Experiences in the detection of drugs of abuse in smuggling seizures and forensic samples using electronic tongue principles

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Abstract—The application of voltammetric sensors to the analysis of illicit drugs in combination with different chemometric tools to achieve their identification and quantification is explored herein. The aim is to process the whole voltammograms obtained from different sensors as a unique profile, and analyze those with the aid of pattern recognition methods that allow the extraction of a characteristic fingerprint, rather than focusing on the oxidation peaks associated to each of the drugs. To this aim, different arrays of electrodes were prepared to analyzed samples employing square wave voltammetry (SWV). Next, identification of different drugs was achieved by means of principal component analysis (PCA) and linear discriminant analysis (LDA), while their quantification was attained by partial least squares (PLS) modelling.

Keywords— voltammetric sensors, principal component analysis, partial-least squares, electronic tongue, opioids, cutting agents

I. INTRODUCTION

Over the last years, illicit drugs have become a worldwide burden for the society [1, 2], but also for the different police and border agencies which have to deal with their consequences (e.g. drug dealers, increase in violence, traffic, underground economy, etc.). In order to be able to dismantle such fraudulent activities and safeguard the public, security and law enforcement agencies require of fast and portable methods that allow them to reliably achieve the identification of the drugs upon its interception.

However, the rapid detection of illicit drugs is still a challenge. The low accuracy of color tests, or the high cost and limited portability of spectroscopic testing, are the main limitations of currently utilized on-site procedures for the identification of illicit drugs. Moreover, color tests are directed towards a specific substance, requiring the use of a different test for each of the drugs that we suspect, while in turn those are only available for the more common drugs. As an alternative, immunoassay- and chromatography-based testing methods are reported in the literature as a more powerful approach [3]. Nevertheless, those are still costly (both from the equipment and reagents side), time- consuming and might require a sample pre-treatment step and/or laboratory facilities. Thus, not being suitable for the on-site analysis.

In the light of the pressing need for better drug test systems at border controls, BorderSens project aims to establish the basis for the development of a portable device capable to quickly test for different drugs, precursors and cutting agents, with outstanding accuracy and reduced

false positives and false negatives [4]. In this direction, electrochemical sensors offer fast and accurate information in a cost-effective manner. Besides, their high sensitivity, wide linear range, minimal power requirement, potential for miniaturization and portability, low-cost instrumentation and ease of operation, are some of their several advantages that make them suitable for the development of compact and user-friendly hand-held meters for on-site analysis [5].

Despite the inherent redox activity of most of the drugs and the above mentioned advantages, the simultaneous determination of seized samples might still be challenging given the complexity of the samples and the similar electrochemical response of some drugs and cutting agents. Precisely, one of the main drawbacks faced is the possible overlapping between peaks when mixtures of those are analyzed, which can even lead to the suppression of some peaks [6]. In this direction, the coupling with chemometric processing allows extracting the maximum chemical information from these complex data. Thus, with such an approach is possible to deconvolute complex overlapping electrochemical responses and achieve the simultaneous identification and quantification of several analytes. Moreover, the use of an array of chemically-modified sensors, rather than relying on a single bare electrode can also further improve the potential of the system; an approach that is known as electronic tongue (ET) [7].

In this direction, herein we present an overview of some of the achievements made so far in the detection of illicit drugs and some of their common cutting agents. Given the complexity of the scenario, the analysis of opioids has been taken as a testbed to demonstrate the potential of the approach, with a series of experiments planned in increasing order of complexity. Firstly, the use of different electrodes was investigated for the generation of the voltammetric fingerprints, followed by the qualitative identification of different drugs at fix and varying concentrations. Next, the identification of illicit drugs when mixed with different cutting agents was also attempted, in what represents a more realistic scenario. Finally, the simultaneous quantification of mixtures of three different drugs was evaluated, both in the absence and presences of different cutting agents.

II. EXPERIMENTAL

A. Sensor array

Several voltammetric sensors were prepared using different modifiers such as carbon nanotubes, graphene, cobalt (II) phthalocyanine (CoPc), Prussian blue, polypyrrole as well as palladium nanoparticles (Pd) or oxide nanoparticles of copper, bismuth, titanium, zinc and tin. Those modifiers were selected taking into account previous studies with ETs in other fields. In this manner, two different platforms were evaluated: usage of bulk-modified graphite epoxy composites (GECs) and screen printed electrodes (SPEs) modified with a drop-casted ink-like solution. Briefly, the procedure for its preparation was as follows:

1) GEC sensors: electrodes were prepared by mixing 18% of graphite powder, 2% of the specific modifier and 80% of the epoxy resin. Next, this paste was placed into a PVC tube, in which a cupper disc soldered to a connector had previously been inserted, and cured at 80 ºC for 3 days [8]. Finally, the electrodes were polished and ready to use.

2) SPE sensors: a polystyrene ink was prepared by mixing 58% of graphite, 10% of the specific modifier and 32% of powdered polystyrene with 250 µL of mesytylene. Next, 1 µL of the obtained solution was dropped onto the electrode and dried at 40 ºC for 1h.

