FORENSIC DRUG APPLICATIONS OF ELECTROCHEMICAL SENSORS

Lynsey Shaw, Lynn Dennany*

WestCHEM

Department of Pure and Applied Chemistry

University of Strathclyde

Centre for Forensic Sciences

Technology and Innovation Centre

99 George Street

Glasgow, G1 1RD, UK

* To whom correspondence should be addressed. Email: lynn.dennany@strath.ac.uk

ABSTRACT

Electrochemical based sensors are a powerful analytical tool which can be exploited by the forensic community particularly for the analysis of illicit substances from street and biological samples. This report presents a brief overview on selected recent publications related to the application of electrochemical sensors to forensic drug analysis and gives opinions on the technical developments as well as the future applications in this field.

INTRODUCTION

Within any forensic examination, several scientific methods are utilised to provide scientific evidence on a case to court or as an investigative tool to investigators. The choice of analytical techniques, methods and procedures relies on the assessment of several factors.[1] For example, the ability of the technique or method to analyse a particular sample matrix, the sensitivity, selectivity and robustness of the technique and method are some of the key analytical performance characteristics. Generally, these requirements are not met by any one single technique but often by a combination of techniques and methods. This is especially true of crime scene analysis where often confirmatory analysis is undertaken within a forensic laboratory.[2]

In recent years, the versatility, portability, selectivity, sensitivity and ability to analysis samples with little or no pre-treatment has made electrochemical sensors an attractive option to forensic applications.[3,4] Potentiostatic methods are commonly utilised and this review will focus primarily on the use of voltammetric methods as electrochemical sensors for forensic analysis. The application of electrochemical sensors to forensic science spans a wide range of areas including the detection of poisons[5], drugs[6], explosives[7], gunshot residue (GSR)[8] and more unusually fingerprints[9,10]. Herein, we present a brief overview on recent applications of electrochemical sensors to forensic drug investigation and highlight the unique opportunities electrochemistry presents for this field as well as the most significant advancements in developing the application of electrochemistry to forensic science drug detection and analysis.

CHEMICAL DETECTION

The widespread use of illicit drugs remains an important social and medical problem all over the world.[11,12] Rapid, sensitive, simple and inexpensive procedures for illicit substance detection are needed in the fields of drug analysis and toxicology. As an

alternative to the standard chromatographic and spectroscopic methods, electrochemical sensors have shown great promise. Many illicit substances can be detected by electrochemical methods including cocaine[13,14,15,16,17], cannabis[14,18], amphetamine type substances (ATS)[19,20,21,22], opiates[23,24,25], diverted pharamecuticals[26,27] and novel psychoactive substances (NPS)[28,29,30,31,32] with the approach tailored to the particular illicit substance. A specific analytical challenge for forensic analyse is the wide ranging concentration ranges as well as number and relative concentration of cutting agents both diluents and adulterants. For example, a recent publication found that the purity of cocaine samples within the UK ranged from 1.3 to 78.8% with a mean of 43.1% (expressed as cocaine base).[33] This is slightly higher than that obtained for cocaine street samples in Beligum, where typically cocaine purity was found to be above 30%.[34] These values are significantly higher than does reported for ATS street samples, where values ranged from 1.4 to 6% for traditional ATS samples.[35] Within these samples are also a wide range of impurities and street samples also containing from 3 to 10 cutting agents including caffeine, paracetamol, other illicit substances. This constantly changing composition of street samples, highlights a challenge for forensic analysis. For toxicological samples, the presence of metabolites can also be considered as interferences.[29-32]

Recently, the use of different electrochemical methods for the detection of cocaine and its adulterants have been reported.[13,36,37] In order to obtain the required level of specificity and sensitivity, the most common approach has been to utilise modified electrodes.[38] This has included using cytochrome[39] P450, carbon nanotubes (CNTs)[40], β-cyclodextrin incorporated in polyaniline films with CNTs[41], Schiff base films[42], carbon paste electrodes modified with methoxy-substituted N-N'ethylene-bis(salcylideneiminato)uranyl(VI) complexes and Pt disk electrodes modified with cobalt-hexacyanoferrate films.[43] However, the majority of these did not have the required sensitivity or specificity for widespread applications. To achieve this specificity, the main approach in recent work has been to incorporate either an aptamer or antibody specific or to use an alternative working electrode for cocaine detection.

