This is a peer-reviewed, accepted author manuscript of the following research article: Brown, K., & Dennany, L. (2022). Electrochemiluminescence sensors and forensic investigations: a viable technique for drug detection? *Pure and Applied Chemistry*. https://doi.org/10.1515/pac-2021-1204

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Electrochemiluminescence Sensors and Forensic Investigations: A Viable Technique for Drug Detection?

Abstract:

Novel psychoactive substances (NPS) are today considered one of the major ticking public health time bombs in regard to drug abuse. The inability to identify these substances with current screening methods, sees their distribution remain uninterrupted and contributes to the high death rates amongst users. To tackle this problem, it is vital that new robust screening methods are developed, addressing the limitation of those currently in place, namely colour subjectivity and lack of compatibility with the complex matrices these substances may be found within. To this avail, electrochemical methods have been assessed. These low cost and extremely portable sensors have been successfully applied for the direct detection of a broad range of compounds of interest in a range of matrices including, herbal material, commercial drinks and biological fluids (serum, saliva, sweat and urine). With their high versatility, gifted through a significant degree of flexibility in regard to electrode material a range of sensors have to date been reported. In this review the various electrochemical sensors developed to date for NPS detection will be compared and contrasted, with a special focus upon those utilising electrochemiluminescence (ECL) technology.

Keywords:

2021 IUPAC-Solvay Award; IUPAC-Solvay International Award for Young Chemists; Electrochemiluminescence Sensors; Forensic Electrochemistry; Novel Psychoactive Substances

Introduction

Novel psychoactive substances (NPS), a unprecedented epidemic to hit the drug market, and so called “legal highs” have become a popular drug choice amongst a wide

variety of users. Yet, their popularity with consumers is not mirrored within forensic research. A problem, governments thought tackled through increased legislative controls, still sees the forensic community struggle to remain afloat and stay ahead in the sea of these emerging compounds. NPS pose a significant and dangerous public health threat. Perceived to offer improved quality and safety, their false status as "legal" dilutes the negative stigma surrounding their use, accounting for their popularity. With NPS abuse, the stereotypical drug user no longer exists. Instead, a culture of multi-drug use, with users spanning all classes, from homeless to the "1%", these substances are increasingly difficult to identify. Specifically designed to circumvent legislation, clandestine chemists utilise their knowledge to produce a range of species higher in potency and toxicity than their traditional counterparts, but with the added advantage of easy concealment. With current screening methodologies largely unable to detect these substances, they seem invisible to authorities with distribution concealed within decorative plant material or impregnated book pages. Authorities must therefore become as innovative as the producers to fight this latest trend. Unfortunately, to date the forensic community has been unable to maintain pace with the rapid expansion of NPS in the global drug market, which is adamant when acknowledging the 2000 deaths attributed to NPS use in the UK in 2020, double the number witnessed in 2019.[1, 2] Not only is the inability to identify these substances in transport a significant hurdle but also the ability to rapidly identify their presence in overdose patients presents a reasonably overwhelming challenge.

The ticking-time bomb of NPS abuse threatens public health in ways not previously encountered. NPS are not only a societal problem but a scientific one. They provide today's forensic scientists with a challenging but fascinating problem. How to screen for a substance you have never encountered before? The traditional screenings test, including the NIK™ test, were specifically design for a target compound of known structure. The success of these colorimetric test lies in their simplicity, but if the structure was not known prior to development would they be the success they are considered today? The likely answer is no, as to date no commercial colorimetric test have been successfully implemented for the detection of NPS.

To tackle this epidemic, new approaches must be taken, innovative technologies developed and a multidisciplinary approach adopted. To this extent, the development of electrochemical sensors has been witnessed. Electrochemical sensors are fundamentally amenable to forensic and clinical analysis. Yet, they remain - to a certain degree – a niche area of analytical science. The targeting of NPS, by exploiting the electrochemical behaviour gifted to them by their structural properties, allows electrochemical techniques to succeed where traditional colorimetric tests fail. Unlike the current screening methods, the compound's specific structure need not be known to produce a positive

result but a model constructed upon the functional groups commonly encountered within the NPS species can be built. As such these sensing systems would not be nullified by the inevitable future development of new NPS compounds.

