid sodium salt –NQS–) as a chromogenic reagent and derivatizing agent for the determination of pharmaceutical amines using spectrophotometry [37] or to label AMP for its electrochemical reduction after high-performance liquid chromatography [38]. Interestingly, a proof-of-concept was shown based on the derivatization of AMP with NQS [39]. In the latter case, the presence of AMP was monitored via either the decrease of the voltammetric peak corresponding to the electrochemical reduction of the quinone functionality of the NQS or via the increase in a new reduction peak related to reaction between AMP and NQS. However, the work did not exploit the voltammetric oxidation behavior of the system, it did not study the reactivity with similar compounds (i.e. other illicit drugs and cutting agents), and importantly, it was not used for the detection of AMP in seizures.

The present work demonstrates for the first time the fast and accurate detection of AMP in seized samples using the voltammetric oxidation of a derivatized compound on a graphite SPE. The electrochemical profiling of AMP (an intrinsic non-electroactive compound) is based on the derivatization of AMP with NQS, which is subsequently interrogated under square wave-voltammetry (SWV). An easy mixing process of the suspicious powder with hydrogen carbonate buffer (CB) and NQS triggers the chemical reaction into an oxidizable product (**Fig. 1**). First, the electrochemical behavior of the concept is studied by cyclic voltammetry (CV) and SWV. Subsequently, a careful optimization of the parameters is performed. Thereafter, a preliminary study of the EP approach employing common cutting agents encountered in seizures is deeply addressed. Interestingly, the effect of NQS over illicit drugs containing secondary or tertiary amines does not hinder the identification of AMP. Ultimately, the concept is applied for the quantification of AMP in confiscated samples, and compared with the analysis from forensic laboratories. Overall, the fast and easy-to-use electrochemical detection of AMP is presented as a breakthrough for the screening of suspicious powders, aiming to facilitate the tasks of LEAs in the field.

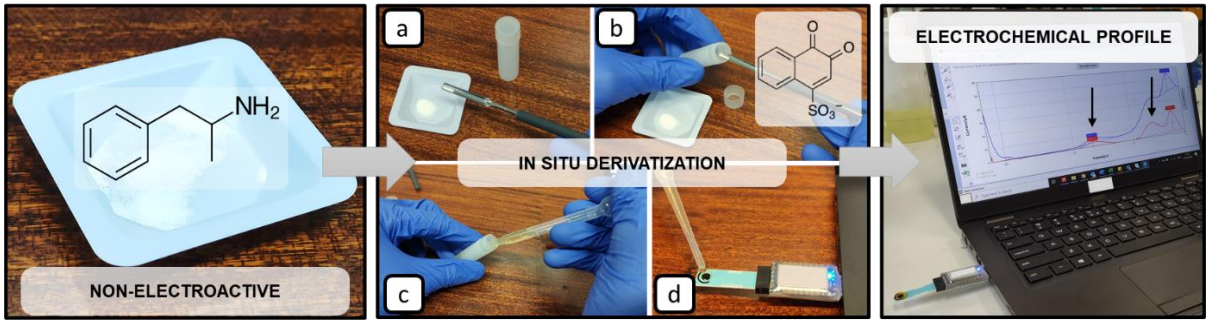

Fig. 1*. Schematics of the concept for the on-site screening of amphetamine (AMP). (a) A suspicious powder is mixed (b) with sodium 1,2-naphthoquinone-4-sulfonate (NQS) in hydrogen carbonate buffer pH 10, (c) thoroughly shaken for in situ derivatization, and (d) deposited on a SPE for the SWV interrogation by a portable potentiostat. The characteristic electrochemical profile is displayed in a laptop or smartphone exhibiting the illicit compound found in the suspicious sample aiming for a confiscation.*

2. Material and methods

2.1. Materials

Standards of d,l-amphetamine·HCl, mephedrone·HCl, methylone·HCl, 4-Cl-alpha-PVP·HCl, methamphetamine·HCl and 3,4-methylenedioxymethamphetamine·HCl

(MDMA) were purchased from Lipomed, Switzerland, and cocaine·HCl and heroin·HCl, were purchased from Chiron AS, Norway. Standards of 3-fluoroamphetamine·HCl, 2-aminoindane·HCl, 5,6-methylenedioxy-2-aminoindane·HCl, cathine·HCl, paracetamol, caffeine and creatine were provided by National Institute for Criminalistics and Criminology (NICC, Belgium). Street samples of AMP in its sulphate form were also provided by the NICC.

Analytical grade salts of potassium chloride, potassium phosphate, sodium borate, sodium bicarbonate, sodium acetate and potassium hydroxide were purchased from Sigma-Aldrich (Overijse, Belgium). 1,2-naphthoquinone-4-sulphonic acid sodium salt (>98%) and N-N-dimethylcyclohexylamine were purchased from Tokyo Chemical Industry Co., LTD., Japan. All solutions were prepared in 18.2 MΩ cm^{-1} doubly deionized water (Milli-Q water systems, Merck Millipore, Germany). The pH was measured using a pH-meter (914 pH/Conductometer, 2.914.0020, Metrohm, Switzerland).

2.2. Methods

Square wave voltammograms and cyclic voltammograms were recorded using a MultiPalmSens4 or EmStat Pico potentiostats (PalmSens, The Netherlands) with PSTrace/MultiTrace. Disposable Dropsens screen-printed electrodes (SPEs) (Metrohm-Dropsens, Spain), containing a graphite working electrode (Ø = 4 mm), a graphite counter electrode, and a (pseudo) silver/silver chloride reference electrode were used for all measurements. The CV parameters that were used: scan rate 0.1V s^{-1} and potential window from -0.6V to 1.4V. The SWV parameters that were used: potential range of 0.0 to 1.4 V, frequency 10 Hz, 25 mV amplitude and 5 mV step potential. All the square wave voltammograms are background corrected using the “moving average correction” (peak width = 1) tool in the PSTrace software.

Electrochemical measurements were performed in 20 mM buffer solutions containing 100 mM KCl by applying 80 µL of the solution onto the SPE. Every measurement was performed with a new SPE and subsequently discarded.

2.3. Amphetamine detection and quantification in street samples

During the analysis of the seized samples, a portable potentiostat connected to a laptop with PSTrace software was used. Regarding sample preparation, a solution of

1.5 mg mL^{-1} of the suspicious powder was prepared in distilled water and thoroughly mixed for 30 s in a 5 mL tube. Thereafter, a 1:10 dilution of the previous solution in CB pH 10 with 5 mM NQS was prepared and let to react for 2.5 min. Finally, a 80 µL drop of the solution is placed at the SPE surface for the electrochemical analysis by SWV .

For the validation of the electrochemical method employing SPEs, qualitative and quantitative analysis of the street samples were performed using the standard methods gas chromatography/mass spectrometry (GC/MS) and gas chromatography/flame ionization detection (GC/FID), respectively, at the forensic laboratory (NICC, Belgium). The applied chromatographic methods are ISO17025 accredited and are continuously evaluated through participation to international quality control programmes (UNODC, ENFSI, NMI).