To allow for more specific and sensitive detection, highly selective sensing molecules, such as short and single-stranded apatmers and antibodies have been incorporated into the

electrochemical sensor. Work by Bozokalfa *et. al.*[16] reported on innovative approach of combining the selective recognition elements with the well known advantages of electrochemical sensor systems. These aptamers were immobilised by electrodepositing thiophene macro-monomer bearing polypetitdes (PT-Pala) followed by conjugation of the cocaine aptamer onto the PT-Pala film using the hetero-bifuncational cross-linker illustrated in Figure 1. This was applied to the detection of cocaine and its metabolite, benzoylecgonine (BE), which exhibited a linear correlation in the range from 2.5 up to 10 nM and 0.5 up to 50 μM for cocaine and BE, respectively. Differential pulse voltammetry (DPV) was utilised to monitor the recognition of the aptamer for the presence of cocaine and BE. An immunoelectrochemical approach to this challenge was investigated by Sengel *et al*.[17]

While the presence of BE would be extremely important in toxicology samples, street samples of cocaine contain a wide variety of adulterants. A simple and robust batch-injection analysis system utilising square-wave voltammetry (BIA-SWV) was utilised as a screening method for the electrochemical determination of cocaine and screening of the most common adulterants.[13] To achieve this, the BIA-SWV incorporated the use of a boron-doped diamond (BDD) working electrode and using an acidic medium to monitor the oxidation of cocaine at +2.1 V vs Ag/AgCl. The proposed mechanism for cocaine oxidation in acidic medium is shown in Figure 2. This oxidation is was well separated from the common adulterants, namely, paracetamol, phenacetin, procaine, benzocaine, caffeine and lidocaine as shown in Figure 3. This figure shows the peak current of cocaine remains relatively constant (RSD = 3.4%) after the addition of all adulterants simultaneously. This highlights that even in the presence of small amounts of cocaine (11% m/m) and high amounts of adulterants (89% m/m) cocaine can be easily detected and discriminated from these adulterants. This illustrates the unique ability of electrochemical sensors to provide a rapid and simple on-site screening of seized street samples.

There are many other reports of the electrochemical detection of a range of drugs including amphetamine type stimulants (ATS)[19,20] and cannabis as well as the ever expanding field of novel psychoactive substances.[28-32] The market and number of such substances has grown substantially as reported by the United Nations Office on Drugs and Crime.[11,12] Extending the capabilities of forensic electrochemistry to these NPS has been

addressed.[44] The majority of these studies have addressed particular groups of NPS, such as synthetic cannabinoids[29], to develop a portable electrochemical system for forensic screening. These often develop from sensors based upon ATS which could be detected electrochemically[19,20] and discriminated against different members based upon their pK_a values at different pHs similar to other amine based compounds.[45,46] For example, the chemiluminescence achieved from electrochemical oxidation was maximized at pH values near the pK_a of the N-terminal amine site.[47] Similar results were obtained for amphetamine type stimulants when electrochemically analysed in solution phase approaches.[48] The understanding of the ATS allowed for the extension of electrochemical sensors to NPS such as benzylpiperazine[28], which achieved a limit of detection of 20 μM. This is well within the concentration range required since typical BZP tablets contain between 50 and 200 mg. However, to be applied to toxicological samples, this system would need to assess the resolution between BZP and the hydroxylated metabolites.

The analysis of both street samples and biological samples was addressed by Dronova *et al*[29] who examined the use of differential pulsed voltammetry as a pre-screening procedure for confiscated street samples thought to contain synthetic cannabinoids. This work developed from research focusing on the direct electrochemical detection of Δ^9-tetrahydrocannabinol (Δ^9-THC). Δ^9-THC can be directly detected by monitoring the anodic peak at 0 V vs Ag/AgCl on a glassy carbon electrode.[18,49,50] This research presented for the first time a direct electrochemical oxidation sensor which could provide meaningful voltammetric signatures for synthetic cannabinoids thus allowing the detection of these NPS in seized materials and biological samples, as shown in Figure 4. These results were also evaluated against standard techniques such as gas chromatography mass spectrometry (GC MS) and liquid chromatography MS (LC MS) demonstrating excellent agreement. However, the electrochemical sensor could not provide unequivocally identification of the synthetic cannabinoid present. Therefore, this sensor would only be utilised as a screening method in the field or as a laboratory screening method for the preliminary quantification of common synthetic cannabinoids found in street sample or biological samples prior to confirmatory analysis. Many reported applications of electrochemical sensors into the field of biomedical diagnostics also supports the promise that these sensors can be utilised in extremely complex matrices such as those biological samples submitted to forensic laboratories.[51,52]

A rapid screening method is highly desirable in the field of forensic drug analysis for both the analysis of street and toxicological samples as well as to respond to the swift evolution of NPS[53] and the subsequent backlogs that develop within forensic laboratories and from this review it is evident that electrochemical sensors can offer a unique capability to address this challenge.