To this end we review the current status of electrochemical sensors for the detection of NPS. Assessment will be made on the recent developments in this field, the benefits these sensors provide and the limitations they face, ultimately aiming to provide a thorough assessment of the feasibility of translation of electrochemical devices into the field for NPS detection.

NPS an Overview

New or novel psychoactive substances are a range of purposely designed compounds with the unique purpose of circumventing legislation but with effects which mimic traditional illicit substances.[3, 4] Gaining popularity and recognition under labels such as “legal highs”, “herbal highs”, “research chemicals” or “spice”.[5] Despite their title of psychoactive, the connotations associated with this does not represent their properties or effects. Indeed, these compounds have been synthetized to mimic a wide range of different illicit compounds, including hallucinogens, sedatives, stimulants and opioids.[5] The wide-ranging types of NPS available can be comprehended with through consultation of the “Drug Wise Drug Wheel”[6], shown within Figure l, which was developed as an educational tool in order to educate the public about these substances. A worrying trend surrounding these substances is their unpredictable usage. Unlike a number of traditional substances NPS are not restrictive in regard to their user group, with users documented from school age children, to business personal and party goers.[7, 8] Their legality can largely be considered responsible for the wide-ranging user groups. Their perception as legal results in the false opinion of “safe to use” and decrease in the negative stigma surrounding these compounds. Subsequently, leading to increase in the frequency of hospitalisations and fatalities attributed to their use.[9] Indeed, psychoactive substances which are legal, such as alcohol, see a wider public acceptance and consequently are consumed to a greater extent than those considered illegal. Their availability, ease of access and low detectability during drug screening tests have all been documented as motivators behind the increased use of NPS.[10, l1] Despite the increased legislation to control their use, NPS still remain a prevalent global problem with over 1000 new species identified across l35 countries since 2008.[12]

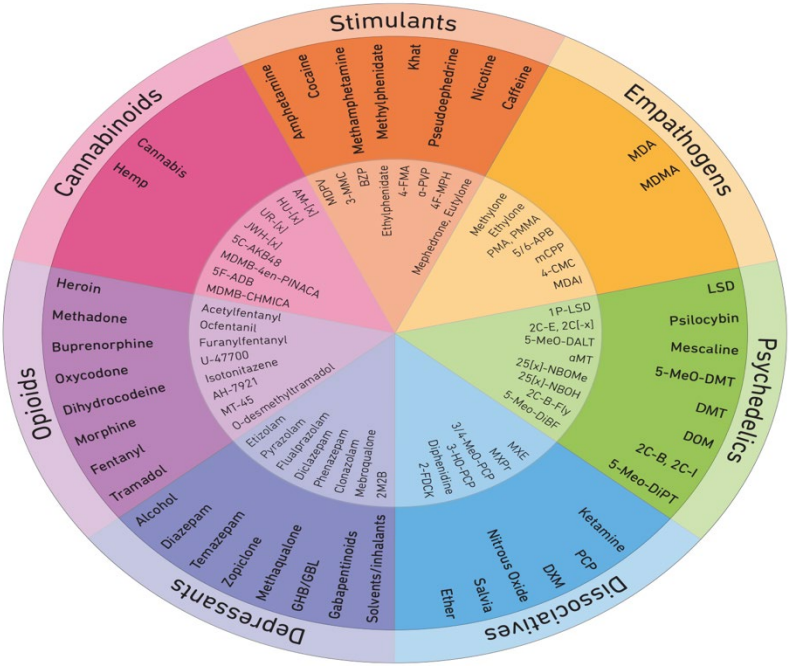

Figure 1: The drugs wheel (NPS vs established) where the outer ring represents established or traditional drugs and the inner ring represents NPS, reproduced from ref. [6] with permission from "the drugs wheel Mark Adley", Copyright 2021.

NPS are typically grouped into four main categories based upon their mechanism of action; stimulants (including cathinone and piperazines), depressants (including benzodiazepines and opioids), hallucinogens and synthetic cannabinoids.[5, 9] Typically, NPS classifications are based upon species possessing similar structures but with varying effects (such as cathinones) or similar effects but with dissimilar structures (such as synthetic cannabinoids).[9] The inconsistency in the chemical structure of NPS across classes and within has likely contributed to the difficulty in developing screening methods appropriate for these species. Typically, colorimetric methods identify the class of drug present based upon their corresponding functional groups. However, with such variation and no consistency in regard to functional groups present within the same NPS classes, these methodologies fall down. This presents a unique challenge in regard to screening technologies, where it must be specific enough to assign class but diverse enough to encompass a range of functional groups within that single class.