3. Results and discussion

3.1. Exploration of the electrochemical behavior after AMP derivatization

The electrochemical behavior of AMP through its derivatization with NQS was firstly evaluated by CV (**Fig. 2a**). It is suggested that after mixing the reagents, the primary amine of AMP reacts with the sulfonate group of NQS potentially leading to a secondary amine [39] (**Fig. S1a**). Particularly, the lone pairs of the electron of nitrogen can attack the electron deficiency center of the 4-C of NQS (4-C=C bond conjugates with 2-C=O) leading to a condensation reaction [40]. However, different products have been elucidated and the exact reaction is still unclear [41]. Despite the unknown products being formed, a product of the chemical reaction can be subsequently oxidized at SPE leading to a characteristic electrochemical signal at ca. 0.66V which can be analytically used (**Fig. 2a**). The oxidation and reduction peaks at negative potentials were accounted to the redox behavior of the benzoquinone moiety of NQS (**Fig. 2a**). **Fig. 2b** shows CV consecutive scans of the mixture AMP with NQS showing the redox wave at ca. 0.66V while a decrease in an oxidation peak at ca. 1.2V in comparison to the results obtained with the consecutive scans over a blank SPE (**Fig. S2a**) and with 5 mM NQS (**Fig. S2b**). Indeed, **Fig. S2b** confirmed that the redox wave at ca. 0.66V is due to the formation of a product as a result of the interaction between AMP and NQS. Subsequently, the concept was explored employing SWV technique to unravel a characteristic EP for AMP in a rapid and sensitive manner as well as

avoiding high capacitive background currents [27]. Clearly, **Fig. 2c** exhibited an oxidation peak (P1) at 0.66V only when AMP is present with NQS, proving the oxidation of the derivative product formed during the chemical reaction (see **Fig. S1b** for the suggested electrochemical oxidation at SPE). Moreover, the second oxidation peak from NQS (P2, at 1.18V) decreased, suggesting that a chemical reaction is occurring. The origin of the latter oxidation peak is not elucidated yet and further experiments will follow to understand the nature of the signal. **Fig. 2d** exhibited the SWV with the moving average algorithm from the software which facilitates the interpretation of the results. Note that this data treatment was also employed in the following experiments.

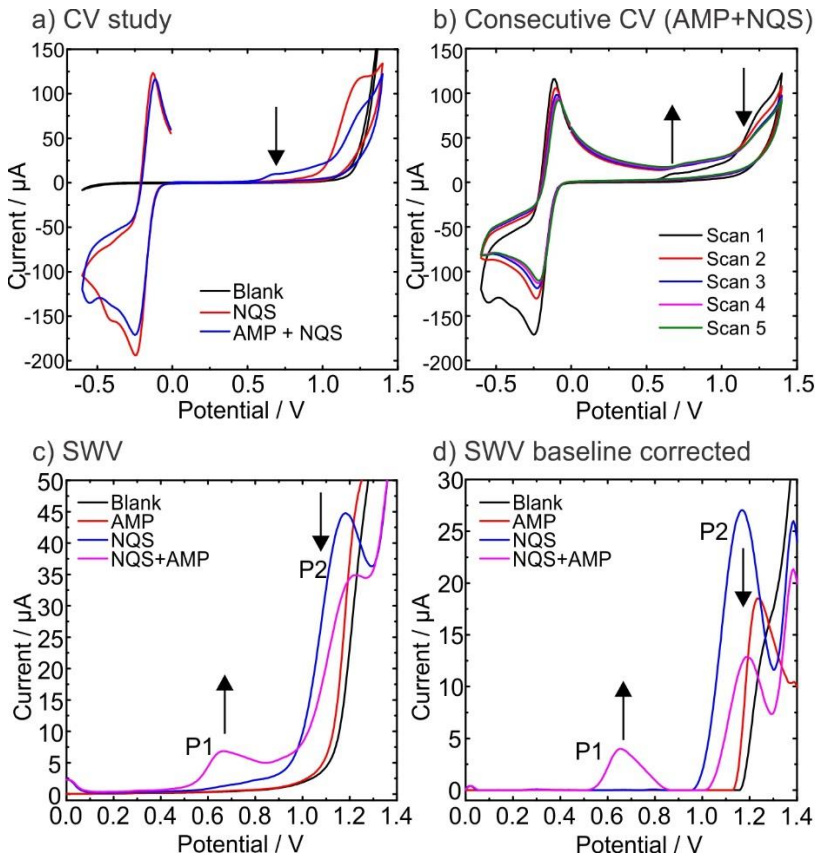

Fig. 2. *Electrochemical study of the sensing method to detect AMP at SPE: a) CV of buffer, 5 mM NQS and 0.5 mM AMP + 5 mM NQS. Start potential at 0V; b) Consecutive CV scans of the mixture of 0.5 mM AMP + 5 mM NQS; c) SWV of buffer, 0.5 mM AMP, 5 mM NQS and 0.5 mM AMP + 5 mM NQS; and d) corrected baseline SWV of the conditions in c). All measurements are performed in 20 mM hydrogen carbonate buffer pH 10. CV scan-rate was performed at 0.1V* s^{-1}*.*

3.2. Optimization of the parameters

3.2.1. Buffer and pH influence

In order to obtain the best analytical performance for the use of the approach in the field, the optimization of the sensor was carefully addressed. Note that all the SWV experiments were launched after 2.5 min of the chemical reaction (i.e. after mixing AMP with NQS) as an optimal time of operation for an on-site test. Following the reported conditions for the chemical reaction between primary amines with NQS [39,42,43], CB was tested at different pH (from 9 – 12) using SWV (**Fig. 3a**). **Fig. 3b** exhibits the shift in peak potential (E_p) as well as in peak current (I_p) according to the pH at test for 1 mM AMP with 5 mM NQS. As the pK_a of amphetamine is 9.9 [5], it is suggested that as more amino group ($-NH_2$) with nucleophilic capability and less protonated amine ($-NH_3^+$) which loses capability as nucleophile for NQS, the better the performance of the chemical reaction, and consequently, higher the electrochemical signal (**Fig. 3b**). Therefore, alkaline pHs effectively remove the proton, facilitating the nucleophilic substitution reaction. However, strong alkaline conditions generate high concentration of hydroxide ion (also with nucleophilic activity) which might compete against the amino group to attack NQS, in consequence, showing a decrease of peak current in strong alkaline media [44]. For this reason, pH 10 was chosen as the optimal condition exhibiting the highest peak intensity. Concerning the oxidation mechanism of the product, E_p displayed a pH relationship with the electrochemical process indicating the participation of protons (**Fig. 3b**). The E_p shifted towards less positive values at more alkaline conditions following the linear relationship E_p (V) =−0.064 pH + 1.31, showing close Nernstian slope (0.059 V pH^{-1} at 298 K), that suggested the transfer of an equal number of protons and electrons in the electrochemical oxidation process.

Fig. 3c shows the comparison between CB and Britton-Robinson buffer (BR) at the selected pH, proving the need for CB to trigger the chemical reaction [39,42,45]. From the SWV analysis of the NQS sample (without AMP) which exhibits an oxidation process at high potential values (<1V) in CB, it is suggested that CB catalyzes the oxidation of AMP-NQS in comparison to BR buffer. Moreover, the influence of the buffer on the chemical reaction was evidenced by the change in color which is visually showed in **Fig. S3**.

3.2.2. Evaluation of NQS concentration and time in the reaction

Importantly, the influence of the concentration of NQS in the EP of 1 mM AMP was evaluated (**Fig. 3d**). As expected, the higher the concentration of NQS, the higher the oxidation peak of the derivatized AMP. In this case, 5 mM was chosen as the optimal concentration as it exhibited the highest current for P1. Higher concentrations of NQS were not evaluated to avoid an increase in the cost per analysis.