CONCLUDING REMARKS

Electrochemical sensors have been widely applied to forensic science applications particularly in the field of drug analysis and detection utilising a wide range of platforms to achieve the sensitivity and specificity required. Despite its obvious advantages, electrochemical sensors still need to expand to screening for multiple drugs or illicit substances as well as common adulterants and metabolites in order to provide a robust and effective screening tool to the forensic community. The majority of these studies primarily focus on one illicit substance or one family of illicit substances. However, to truly be established as an effective tool for forensic science investigation a technique which can be applied to more than one family of illicit substances is required. Electrochemical sensors should be developed further to provide for high-throughput analysis of street and toxicological samples to meet the requirements of the forensic investigator. Therefore, research should be expanded to investigate the analysis of metabolites particularly those from NPS. With this research, electrochemical sensors would represent an extremely important investigative tool which would be translated to both laboratory and on-site screening of illicit substances. Achieving this would also open up potential avenues such as the application of electrochemical sensors to roadside drug testing. The continuing work within this field, illustrates the potential of electrochemical sensors to address these forensic challenges.

LEGENDS

Figure 1: Schematic representation how the PT-Pala modified with cocaine aptamer allows for cocaine detection. Reprinted from Ref [16] with permission of American Chemical Society (2017).

Figure 2: (a) Schematic representation of BIA-SWV detection of cocaine and its common adulterants. (b) Proposed mechanism for the electrochemical oxidation of cocaine in acid medium. (c) BIA-SWV voltammograms obtained for solutions containing a fixed concentration of cocaine (20 mgL^{-1}) without (black line) and with the addition of increasing concentrations of lidocaine, caffeine, phenacetin, and paracetamol (2 – 40 mg L^{-1}). Reprinted from Ref [13] with permission of Elsevier (2017).

Figure 3: DPV response of herbal plant extract that did not contain any synthetic cannabinoids (A); herbal plant material that contained two indazole-based synthetic cannabinoids (B); one indole-, one indazole-based synthetic cannabinoids (C and D). Potentials are recorded vs Ag/Ag^{+}. Reprinted from Ref [29] with permission of American Chemical Society (2017).

FIGURE 1

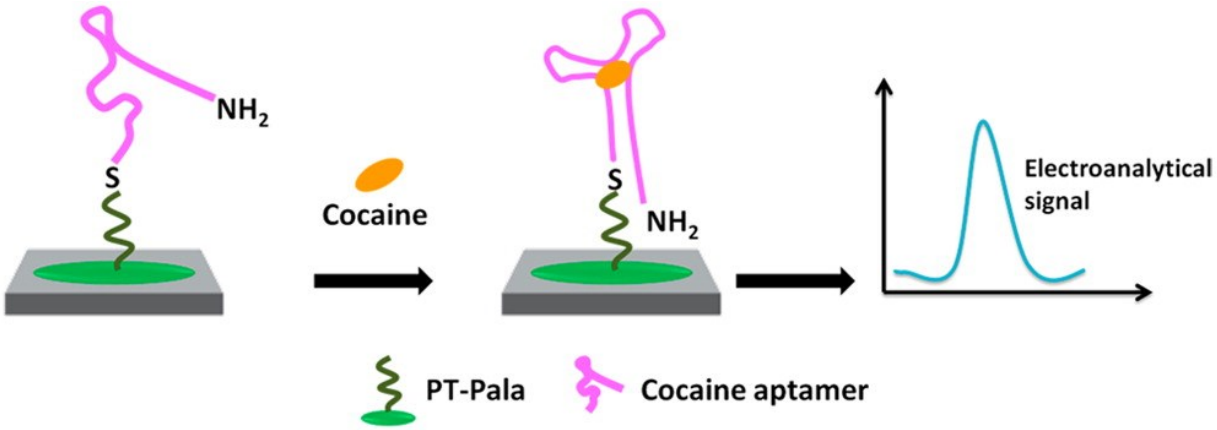
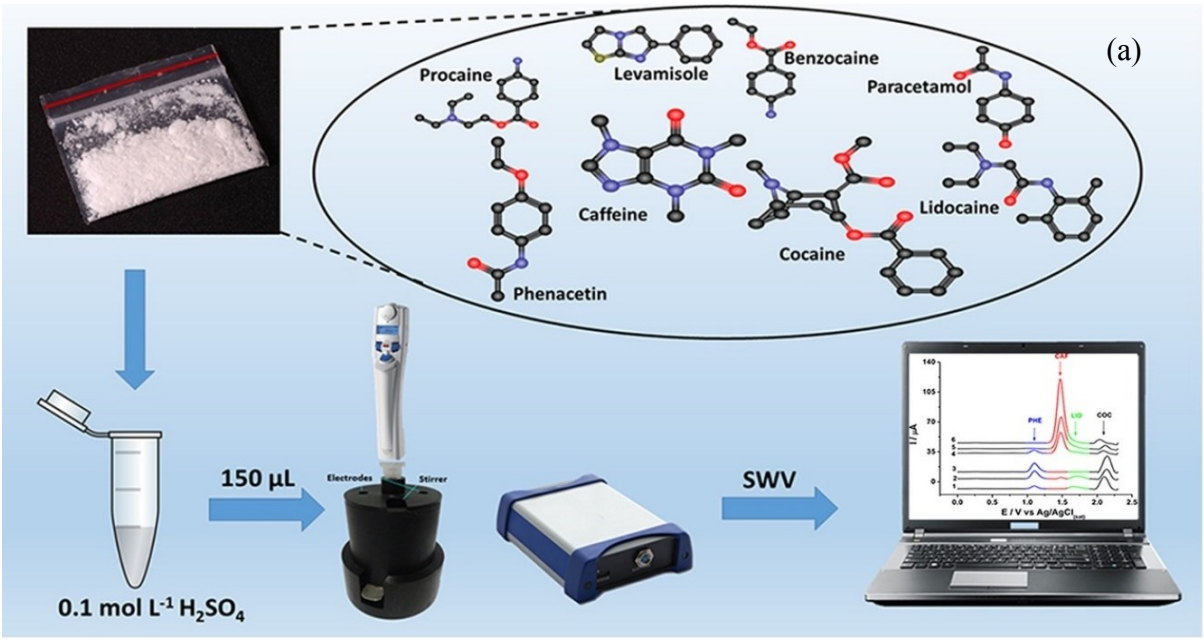
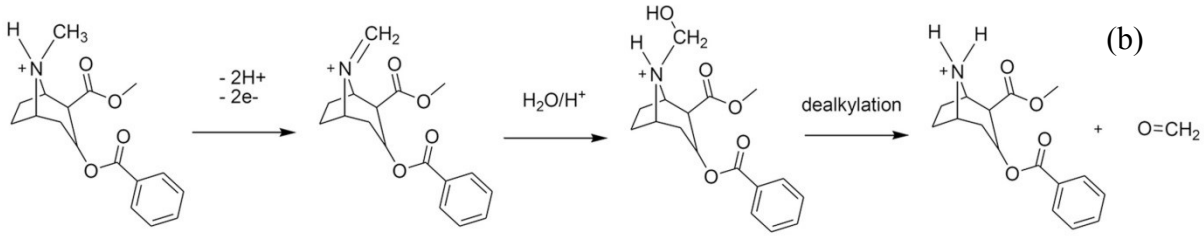