B. Electrochemical measurements

Square wave voltammetric (SWV) measurements were carried out at room temperature using a 4-channel Palmsens MultiEmStat potentiostat (Houten, The Netherlands) controlled with the MultiTrace software package. In this way, drug samples were analyzed with the sensor arrays above mentioned by placing a small drop of the solution on top of the electrodes, and recording a single oxidative scan for each of the samples and electrodes. Besides, to prevent any fouling effect on the electrodes and to avoid performing any physical surface regeneration of those, a blank measurement was carried under the same conditions as cleaning stage between samples.

C. Data processing

Chemometric analysis was accomplished by means of scripts implemented in Matlab (MathWorks, Natick, MA, USA), using its Statistics toolbox. Concretely, genetic algorithms (GAs) were used as feature selection tool to reduce the number of inputs fed to the quantitative chemometric models given the large dimensionality of the voltammetric data [9]. Next, qualitative analysis was done by means of principal component analysis (PCA) which allowed to assess initial patterns in the data and evaluate samples (dis)similarities, while linear discriminant analysis (LDA) was used next to build the classifier model which allowed the categorization of the different samples. Finally, quantification of drugs mixtures was achieved by means of partial least square regression (PLS).

In all cases, considering that the ultimate goal is the development of a user-friendly hand-held device, the effort was to develop the simplest model possible able to fulfill the desired task. In this regard, the choice of GAs as feature selection tool, provide a double advantage as, on the one side, allow to significantly reduce the computing processing, while, on the other side, an improvement in the model performance and generalization ability could be attained. Similarly, PLS was preferred over artificial neural networks (ANNs) due to its simplicity and lower computational requirements.

III. RESULTS AND DISCUSSION

To illustrate the potential of the proposed approach, four different scenarios of increasing complexity were considered; namely, identification of different opioids without and with mixing them with different cutting agents, and the quantification of opioids mixtures, without or with the presence of different cutting agents. For each of them, a different set of samples was prepared and measured with the proposed sensor arrays (after optimization of the sensors chosen [10]), submitting afterwards the obtained responses to the appropriate chemometric model depending whether a qualitative or quantitative response was sought. For

all the supervised models, the sets of samples were split into two subsets: train subset (used to fit the model) and test subset (used to assess its performance).

A. Identification of different drugs

The first step was the analytical characterization of the voltammetric responses of the different electrodes towards the different dugs considered, to ensure that there is some response, and that differentiated responses are also obtained between the different electrodes. Next, voltammograms were submitted to PCA, and the clustering observed was used to select the optimal sensor array for each scenario [10].

As an example, the voltammetric responses for three different modified SPE are shown in Fig. 1, where it can be seen how distinguished signals are generated by each of them. The obtained scores plot with those three sensors is shown in Fig. 2, where a clear clustering of the drugs can be observed, confirming that different fingerprints are obtained. Significantly, even when varying the concentration of those, the algorithm is still able to correctly identify each substance.

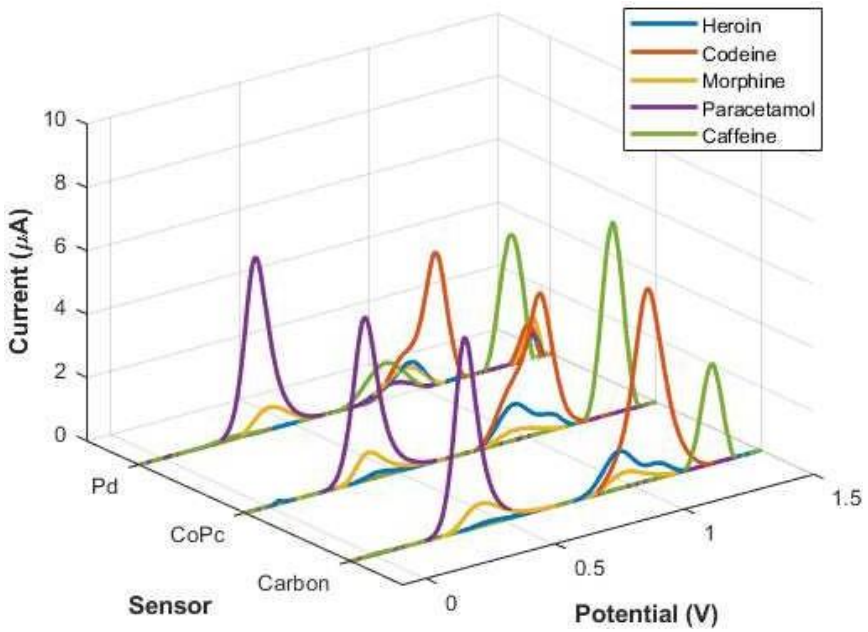

Fig. 1. Example of the voltammetric responses towards three different opioids and two cutting agents at 300 µM, with SPE-modified sensor array.

B. Identification of drugs mixed with cutting agents

In another qualitative approach, the identification and classification of four different drugs when mixed with different cutting agents was attempted. For this purpose, a new set of samples was analyzed with the different sensors, and responses modelled with the aid of LDA as a supervised method to achieve the classification into 5 different groups: one for each of the drugs considered (mixed or not with the cutting agents) and one for all the different cutting agents. Again, clear clusters were obtained for each of the drugs, achieving a percentage of classification success for the testing subset of 100%.