The reaction time is a key parameter for a sensitive electrochemical reaction. For this reason, 5 mM NQS (without AMP) and a mixture of 0.5 mM AMP with 5 mM NQS were interrogated by SWV after increasing reaction times (**Fig. 3e** and **Fig. 3f**, respectively). **Fig. 3e** shows a decrease in P2 after some time and the insurgence of a small oxidation peak at 0.78V which might be attributed to the oxidation of a byproduct generated during a possible degradation of NQS at alkaline pH. Presumably, the hydroxide ion with high nucleophilic ability attacks the 4-position sulfonate of NQS at high alkaline conditions producing an oxidizable byproduct [44]. However, further confirmation will be performed in future works to assess the nature of that peak. When AMP is present with NQS (**Fig. 3f**), an oxidation peak appears at 0.66V (P1) which increases while P2 decreases, suggesting that the chemical reaction is occurring over time. As a compromise situation between time of operation and sensitivity of the EP, 2.5 min reaction time was chosen.

The influence of the ionic strength of the buffer over the electrochemical signal was also evaluated exhibiting 20 mM as optimal condition due to buffering capacity and P1 peak intensity (**Fig. 3g**). **Fig. S4** displays the raw voltammograms from **Fig. 3g**, showing an enhancement of the background current at high buffer concentration, thus confirming that 20 mM was the optimal condition.

3.2.3. Assessment of the product formation

To further prove the formation of a product (potentially a secondary amine, **Fig. S1a**) between AMP and NQS, a pH screening test with BR was developed at different pH after performing a previous reaction in a separate batch during 1h containing 1 mM AMP and 5 mM NQS in CB at room temperature. Subsequently, an aliquot from the reaction batch (1 mM AMP with 5 mM NQS after 1 h reaction) was diluted into the corresponding BR buffer at suitable pH (to stop the reaction from the CB) to a concentration of 100 µM, and interrogated by SWV. BR was used because it hinders the chemical reaction between AMP and NQS (**Fig. 3c**), whereas it allows a pH

screening. **Fig. 3h** displays the EP of the product of the reaction at different pHs (black SWV) overlapped with a control experiment (i.e. NQS incubated for the same period without AMP) (green dashed SWV), confirming the formation of an oxidizable product in the presence of AMP. Finally, a complete pH screening of the aforementioned aliquot and the comparison with a compound containing a tertiary amine in its structure (i.e. N-N-dimethylcyclohexylamine) was carried out (**Fig. S5**). The EPs of the product from AMP+NQS reaction and the N-N-dimethylcyclohexylamine exhibited similar behavior in the peak potential of both compounds at pH 9 and 10, showing an evidence of the potential formation of a tertiary amine. In contrast, an expected enhancement of the peak current at pH 11 and 12 did not occurred in comparison to the model molecule N-N-dimethylcyclohexylamine. As previously suggested, the hydroxide ion might strongly attack the NQS at alkaline conditions [44] possibly breaking the former product of AMP and NQS, thus decreasing the expected signal at alkaline conditions (i.e. pH 11 and pH 12).

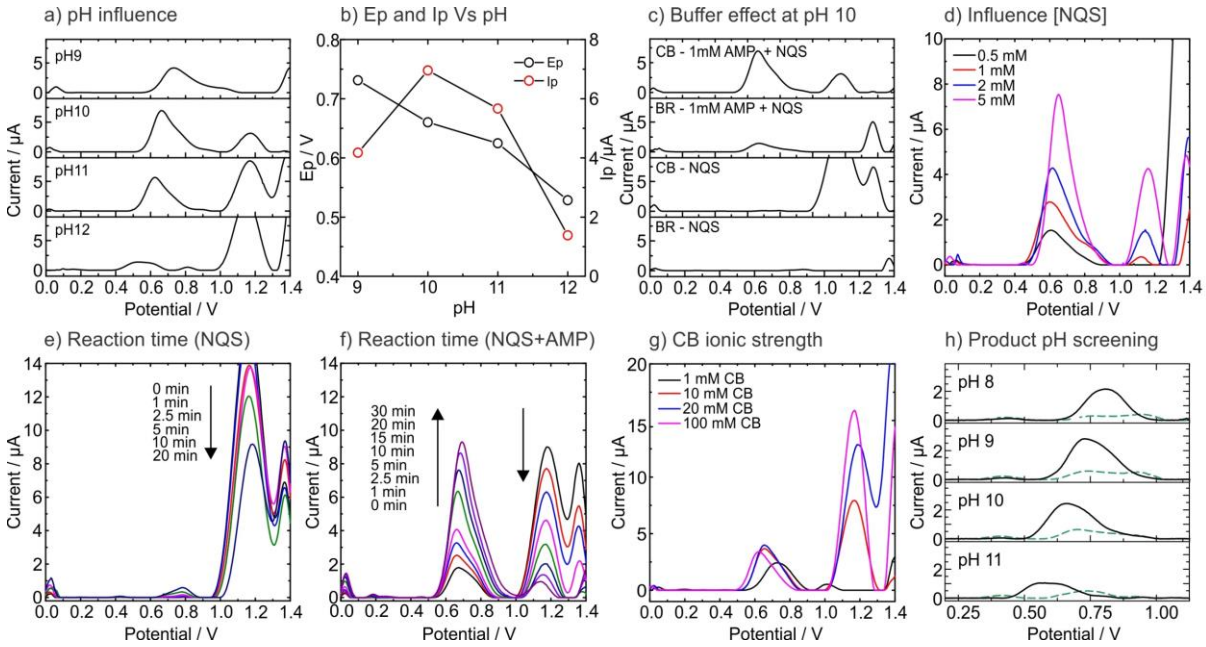

Fig. 3*. Optimization of the electrochemical detection of AMP at SPE: a) Influence of the pH in 20 mM hydrogen carbonate buffer: SWV of 1 mM AMP + 5 mM NQS. b) Representation of the peak potential (E_p) and peak current (I_p) from the SWV at each pH. c) Effect of the buffer at pH 10 on the 5 mM NQS, and 1 mM AMP + 5 mM NQS mixture. d) Influence of the concentration of NQS on 1 mM AMP. e) Study of the time of reaction upon the 5 mM NQS. f) Study of the time of reaction upon the 0.5 mM AMP + 5 mM NQS. g) Influence of the ionic strength of CB (1, 10, 20 and 100 mM) on the electrochemical response of 0.5 mM AMP + 5 mM NQS. h) pH screening (from pH 8 to 11 in BR) of 100 µM of the product (black SWV)*

formed after 1h reaction with 1 mM AMP and 5 mM NQS in CB buffer pH 10 and blank without AMP (green dashed SWV) using same conditions. The reaction time was set at 2.5 min in all the experiments except for the reaction time and product pH screening studies.