NH2
S
Cocaine
S
NH2
Electroanalytical signal
PT-Pala
Cocaine aptamer

FIGURE 2


(a)
Procaine
Levamisole
Benzocaine
Paracetamol
Caffeine
Lidocaine
Cocaine
Phenacetin
150 µL
Electrodes
Stirrer
SWV
0.1 mol L-1 H2SO4


(b)
- 2H+
- 2e-
H2O/H+
dealkylation
O=CH2

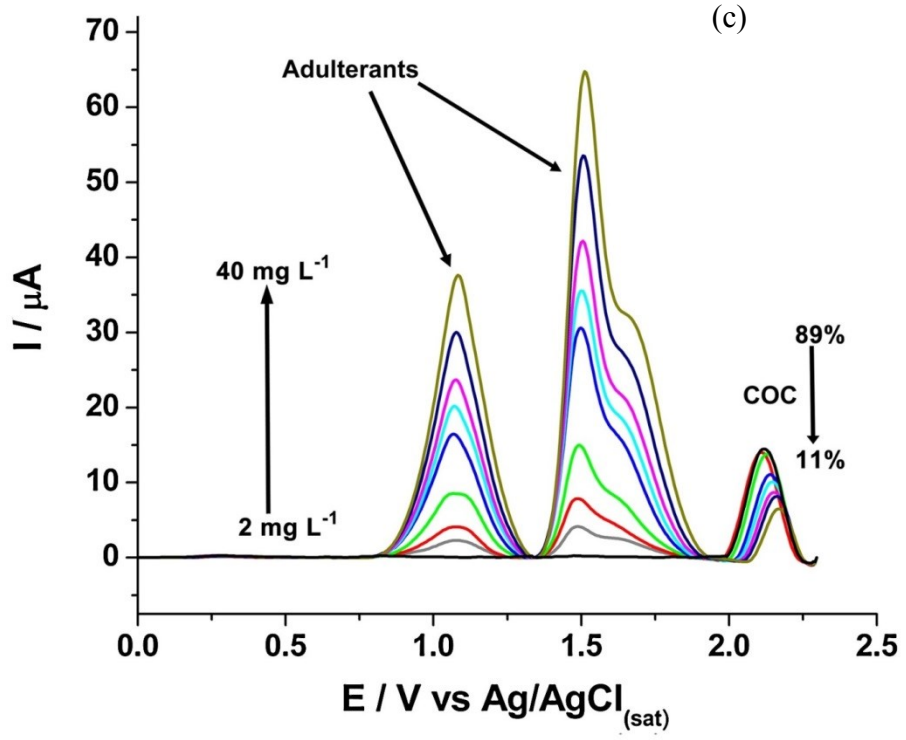

(c)
Adulterants
40 mg L-1
2 mg L-1
89%
COC
11%
I / µA
E / V vs Ag/AgCl(sat)

FIGURE 3

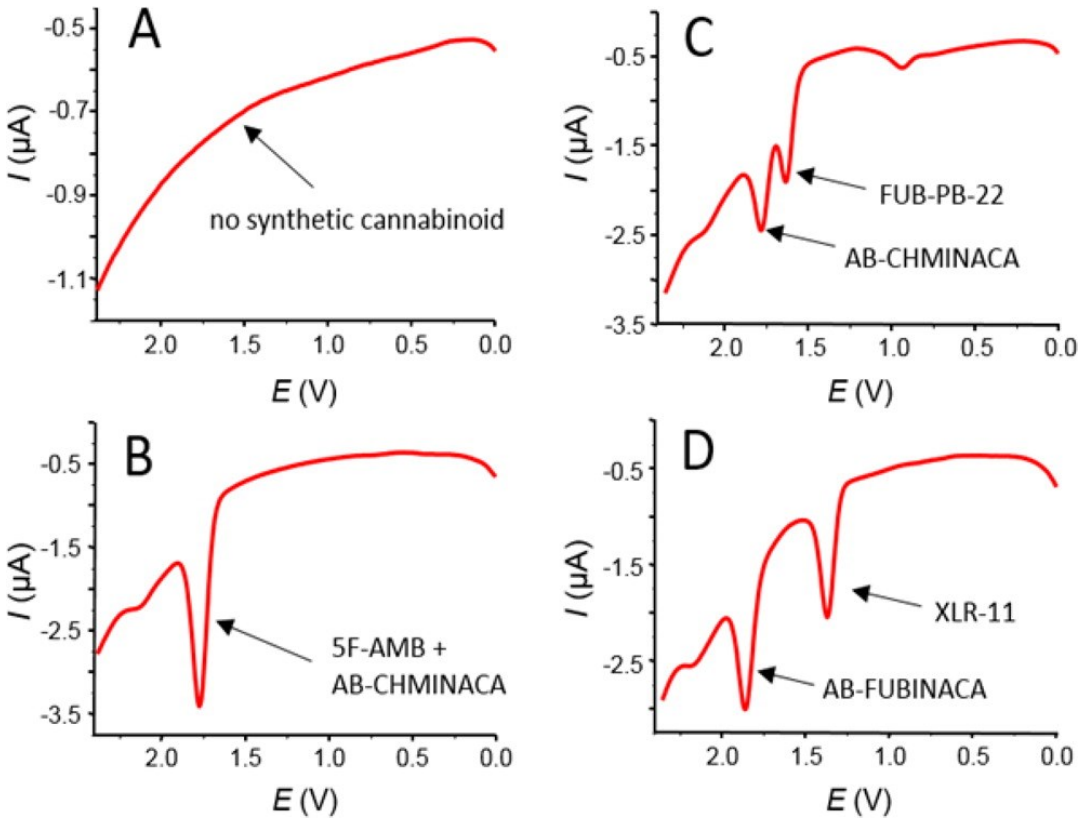


FIGURE 4

REFERENCES

[1] JG Bramness, MJ Reid, KF Solvik, V Vindenes, Recent trends in the availability and use of amphetamine and methamphetamine in Norway, For Sci Int, 2015, 246, 92-97.

[2] L.S. Castillo-Peinado, M.D. Luque de Castro, An overview on forensic analysis devoted to analytical chemists, Talanta, 2017, 167, 181-192.

[3] J.P. Smith, E.P. Randviir, C.E. Banks, An introduction to forensic electrochemistry in E. Katz, J. Halámek (Eds) Forensic Science: A Multidisciplinary Approach, Wiley-VCH, Weinheim, Germany, 2016, pp. 89-102.

[4] P. Norouzi, H. Haji-Hashemi, B. Larijani, M. Aghazadeh, E. Pourbasheer, M.R. Ganjali, Application of new advanced electrochemical methods combine with nano-based materials sensors in drug analysis, Curr Anal Chem, 2017, 13, 70-80.