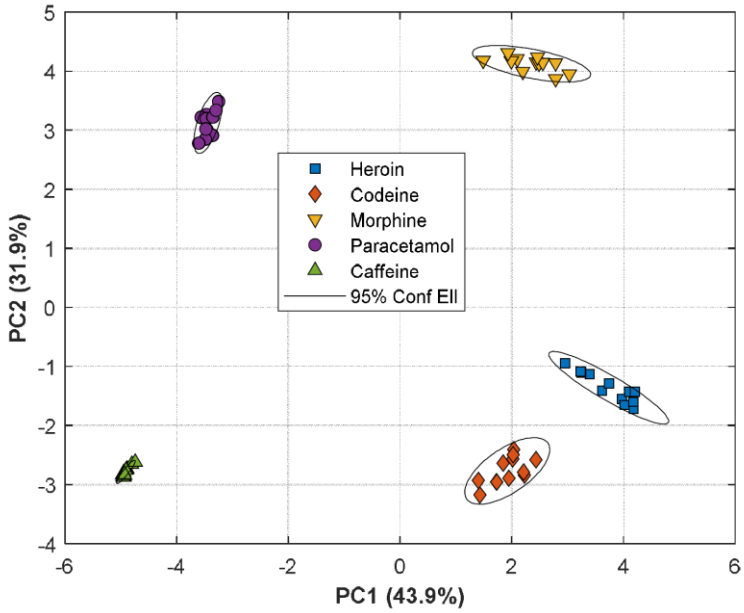

Fig. 2. Score plot obtained from the PCA of the voltammetric responses of different drugs at different concentrations (100-400 µM). Ellipses plotted correspond to 95% confidence limits for each of the clusters.

C. Quantification of drugs mixtures (pure substances)

Next, the simultaneous quantification of mixtures of the three opioid drugs considered in III.A was evaluated. To this aim, a set of samples was prepared, measured with the sensor array, and the quantitative model was then built employing GAs-PLS. To visualize its performance, comparison graphs of predicted vs. expected concentrations were built (Fig. 3), from which the linear regression parameters were also calculated. As can be seen, a satisfactory trend was obtained for each of the drugs and subsets, with regression lines close to the ideal ones, being the ideal values of slope, correlation and intercept within the confidence intervals. Moreover, to demonstrate that neither the use of GAs nor the high dimensionality of the data is resulting in over-fitted models, a permutation test was carried out and the performance of the test compared to those from the actual model.

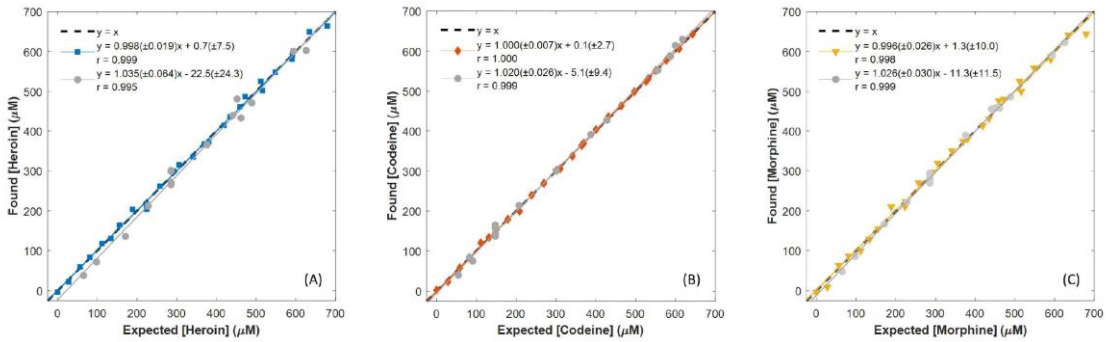

Fig. 3. Modelling ability of the GA-PLS model for the quantification of (A) heroin, (B) morphine and (C) codeine mixtures in the range 0-700 µM. Set adjustments of obtained vs. expected concentrations for the train and test subsets. Additionally, the ideal comparison line (y=x) is also plotted.

D. Quantification of drugs mixtures and cutting agents

Finally, the same approach above mentioned, but making use of a different set of samples, was used to achieve the quantification of mixtures of the same three opioids in the presence of two different cutting agents (paracetamol and caffeine). As before, GA-PLS was used to build the quantification model that allowed not only the quantification of the different drugs, but also the cutting agents. Again, showing a satisfactory trend and regression parameters close to the ideal values.

IV. CONCLUSIONS

The combination of modified voltammetric sensors with different chemometric tools have proven to be a useful approach for the analysis of drugs. A very satisfactory performance has been obtained both in the qualitative discrimination of different substances or in its simultaneous quantification, even when mixed with other drugs and/or different cutting agents. Consequently, taking into account the performance demonstrated herein and the inherent advantages of electrochemical methods such as its simplicity, low-cost and portability, the suitability of the current approach for the development of portable system for decentralized analysis is confirmed.

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