3.3. Analytical performance

Fig. 4 shows the analytical performance of the sensor under optimal conditions (i.e. 5 mM NQS, 2.5 min reaction time and 20 mM CB pH 10). **Fig. 4a** exhibits the EP upon increasing concentrations of AMP. Clearly, **Fig. 4a** and **Fig. S6a** (corresponding to the raw SWVs) show an increase in P1 current upon increasing concentrations of AMP while a current decrease at P2. Accordingly, **Fig. 4b** displays the calibration curve from P1 which exhibits a slope of 7.9 µA mM^{-1} within a linear range from 50 to 500 µM and a limit of detection (LOD) of 22.2 µM based on the standard deviation of the response (S_y) and the slope of the calibration curve (S) according to the formula: $LOD = 3.3(S_y/S)$. Standard deviations of the calibration curves were obtained from peak current at P1 (0.66V) by triplicates (**Fig. S6b**). Besides, an excellent reproducibility was obtained at 500 µM for intraday measurements with different SPEs (RSD= 4.3%, n=5, **Fig. S7a**) and 1 mM (RSD= 8.9%, n=4, **Fig. S7b**). In comparison to other electrochemical methods for the detection of AMP which use antibodies or deposition of complex membranes and setups (**Table 2**), the proposed method exhibits a similar analytical performance, but remarkably, a much affordable and easy-to-use solution by the employment of disposable SPEs for the applicability in the on-site detection of AMP.

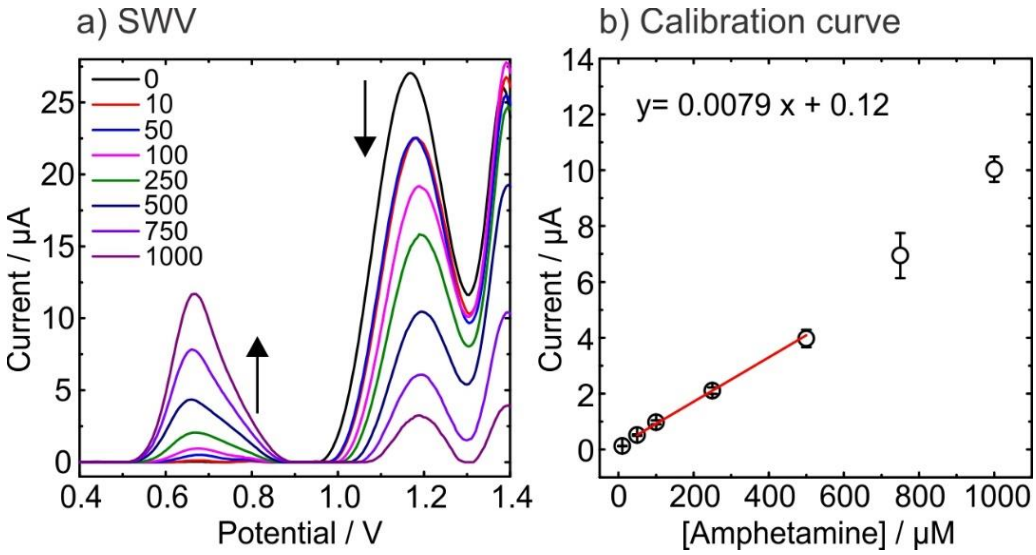

Fig. 4*. AMP detection at SPE: a) SWVs of increasing concentration of AMP from 10 to 1000 µM, and b) corresponding calibration curve with 5 mM NQS in CB pH 10 obtained from the current at 0.66V. Linear range from 50 µM to 500 µM at SPE (n=3) (R^2=0.99). The reaction time was set at 2.5 min.*

Table 2. Electrochemical sensors for AMP detection.

Method	Electrode	LOD	Sensitivity	Linear range	Reproducibility	Recovery or Accuracy	Time of analysis	Ref
AM	Ab/Membrane/Pt	2.5 µM	-	0.74 – 14.8 µM	<15%	-	12 min	[35]
CV and SWV	Gold disk E	30.9 µM	200 µA cm^{-2} mM^{-1}	110.9 – 258.9 µM	-	97.4 – 98.5 % urine	-	[46]
LSV	PGE	22 µM	91 µA mM^{-1}	80 - 560 µM	-	-	-	[39]
PT	ISE	12 µM	60.1 mV $decade^{-1}$	10 - 1000 µM	-	-	10 s	[36]
Transistor	Cucurbit[7]uril / gold E	1 pM	-	1 pM – 1 µM	-	-	-	[47]
ECL	$Ru(bpy)_3]^{2+}$ – Nafion composite	50 pM	2.3 A.U. mM^{-1}	5 nM – 1 mM	4.8%	-	15 s	[48]
SWV	SPE	22.2 µM	7.9 µA mM^{-1}	50 - 500 µM	4.3%	83-113.6% drug seizures*	3 min	This work

Abbreviations: AM: amperometry; DPV: differential pulse voltammetry; ECL: Electrochemiluminescent; GCE: glassy carbon electrode; ISE: ion-selective electrode; LSV: linear sweep voltammetry; PGE: pyrolytic graphite electrode; PT: potentiometry; Pt: platinum; SPE: screen-printed electrode; SWV: square-wave voltammetry.

*Values from the accuracy can be found in **Table S1**.

3.4. Evaluation of the approach with cutting agents and other illicit drugs

AMP is usually adulterated to enhance the psychoactive response, to avoid undesired effects, and to increase drug traffickers' profits while maintaining the drug's weight [7]. **Table 1** reports common adulterants encountered in AMP seizures. Accordingly, the EP of AMP with the most popular adulterants and diluents (i.e. caffeine, creatine, paracetamol, lactose) was investigated at equimolar concentrations (0.5 mM AMP + 0.5mM corresponding cutting agent). **Fig. 5a** clearly exhibits the oxidation peak of the derivatized AMP (P1, 0.66V) as well as the oxidation peaks corresponding to other adulterants (e.g. paracetamol at 0.2V). The diluent lactose did not show any electrochemical signal as it does not contain any electroactive moiety as well as it does not react with NQS. Caffeine oxidation peak occurs at high potentials (< 1V), thus overlapping with the NQS signal. Interestingly, cutting agents were evaluated with

NQS as a control experiment (dashed green line), showing no interaction with the derivatization agent. Therefore, the proposed method allows the selective detection of AMP in commonly adulterated samples.

The derivatization approach was conducted in other illicit drugs with similar structures to AMP containing primary and secondary amines to evidence its potential for forensic applications. First, 3-fluoroamphetamine (3-F-AMP), 2-aminoindaine, 5,6-methylenedioxy-2-aminoindane (MDAI) and cathine were tested as primary amines containing substances (**Fig. 5b**). The same reaction mechanism as in AMP occurred with the aforementioned illicit drugs unravelling an oxidation peak (0.66V) after the NQS reaction in comparison to the voltammetric interrogation without NQS (dashed blue SWV). The only issue was found with MDAI as the electrochemical signal was overlapping with the oxidation peak from the methylenedioxy group, thus widening the output EP. Second, the method was applied to ATS and new psychoactive substances (NPS) containing secondary amines (i.e. methylone, mephedrone, methamphetamine, and MDMA) which are electroactive at the potential window of a carbon SPE (**Fig. 5c)**. In this case, NQS scarcely modified the EP of each drug (comparison with dashed blue SWV for drug without NQS), and importantly, no oxidation peak appeared in the oxidation window of AMP at P1. As an example of a cyclic amine (i.e. pyrrolidine ring), 4-chloro-alpha-pyrrolidinovalerophenone (Cl-PVP) was used. In this case, Cl-PVP overlaps the electrochemical signal of the derivatized AMP. Fortunately, Cl-PVP is not as commonly encountered as MDMA or methamphetamine in street samples, thus it should not be an issue for the implementation of the method in the field. Finally, binary mixtures at equimolar 0.5 mM concentrations of AMP with popular illicit drugs (i.e. cocaine, heroin, MDMA, methamphetamine, mephedrone) were tested to evaluate the capabilities of the method to identify both illicit drugs in a potential sample. **Fig. 5d** unravels the oxidation peak of AMP as well as other illicit drugs, thus allowing for the detection of both drugs in mixtures. The only issue was found in the heroin mixture in which exists a peak overlap shown as a broaden peak in the EP in comparison to pure heroin (green dashed line). The integration of data treatment which facilitates peak separation might overcome this issue similar to previous reported work [31,32]. Overall, the sensor exhibits outstanding performance for the selective detection of AMP in adulterated samples and drugs-of-abuse mixtures.