[5] N. Khan, T Athar, H. Fouad, A Umar, Z.A. Ansari, S.G. Ansari, Application of pristine and doped SnO_2 nanoparticules as a matrix for agro-hazaedous material (organophosphate) detection, Sci Rep, 2017, 7, 42510.

[6] A.N. Amitkumar, A. Pandya, Y.K. Agrawal, Overview of nano-enabled screening of drug facilitated crime: A promising tool in forensic investigation, Trends Anal Chem, 2016, 80, 458 – 470.

[7] F. Shahdost-fard, M. Roushani, Designing an ultra-senstive aptasensor based on an AgNPs/thio-GQD nanocomposite for TNT detection at femtomolar levels using the electrochemical oxidation of Rutin as a redox probe, Biosen. Bioelectron. 2017, 87, 724-731.

[8] M. Maitre, K.P. Kirkbride, M. Horder, C. Roux, A. Beavis, Current perspectives in the interpretation of gunshot residues in forensic science: A review. For Sci Int 2017, 270, 1-11.

[9] Z. Zhou, R.N. Zare, Personal information from latent fingerprints using desorption electrospray ionization mass spectrometry and machine learning, Anal Chem, 2017, 89, 1369-1372.

[10] Y. Zhand, M. Zhang, Q. Wei, Y. Gao, L. Gao, X. Zhang, Latent fingermarks enhancement in deep eutectic solvent by co-electrodepositing silver and copper particles on metallic substrates, Electrochimica Acta, 2016, 211, 437-444.

[11]UNODC World Drug Report, 2016 Available online from http://www.unodc.org/doc/wdr2016/WORLD_DRUG_REPORT_2016_web.pdf (assessed 28th March 2017).

[12] European Drug Report 2016, Available online from http://www.emcdda.europa.eu/system/files/publications/2637/TDAT16001ENN.pdf (assessed 28th March 2017).

[13] J.M. Freitas, D.L.O. Ramos. R.M.F. Sousa, T.R.L.C. Paixão, M.H.P. Santana, R.A.A. Muñoz, E.M. Richter, A portable electrochemical method for cocaine quantification and rapid screening of common adulterants in seized samples, Sensors Actuators B, 2017, 243, 557-565.

••A portable and rapid electrochemical method for screening of cocaine street samples. This work highlights the innovations required to be able to discriminate an illicit substance from the many adulterants typically present in street samples. This research allows for the quantification of cocaine and its adulterants while proposing its use as an on-site or laboratory based screening method.

[14] M.A. Balbino, E.N. Oiye, M.F.M. Ribeiro, J.W. Cruz Júnio, I.C. Eleotério, A.J. Ipolito, M.F. de Oliveira, Use of screen printed electrodes for quantification of cocaine and Δ^9-THC: adaptions to portable systems for forensic purposes. J Solid State Electrochem, 2016, 20, 2435-2443.

•• One of the first papers examining more than one group of illicit substances. This is a challenge for electrochemical sensors but one that does need to be addressed for its application by forensic science.

[15] F. Shahdost-fard, M. Roushani, Conformation switching of an aptamer based on cocaine enhancement on a surface of modified GCE, Talanta, 2016, 154, 7-14.

[16] G. Bozokalfa, H. Akbulut, B. Demir, E. Guler, Z.P. Gumus, D.O. Demirkol, E. Aldemir, S. Yamada, T. Endo, H. Coskunol. S. Timur, Y. Yagci, Polypeptide functional surface for the aptamer immolization: Electrochemical cocaine biosensing, Anal Chem, 2016, 88, 4161-4167.

••A novel approach to forensic analysis of cocaine, incorporating the benefits of electrochemical analysis with the sensitivity of aptamers to obtain a highly sensitive and selective approach for monitoring not only cocaine but also its metabolite benzoylecgonine which is crucial for the application of electrochemical sensors to toxicological analysis.

[17] T.Y. Sengel, E. Guler, Z.P. Gumus., E. Aldemir, H. Coskunol, H. Akbulut, D.G. Colak, I. Cianga, S. Yamada. S. Timur, T. Endo, Y. Yagci, An immunoelectrochemical platform for biosensing of "Cocaine use", Sensors Actuators B, 2017, 246, 310-318.

[18] M.A. Balbino, L.A. de Oliveira, I.C. Eleotério, E.N. Oiye, M.F.M. Ribeiro, B.R. McCord, A.J. Ipolito, M.F. de Oliveira, The application of voltammetric analysis of Δ^9-THC for the reduction of false positive results in the analysis of suspected marijuana plant matter, J For Sci, 2016, 61, 1067-1073.