Electrochemical Strategies for NPS Detection

Electrochemical sensors are highly amenable toward employment as screening strategies. These versatile methodologies encompass a wide variety of the necessary criteria making them particularly appealing toward employment within the forensic science field. Recent advances in the technology required to perform electrochemical measurements see them offering tremendous portability, both with commercial portable systems or in-house manufactured systems, with some even involving manipulation of mobile phone auxiliary outputs to supply the required system voltages.[13-15] The instrumentation required is significantly less than their spectroscopy or chromatographic counterparts, making they ideally suited toward in-field analysis and with no necessary separation strategies required negates the need for gas cylinders as is the case with the gold standard chromatographic mass spectrometry techniques. What's more flexibility in regard to electrode materials and potential surface functionalisation allows for fabrication toward specifically identified target analytes or toward a wide variety of substances. Surface modification has indeed never been more attainable, with facilities allowing electrode fabrication in-house at minimum cost. The increased presence of screen-printed electrodes (SPE) not only minimises the risk of cross contamination of samples due to their disposability, their smaller geometry requires only µL volumes, maximising available sample amounts for subsequent analysis. Electrochemical sensors have proven success in the detection of forensically relevant substances, including illicit drugs but more importantly NPS.[16-23] With a growing amount of literature available on the detection of NPS via these methodologies it begins to feel somewhat inevitable that their use will transition from theoretical research laboratory use into real-world field applications.

The electrochemical sensing of NPS dates back to 2014, where Smith *et al.[24]* discussed the ability to reliably detect synthetic cathinone's as a consequence of irreversible oxidation at their amine functionality. Utilising graphite SPE a significant attempt was made toward the reliable detection of synthetic cathinone's by the authors, they were able to reliably detect these target NPS individually within an ideal matrix. However, where their methodology fell down was the inability to detect the synthetic cathinone's when in the presence of other electroactive substances, notably caffeine and benzocaine. This early work however set a precedence for the utilisation of electrochemistry for the detection of NPS, which has expanded in the subsequent years.[24] The detection of synthetic cathinone's has progressed considerably from that of Smith *et al.* [24] initial work, with a system based upon reductive identification and metabolite identification.[23, 25, 26] Indeed, last year Lima *et al.[27]* built upon the methodologies

of Smith *et al.* [24] and assessed graphite SPE for the detection of 3,4-methylenedioxypyrovalerone (MDPV). Through the pairing of these SPE with adsorptive stripping differential pulse voltammetry (AdSDPV) the authors were able to achieve detection of MDPV down the forensically relevant concentrations, with a sensor which was reusable with no cross contamination or carry over observed.[27] Of more note however, was their ability to address the lack of specificity which plagued Smith *et al.* [24] Through their AdSDPV method and utilising the multiple oxidation processes which occurred when MDPV was interrogated via electrochemical techniques, the authors were able to accuracy identify and quantify MDPV in the presence of common interferents including, caffeine (previously indistinguishable with Smith *et al.'s* method), paracetamol, MDMA and two other synthetic cathinone's, mephedrone (4-MMC) and methylone (bk-MDMA).[27] Through monitoring of the initial oxidation peak, the authors were able to accurately monitoring MDPV amongst the other electroactive interferents, and achieved recoveries well within the typical analytical limits of 90-110%, as demonstrated in Figure 2.[27] They further provide the merit in their sensor by then applying it to seized street samples, achieving recoveries of 103% for samples known to contain ethylpentylone and 95% in the presence of MDMA, in comparison to the gold standard LC-MS method.

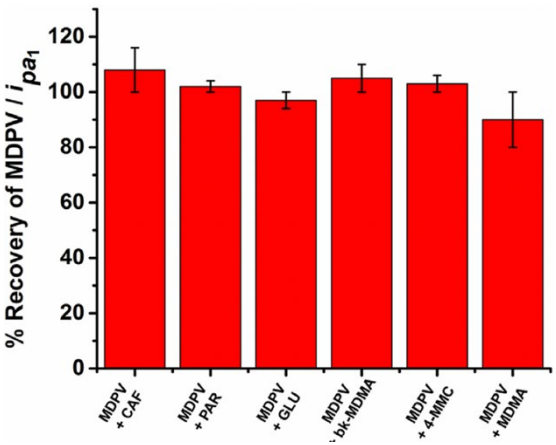

Figure 2: Recovery results obtained for the first oxidation process of MDPV in the presence of potential interferents caffeine, paracetamol, methylone, 4-MMC and MDMA (CAF, PAR, GLU, bk-MDMA, 4-MMC and MDMA). Reproduced from ref. [27] with permission from Elsevier, Copyright 2020.