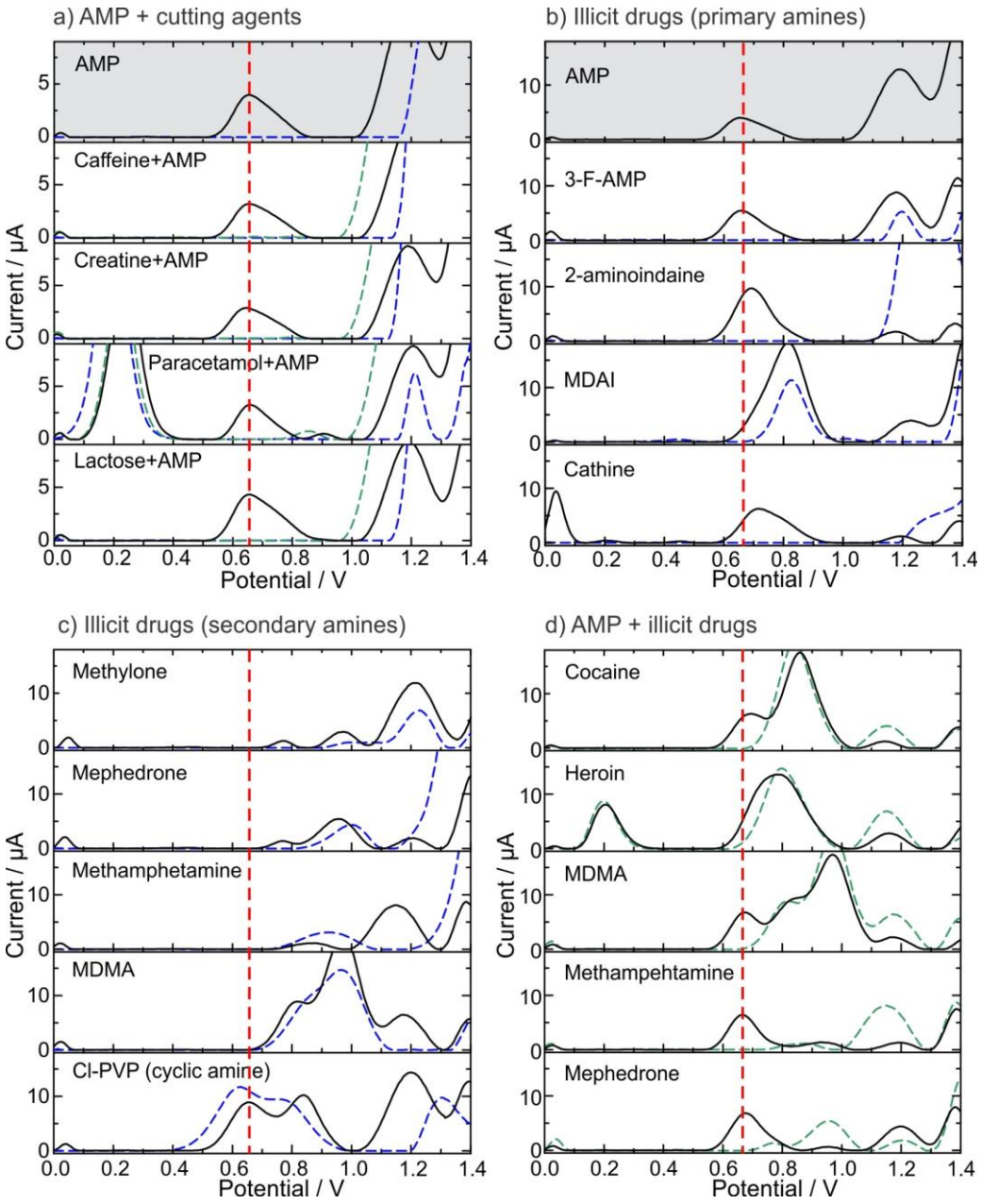

Fig. 5*. Influence of cutting agents and illicit drugs in the chemical reaction with NQS. a) Electrochemical profiles (EP) by SWV of mixtures of AMP and cutting agents (equimolar 0.5 mM). b) EP of illicit drugs holding a primary amine after reaction with NQS. c) EP of ATS and new psychoactive substances (NPS) holding a secondary amine after reaction with NQS. Cl-PVP is included as an example of a cyclic amine. d) EP of binary mixtures of AMP with popular illicit drugs (equimolar 0.5 mM). Dashed blue SWV corresponds to pure cutting agent or illicit drug in CB pH 10. Dashed green SWV corresponds to pure cutting agent or illicit drug in 5 mM NQS CB pH 10. The red dotted line indicates the oxidation peak potential of AMP at 0.66V. 3-F-AMP=3-fluoroamphetamine; Cl-PVP=4-chloro-alpha-pyrrolidinovalerophenone; MDAI=5,6-methylenedioxy-2-aminoindane; MDMA=3,4-methylenedioxymethamphetamine.*

3.5. Testing the concept in confiscated samples

The rapid detection of AMP in the field is an essential duty for LEAs to accurately determine when a cargo needs to be seized. For this reason, this sensing concept aims to assist in the decision-making process of regular LEAs' tasks. Hence, the sensing capabilities of the approach were evaluated in 20 confiscated samples provided by NICC (compositions described in **Table S1**). After the EP analysis, the 20 samples were all positive for AMP reporting consisting results in comparison to the standard methods form the forensic laboratory of GC/MS for the identification of the compounds, and GC/FID for the quantification of each compound (wt. %) in the seized samples. The intraday reproducibility of confiscated samples was also tested by the electrochemical method in sample SS 6.63 (RSD_{Ip}=8.6%, n=3) (**Fig. S7c**). **Fig. 6** displays the EP of the street samples exhibiting an oxidation signal after NQS reaction at ca. 0.66V (black straight line) in comparison to a flat EP when the street samples were analyzed in CB (blue dashed line). Moreover, the peak current at 0.66V corresponding to the oxidation of the AMP-NQS product allowed to calculate the concentration of AMP in the solution according to the previous calibration curve, and consequently, perform the validation with the standard method. Hence, the concentrations of 18 samples examined by the forensic laboratory employing the GC-FID technique, were used for comparison. Remarkably, the electrochemical sensor exhibited an accuracy of 97.3±10.5% (n=17) in confiscated samples ranging from 4.9 to 100 wt. % of AMP (**Table S1**). Besides, a paired t-test suggested that there is no significant difference between the two methods assuming the null hypothesis (p=0.75). It is worth to mention that samples containing a mixture of AMP and 3-F-AMP, the sum of concentrations from the GC-FID was used to compare with the EP approach as the EP measures the oxidation product formed by the primary amine with the NQS. However, this feature should not represent an issue for LEA for the detection of AMP in the field as both compounds are illegal and classified as AMP type substance in many countries (e.g. Belgium). The only issue was risen by the SS 11 sample which accuracy against the standard method was not satisfactory in comparison to the other seized samples. Interestingly, SS 14 sample displayed an oxidation peak at 0.8V before and after the NQS treatment, showing the presence of an electroactive compound from an impurity or an added cutting agent (information from this compound was not provided by the standard method). Nevertheless, it did not interfere in the

identification and accurate quantification of AMP (i.e. accuracy of 92.6%), proving a reliable method to quantify AMP even in the presence of other electroactive compounds. Finally, the minimum mass of the sample required to be detected by the electrochemical approach could be in the µg range of AMP in a seizure if the dilution step (10-fold) is avoided in the preparation of the sample. For example, considering the successful detection of the 4.9 wt.% AMP powder, a sample with 0.49 wt.% should be detected by using direct powder mixing with the buffer. Overall, the electrochemical analysis demonstrates an excellent analytical performance in confiscated samples for its identification and even quantification, thus being a promising tool for the rapid on-site screening of AMP in border and laboratory settings, respectively.