[19] •J. McGeehan, L. Dennany, Electrochemiluminescent detection of amphetamine type stimulants, *For Sci Int*, 2016, 264, 1-6.

[20] L. Dennany, Z. Mohsan, A.L. Kanibolotsky, P.J. Skabara, Novel Electrochemiluminescent Materials for Sensor Applications, Faraday Dis., 2014, 174, 357-367.

[21] •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, 2016, 8, 142-152.

[22] F. Tan, J.P. Smith, O.B. Sutcliffe, C.E. Banks, Regal electrochemistry: sensing of the synthetic cathinone class of new psychoactive susbtances (NPSs), Anal Methods, 2015, 7, 6470-6474.

[23] B. Habibi, M. Abazari, M.H. Pournaghi-Azar, Simultaneous determination of codeine and caffeine using single walled carbon nanotubes modified carbon-ceramic electrode, Colloids Surface B, 2014, 114, 89-95.

[24] A.S. Lodha, A. Pandya, P.G. Sutariya, S. Menon, A smart and rapid colorimetric method for the determination of codeine sulphate using unmodified gold nanprobe, RSC Adv, 2014, 4, 50443-50448.

[25] A. Mokhtari, H. Karimi-Maleh, A.A. Ensafi, H. Beitollahi, Application of modified multiwalled carbon nanotube paste electrode for simultaneous voltammetric determination of morphine and diclofenac in biological and pharmaceutical samples, Sens Actuators B, 2012, 169, 96-105.

[26] M. Rahimi-Nasrabadi, A. Khoshroo, M. Mazloum-Ardakani, Electrochemical determination of diazepam in real samples based on fullerene-functionalized carbon nanotubes/ionic liquid nanocomposite, Sen Actuators B, 2017, 240, 125-131.

[27] B. Deiminiat, G.H. Rounaghi, M.H. Arbab-Zavar, Development of a new electrochemical imprinted sensor based on poly-pyrrole, sol-gel and multiwall carbon nanotubes for determination of tramadol, Sen Actuators B, 2017, 238, 651-659.

[28] S.A. Waddell, C. Fernandez, C.C. Inverarity, R. Prabhu, Extending the capability of forensic electrochemistry to the novel psychoactive substance benzylpiperazine, Sensing Bio-sensing Res, 2017, 13, 28-39.

[29] M. Dronvoa, E. Smolianitski, O. Lev, Electrooxidation of new synthetic cannabinoids: Voltammetric determination of drugs in seized street samples and artificial saliva, Anal Chem, 2016, 88, 4487-4494.

••A voltammetric method for the direct screening of synthetic cannabinoids, one of the most common NPS compounds. This work was validated against current analytical methods utilised for forensic analysis of street samples.

[30] •J.P. Smith, J.P. Metter, O.I.G. Kherit, O.B. Sutcliffe, C.E. Banks, Forensic chemistry applied to the sensing of new psychoactive substances: Electroanalytical sensing of synthetic cathinones and analytical validation in the quantification of seized street samples, Anal Chem, 2014, 86, 9985-9992.

[31] B.G. Mahmoud, M. Khairy. F.A. Rashwan, C.E. Banks, Simultaneous voltammetric determination of acetaminophen and isoniazid (hepatotoxicity-related rugs) utilising bismuth oxide nanorod modified screen printed electrochemical sensing platforms, Anal Chem, 2017, 89, 2170-2178.

[32] L.R.Cumba, A.V. Kolliopoulos, J.P. Smith, P.D. Thompson, P.R. Evans, O.B. Sutcliffe, D.R. do Carmo, C.E. Banks, Forensic electrochemistry: indirect electrochemical sensing of the components of the new psychoactive substance "Synthacaine", Analyst, 2015, 140, 5536-5545.

[33] L. Brockbals, M. Karlsen, J. Ramsey, B. Miserez, Single injection quantification of cocaine using multiple isotopically labelled internal standards, For Tox, 2017, 35, 153-161.

[34] J. Eliaerts, P. Dardenne, N. Meert, F. Van Durme, N. Samyn, k. Janssens, K. De Wael, Rapid classification and quantification of cocaine in seized powders with ATR-FTIR and chemometrics, Drug Test Analysis, 2017, doi: 10.1002/dta.2149.

[35] D Van Der Gouwe, T.M. Brunt, M. Van Laar, P. Van Der Pol, Purity, adulteration and price of drugs bought on-line versus off-line in the Netherlands, Addiction, 2017, 112, 640-648.

[36] M.O. Salles, W.R. Araujo, T.R.L.C. Paizão, Development of a molecularly imprinted modified electrode to evaluate phenacetin based on the preconcentration of acetaminophen, J Braz Chem Soc, 2015, 27, 54-61.