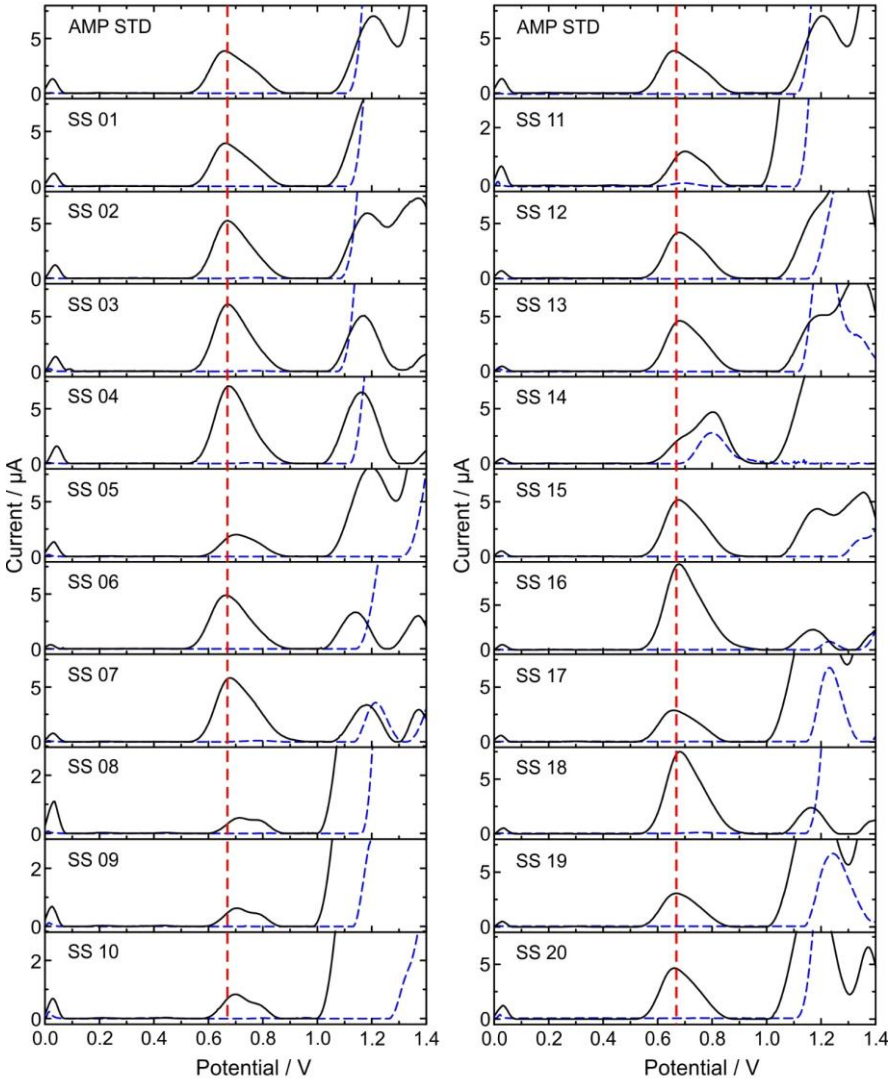

***Fig. 6**. Electrochemical profile of confiscated samples (SS) at SPE in 5 mM NQS CB pH 10. Black SWV corresponds to tests in 5 mM NQS CB pH 10. Dashed blue SWV corresponds to the street samples tests in CB pH 10. The red dotted line indicates the oxidation peak potential*

of AMP at 0.66V. Samples were solved in distilled water at 1.5 mg mL^{-1} and subsequently diluted 1:10 in 5 mM NQS in CB pH 10 for its incubation during 2.5 min before the electrochemical analysis. Samples SS 19 and SS 20 were diluted 1:20.

4. Conclusions

In this article, the electrochemical oxidation of AMP on a SPE employing an easy derivatization step with NQS is for the first time demonstrated to be a viable analytical method for the quantification of AMP in drug seizures. This work provides an investigation based on a chemical reaction between NQS and AMP that unravels the EP of AMP, an illicit drug that cannot be directly determined by electrochemical methods in a conventional graphite SPE. The analytical performance of the derivatized AMP is fully characterized exhibiting a significant oxidation peak at 0.66V in SPE after 2.5 min reaction in hydrogen carbonate solution at pH 10. To prove the selectivity of the sensor to detect AMP in confiscated samples, the EP of AMP with common cutting agents and other illicit drugs containing secondary and tertiary amines moieties was successfully evaluated. Remarkably, the analytical performance of the sensor shows the feasibility of the method to detect and quantify AMP in 20 real confiscated samples from forensic laboratories in ca. 3 min. Overall, this work demonstrates the applicability of a rapid, accurate, easy-to-use and sensitive method for the detection and quantification of AMP in confiscated samples via the use of a characteristic EP on a disposable SPE. This approach will pave the way toward the electrochemical detection of AMP in the field, assisting LEAs in the selective confiscation of cargos in border settings.

CRediT authorship contribution statement

Marc Parrilla: Conceptualization, methodology, visualization, electrochemical analysis, writing original draft. **Noelia Felipe Montiel:** electrochemical analysis, review. **Filip Van Durme:** analysis of confiscated samples with standard methods. **Karolien De Wael:** Resources, funding acquisition, writing review and editing.

Declaration of Competing Interest

The authors declare no competing financial interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version.

References

[1] R.B. Rothman, M.H. Baumann, C.M. Dersch, D. V. Romero, K.C. Rice, I. Carroll, J.S. Partilla, Amphetamine-type central nervous system stimulants release norepinephrine more potently than they release dopamine and serotonin, Synapse. 39 (2001) 32–41. https://doi.org/10.1002/1098-2396(20010101)39:1<32::AID-SYN5>3.0.CO;2-3.

[2] S.M. Berman, R. Kuczenski, J.T. McCracken, E.D. London, Potential adverse effects of amphetamine treatment on brain and behavior: A review, Mol. Psychiatry. 14 (2009) 123–142. https://doi.org/10.1038/mp.2008.90.

[3] B. Knutson, J.M. Bjork, G.W. Fong, D. Hommer, V.S. Mattay, D.R. Weinberger, Amphetamine modulates human incentive processing, Neuron. 43 (2004) 261–269. https://doi.org/10.1016/j.neuron.2004.06.030.

[4] T.L. White, D.C. Lott, H. De Wit, Personality and the subjective effects of acute amphetamine in healthy volunteers, Neuropsychopharmacology. 31 (2006) 1064–1074. https://doi.org/10.1038/sj.npp.1300939.