[37] W.R. de Arajo, A.O. Maldaner, J.L. Costa, T.R.L.C. Paizão, Development of an electroanalytical method for the quantification of aminopyrine in seized cocaine samples, Microchem J, 2015, 121, 213-218.

[38] M. Hosseini, M.R.K. Pur, P. Norouzi, M.R. Moghaddam, M.R. Ganjali, An enhanced electrochemiluminescence sensor modified with a $Ru(bpy)_3^{2+}/Yb_2O_3$ nanopartical/nafion composite for the analysis of methadone samples, Mat Sci Eng C, 2017, 76, 483-489.

[39] L. Asturias-Arribas, M.A. Alonso-Lomillo, O. Domínguez-Renedo, M.J. Arcos-Martínez, Electrochemical detection of cocaine using screen-printed P450 2B4 based biosensors, Talant, 2013, 105, 131-134.

[40] L. Asturias-Arribas, M.A. Alonso-Lomillo, O. Domínguez-Renedo, M.J. Arcos-Martínez, Sensitive and selective cocaine electrochemical detection using disposable electrodes, Anal Chim Acta, 2014, 834, 30-36.

[41] J.M.P.J. Garrido, F. Borges, C.M.A. Brett, E.M.P.J. Garrido, Carbon nanotube β-cyclodextrin-modified electrode for quantification of cocaine in seized street samples, Ionics, 2016, 1-8.

[42] M.F. Muzetti Ribeiro, J.W. da Cruz Júnior, E.R. Dockal, B.R. McCord, M.F. de Oliveira, Voltammetric detection of cocaine using carbon screen printed electrodes chemically modified with uranyl Schiff base films, Electroanalysis, 2016, 28, 320-326.

[43] N.E. Oiye, N.B. de Figueiredo, J.F. de Andrade, H.M. Tristão, M.F. de Oliveira, Voltammetric detection of cocaine in confiscated samples using a cobalt hexacyanferrate film-modified electrode, For Sci Int, 2009, 192, 94-97.

[44] •J.P Smith, O.B. Sutcliffe, C.E. Banks, An overview of recent developments in the analytical detection of new psychoactive substances (NPSs), Analyst, 2015, 140, 4932-4948.

[45] •A.J. Stewart, J. Hendry, L. Dennany, Whole blood electrochemiluminescent detection of dopamine, *Anal Chem*, 2015, 87 (23), 11847-11853.

[46] L. Dennany, E.J. O'Reilly, T. Keyes, R.J. Forster. Electrochemiluminescenct monolayers on metal oxide electrodes: Detection of amino acids, *Electrochem. Comm.* 2006, 8, 1588-1594.

[47] E.J. O'Reilly, P. Conroy, T.E. Keyes, R. O'Kennedy, R.J. Forster, L. Dennany, Combining recombinant Antibody technology and highly sensitive Electrochemiluminescence for the detection of the Cardiac Biomarker C-Reactive protein at sub fg Limits of Detection, RSC Advances, 2015, **5**, 68874-67877.

[48] A.J. Stewart, E.J. O'Reilly, P. Bertoncello, T.E. Keyes, R.J. Forster, L. Dennany, A Cholesterol Biosensor based on the NIR Electrogenerated-Chemiluminescence (ECL) of water-soluble CdSeTe/ZnS quantum dots Electrochimica Acta., 2015,**157**, 8-14.

[49] M.A. Balbino, M.M.T. de Menezes, I.C. Eleotério, A.A. Saczk, L.L. Okumura, H.M. Tristão. M.F. de Oliveria, Voltammetric determination of Δ9-THC in glassy carbon electrode: An important contribution to forensic electroanalysis, For Sci Int, 2012, 221, 23-32.

[50] E.R. Lowe, C.E Banks, R.G. Compton, Indirect detection of substituted phenols and cannabis based on the electrochemical adaptation of the Gibbs reaction, Anal Bioanal Chem. 2005, 383, 523-531.

[51] A.J. Stewart, E.J. O'Reilly, P. Bertoncello, T.E. Keyes, R.J. Forster, L. Dennany, A Cholesterol Biosensor based on the NIR Electrogenerated-Chemiluminescence (ECL) of water-soluble CdSeTe/ZnS quantum dots, *Electrochimica Acta.,* 2015,**157**, 8-14.

[52] P. Bertoncello, A.J. Stewart, L. Dennany, Analytical Applications of Nanomaterials in Electrogenerated Chemiluminescence, *Anal. Bioanal. Chem.,* 2014, 406(23), 5573-5587.

[53] The challenge of new psychoactive substances report 2013 UNODC, https://www.unodc.org/documents/scientific/NPS_Report.pdf, (assessed 28th March 2017).