[5] M. Carvalho, H. Carmo, V.M. Costa, J.P. Capela, H. Pontes, F. Remiao, F. Carvalho, M. de L. Bastos, Toxicity of amphetamines : an update, Arch. Toxicol. 86 (2012) 1167–1231. https://doi.org/10.1007/s00204-012-0815-5.

[6] J.G. Bramness, Ø.H. Gundersen, J. Guterstam, E.B. Rognli, M. Konstenius, E.M. Løberg, S. Medhus, L. Tanum, J. Franck, Amphetamine-induced psychosis - a separate diagnostic entity or primary psychosis triggered in the vulnerable?, BMC Psychiatry. 12 (2012) 221. https://doi.org/10.1186/1471-244X-12-221.

[7] European Monitoring Centre for Drugs and Drug Addiction, European drug report: trends and developments, 2020. https://doi.org/10.2810/420678.

[8] European Monitoring Centre for Drugs and Drug Addiction, EU Drug Markets Report, 2019. https://doi.org/10.2810/53181.

[9] C. Cole, L. Jones, J. McVeigh, A. Kicman, Q. Syed, M.A. Bellis, Cut, a guide to adulterants, bulking agents and other contaminants found in illicit drugs, 2010. https://doi.org/10.5948/9781614441106.011.

[10] C. Cole, L. Jones, J. McVeigh, A. Kicman, Q. Syed, M. Bellis, Adulterants in illicit drugs: A review of empirical evidence, Drug Test. Anal. 3 (2011) 89–96. https://doi.org/10.1002/dta.220.

[11] BorderSens. Border detection of illicit drugs and precursors by highly accurate electrosensors. http://bordersens.eu/.

[12] S. Pichini, F.P. Busardò, A. Gregori, P. Berretta, S. Gentili, R. Pacifici, Purity and adulterant analysis of some recent drug seizures in Italy, Drug Test. Anal. 9 (2017) 485–490. https://doi.org/10.1002/dta.2134.

[13] E. Katainen, M. Elomaa, U.M. Laakkonen, E. Sippola, P. Niemelä, J. Suhonen, K. Järvinen, Quantification of the amphetamine content in seized street samples by Raman spectroscopy, J. Forensic Sci. 52 (2007) 88–92. https://doi.org/10.1111/j.1556-4029.2006.00306.x.

[14] M.F. Andreasen, C. Lindholst, E. Kaa, Adulterants and Diluents in Heroin, Amphetamine, and Cocaine Found on the Illicit Drug Market in Aarhus, Denmark, Open Forensic Sci. J. 2 (2009) 16–20. https://doi.org/10.2174/1874402800902010016.

[15] B. Miserez, O. Ayrton, J. Ramsey, Analysis of purity and cutting agents in street mephedrone samples from South Wales, Forensic Toxicol. 32 (2014)

305–310. https://doi.org/10.1007/s11419-014-0232-y.

[16] A. Guirguis, J.M. Corkery, J.L. Stair, S.B. Kirton, M. Zloh, F. Schifano, Intended and unintended use of cathinone mixtures, Hum. Psychopharmacol. 32 (2017) 1–17. https://doi.org/10.1002/hup.2598.

[17] E. Gerace, F. Seganti, C. Luciano, T. Lombardo, D. di Corcia, H. Teifel, M. Vincenti, A. Salomone, On-site identification of psychoactive drugs by portable Raman, Drug Alcohol Rev. 38 (2020) 50–56. https://doi.org/10.1111/dar.12887.

[18] T.L.E. Lockwood, T.X. Leong, S.L. Bliese, A. Helmke, A. Richard, G. Merga, J. Rorabeck, M. Lieberman, idPAD: Paper Analytical Device for Presumptive Identification of Illicit Drugs, J. Forensic Sci. 65 (2020) 1289–1297. https://doi.org/10.1111/1556-4029.14318.

[19] J.M. Płotka, M. Biziuk, C. Morrison, Common methods for the chiral determination of amphetamine and related compounds I. Gas, liquid and thin-layer chromatography, TrAC - Trends Anal. Chem. 30 (2011) 1139–1158. https://doi.org/10.1016/j.trac.2011.03.013.

[20] H. Chung, S. Choe, Amphetamine-type stimulants in drug testing, Mass Spectrom. Lett. 10 (2019) 1–10. https://doi.org/10.5478/MSL.2019.10.1.1.

[21] E. Cuypers, A.J. Bonneure, J. Tytgat, The use of presumptive color tests for new psychoactive substances, Drug Test. Anal. 8 (2016) 137–141. https://doi.org/10.1002/dta.1847.

[22] L. Pereira De Oliveira, D.P. Rocha, W. Reis De Araujo, R.A. Abarza Muñoz, T.R. Longo Cesar Paixão, M. Oliveira Salles, Forensics in hand: New trends in forensic devices (2013-2017), Anal. Methods. 10 (2018) 5135–5163. https://doi.org/10.1039/c8ay01389f.

[23] W.R. de Araujo, T.M.G. Cardoso, R.G. da Rocha, M.H.P. Santana, R.A.A. Muñoz, E.M. Richter, T.R.L.C. Paixão, W.K.T. Coltro, Portable analytical platforms for forensic chemistry: A review, Anal. Chim. Acta. 1034 (2018) 1–21. https://doi.org/10.1016/j.aca.2018.06.014.

[24] B. Zanfrognini, L. Pigani, C. Zanardi, Recent advances in the direct

electrochemical detection of drugs of abuse, J. Solid State Electrochem. (2020). https://doi.org/10.1007/s10008-020-04686-z.

[25] H. Teymourian, M. Parrilla, J.R. Sempionatto, N.F. Montiel, A. Barfidokht, R. Van Echelpoel, K. De Wael, J. Wang, Wearable Electrochemical Sensors for the Monitoring and Screening of Drugs, ACS Sensors. 5 (2020) 2679−2700. https://doi.org/10.1021/acssensors.0c01318.

[26] E. De Rycke, C. Stove, P. Dubruel, S. De Saeger, N. Beloglazova, Recent developments in electrochemical detection of illicit drugs in diverse matrices, Biosens. Bioelectron. 169 (2020) 112579. https://doi.org/10.1016/j.bios.2020.112579.

[27] G. Moro, H. Barich, K. Driesen, N. Felipe Montiel, L. Neven, C.D. Mendonça, S.T. Shanmugam, E. Daems, K. De Wael, Unlocking the full power of electrochemical fingerprinting for on-site sensing applications, Anal. Bioanal. Chem. 412 (2020) 5955–5968. https://doi.org/10.1007/s00216-020-02584-x.

[28] E. Mynttinen, N. Wester, T. Lilius, E. Kalso, B. Mikladal, I. Varjos, S. Sainio, H. Jiang, E.I. Kauppinen, J. Koskinen, T. Laurila, Electrochemical Detection of Oxycodone and Its Main Metabolites with Nafion-Coated Single-Walled Carbon Nanotube Electrodes, Anal. Chem. 92 (2020) 8218–8227. https://doi.org/10.1021/acs.analchem.0c00450.

[29] L.R. Rocha, J. de Cássica Mendonça, T. Boareto Capelari, R. Antigo Medeiros, C.R. Teixeira Tarley, Development of a reliable and selective voltammetric method for determination of designer drug 1-(3-chlorophenyl)piperazine (mCPP) using boron-doped diamond electrode and exploiting surfactant-mediated measurements, Sensors Actuators, B Chem. 310 (2020) 127812. https://doi.org/10.1016/j.snb.2020.127812.

[30] M. de Jong, N. Sleegers, J. Schram, D. Daems, A. Florea, K. De Wael, A Benzocaine-Induced Local Near-Surface pH Effect: Influence on the Accuracy of Voltammetric Cocaine Detection, Anal. Sens. (2020). https://doi.org/10.1002/anse.202000012.

[31] N. Felipe Montiel, M. Parrilla, V. Beltrán, G. Nuyts, F. Van Durme, K. De Wael, The opportunity of 6-monoacetylmorphine to selectively detect heroin at

preanodized screen printed electrodes, Talanta. 226 (2021) 122005. https://doi.org/10.1016/j.talanta.2020.122005.

[32] J. Schram, M. Parrilla, N. Sleegers, N. Samyn, S.M. Bijvoets, M.W.J. Heerschop, A.L.N. van Nuijs, K. De Wael, Identifying Electrochemical Fingerprints of Ketamine with Voltammetry and Liquid Chromatography–Mass Spectrometry for Its Detection in Seized Samples, Anal. Chem. 92 (2020) 13485–13492. https://doi.org/10.1021/acs.analchem.0c02810.

[33] L.R. Cumba, J.P. Smith, K.Y. Zuway, O.B. Sutcliffe, D.R. Do Carmo, C.E. Banks, Forensic electrochemistry: Simultaneous voltammetric detection of MDMA and its fatal counterpart “dr Death” (PMA), Anal. Methods. 8 (2016) 142–152. https://doi.org/10.1039/c5ay02924d.

[34] J. Schram, S.T. Shanmugam, N. Sleegers, A. Florea, N. Samyn, A.L.N. van Nuijs, K. De Wael, Local conversion of redox inactive molecules into redox active ones: a formaldehyde based strategy for the electrochemical detection of illicit drugs containing primary and secondary amines, Electrochim. Acta. (2020) 137515. https://doi.org/10.1016/j.electacta.2020.137515.

[35] F.M. Ivison, J.W. Kane, J.E. Pearson, J. Kenny, P. Vadgama, Development of a redox mediated amperometric detection system for immunoassay. Application to urinary amphetamine screening, Electroanalysis. 12 (2000) 778–785. https://doi.org/10.1002/1521-4109(200006)12:10<778::AID-ELAN778>3.0.CO;2-#.

[36] J. Gallardo-Gonzalez, A. Saini, A. Baraket, S. Boudjaoui, A. Alcácer, A. Streklas, F. Teixidor, N. Zine, J. Bausells, A. Errachid, A highly selective potentiometric amphetamine microsensor based on all-solid-state membrane using a new ion-pair complex, [3,3″-Co(1,2-closo-C2B9H11)2]− [C9H13NH]+, Sensors Actuators, B Chem. 266 (2018) 823–829. https://doi.org/10.1016/j.snb.2018.04.001.

[37] A.A. Elbashir, A.A. Ahmed, S.M. Ali Ahmed, H.Y. Aboul-Enein, 1,2-naphthoquinone-4-sulphonic acid sodium salt (NQS) as an analytical reagent for the determination of pharmaceutical amine by spectrophotometry, Appl. Spectrosc. Rev. 47 (2012) 219–232.

https://doi.org/10.1080/05704928.2011.639107.

[38] Y. Nakahara, A. Ishigami, Y. Takeda, Electrochemical label for high-performance liquid chromatography I. B-Naphthoquinone-4-sulphonate as an electrochemical detection labelling reagent of amines, J. Chomatography. 489 (1989) 371–376. https://doi.org/10.1016/S0378-4347(00)82916-3.

[39] A. Goodwin, C.E. Banks, R.G. Compton, Tagging of model amphetamines with sodium 1,2-naphthoquinone-4-sulfonate: Application to the indirect electrochemical detection of amphetamines in oral (saliva) fluid, Electroanalysis. 18 (2006) 1833–1837. https://doi.org/10.1002/elan.200603596.

[40] Q. Li, J. Li, Z. Yang, Study of the sensitization of tetradecyl benzyl dimethyl ammonium chloride for spectrophotometric determination of dopamine hydrochloride using sodium 1,2-naphthoquinone-4-sulfonate as the chemical derivative chromogenic reagent, Anal. Chim. Acta. 583 (2007) 147–152. https://doi.org/10.1016/j.aca.2006.09.051.

[41] K. Hartke, U. Lohmann, On the reaction of primary aliphatic amines with 1,2-naphthoquinone-4-sulfonic acid, Chem. Lett. 12 (1983) 693–696. https://doi.org/10.1246/cl.1983.693.

[42] A. Argente-García, N. Jornet-Martínez, R. Herráez-Hernández, P. Campíns-Falcó, A solid colorimetric sensor for the analysis of amphetamine-like street samples, Anal. Chim. Acta. 943 (2016) 123–130. https://doi.org/10.1016/j.aca.2016.09.020.

[43] A.M. Mahmoud, N.Y. Khalil, I.A. Darwish, T. Aboul-Fadl, Selective spectrophotometric and spectrofluorometric methods for the determination of amantadine hydrochloride in capsules and plasma via derivatization with 1,2-naphthoquinone-4-sulphonate, Int. J. Anal. Chem. 2009 (2009) 810104. https://doi.org/10.1155/2009/810104.

[44] Q. Li, Z. Yang, Study of spectrophotometric determination of amoxicillin using sodium 1,2-naphthoquinone-4-sulfonate as the chemical derivative chromogenic reagent, Anal. Lett. 39 (2006) 763–775. https://doi.org/10.1080/00032710600611525.

[45] E.G. Schmidt, Reaction between Amines and Sodium 1,2-Naphthoquinone-4-Sulfonate, Ind. Eng. Chem. 11 (1939) 99–100. https://doi.org/10.1021/ac50130a012.

[46] M.M. Nevešcanin, M.L. Avramov Ivic, S.D. Petrovic, D.Ž. Mijin, S.N. Banovic Stevic, V.M. Jovanovic, The use of a gold electrode for the determination of amphetamine derivatives and application to their analysis in human urine, J. Serbian Chem. Soc. 78 (2013) 1373–1385. https://doi.org/10.2298/JSC121228032N.

[47] Y. Jang, M. Jang, H. Kim, S.J. Lee, E. Jin, J.Y. Koo, I.C. Hwang, Y. Kim, Y.H. Ko, I. Hwang, J.H. Oh, K. Kim, Point-of-Use Detection of Amphetamine-Type Stimulants with Host-Molecule-Functionalized Organic Transistors, Chem. 3 (2017) 641–651. https://doi.org/10.1016/j.chempr.2017.08.015.

[48] J. McGeehan, L. Dennany, Electrochemiluminescent detection of methamphetamine and amphetamine, Forensic Sci. Int. 264 (2016) 1–6. https://doi.org/10.1016/j.forsciint.2016.02.048.

Highlights

- An affordable, rapid and sensitive method for amphetamine detection using screen-printed electrodes.
- The electrochemical oxidation of amphetamine employing 1,2-naphthoquinone-4-sulphonate is proposed.
- The procedure is tested with mixtures of common cutting agents and illicit drugs.
- The quantification of amphetamine in street samples from a forensic institute is performed.

Graphical abstract