Although these works have shown tremendous promise and achievements, they explicitly focus upon a single synthetic cathinone. It is widely known that the NPS market is ever expanding and thus it is vital to truly assess the feasibility of electrochemical methods for the reliable detection of the synthetic cathinone class that some form of grouping system is devised and assessed. Such as that recently performed by Schram *et al*.[28], who divided the parent class up into three groups; N-alkylated (Class I), 3,4-methylenedioxy-N-alkylated (Class II) and N-pyrrolidine (Class III) cathinone's.[28] This classification system was devised to spilt the cathinone class up in regard to their oxidizable groups. Having chosen a specific cathinone as a model compound from each group the authors then investigated each classes electroactivity upon carbon SPE forming the electrochemical profile for each proposed class. As per the prior works, oxidation was readily observed for each class with either a single oxidation peak (Class I) or two redox peaks (Classes II and III), each demonstrating the expected relationships with pH. Of more note was the authors approach to increase sensor specificity. With a basic square wave (SW) voltammetry method interferents of paracetamol, caffeine, procaine, lidocaine, benzocaine, and phenacetin all hindered the identification of the target synthetic cathinone to varying degrees, across all classes.[28] To overcome this the authors devised a simple yet effective pre-treatment steps, whereby cathodic pre-treatment of the sample pH of l2 was performed. Doing so suppressed the effects from the majority of the adulterants. Lidocaine however still presented as problematic with overlapping peaks observed when present alongside Class III, although a quick test at pH 7 was a viable work around. The real strength of this classification method was proven through the analysis of l0 seized samples, with 9 of the samples correctly classified into their respective classes, simply through the developed SW methodology with this cathodic pre-treatment step. Only one sample was not classified and was later confirmed to be cathinone itself, which has no electrochemical functionality in the potential region upon carbon SPE, this was then assigned as Class 0.[28] The strength of the methodology designed by Schram *et al.[28]* for synthetic cathinone detection and classification is to date unparalleled. They successfully addressed the preconceived limitations of electrochemical sensors for the screening of NPS, notably the ability to develop a methodology which is both specific to an NPS class but variable enough to account for the sub-classes within due to the differing functionalities. The promise demonstrated here is undeniable and it becomes difficult to deny the strong possibility of the near future employment of these methodologies into field forensics.

Synthetic cannabinoids (SC) are one, if the not the most, prevalent classes of NPS available on the market. Believed to be amongst the original NPS substances, they remain one of the largest and widely used class of NPS. Synonymous with terminology such as "Spice" "K2" and "Bath Salts", SC remain amongst the deadliest of the NPS available.[29-33] Their full agonist action upon the cannabinoid receptors see's their

toxicity and potency underestimated with connotations from their naming convention giving users a false perception that they share the same potency and effects as Δ^9-THC. However, this is not the case and as such their use is increasingly associated with fatalities and hospitalisation.[3, 29-31, 34] Much like synthetic cathinone's, SC possess a number of different functional sub-classes with some of the most well know being the indole, indazole and imidazole functionalities. These functional groups are associated with electrochemical activity and as such it would be a fair assumption that they would be prime candidates for electrochemical screening. Yet, to date investigations into the ability to detect SC via electrochemical techniques is sparse. The first detection of SC via electrochemical techniques dates back to 2016 when Dronova *et al.*[35] successfully demonstrated the ability to oxidise a number of indole and indazole based SC upon platinum, boron doped diamond and carbon conventional electrodes.[35] At the time of publication SPE and portable potentiostats where not as accessible as today, and such explains the conventional set up adopted by the authors. Despite this though their methodology was thorough and promising with all 11 SC interrogated producing responses, in addition to identifying a classification strategy based upon the number of redox peaks observed with those producing a second anodic peak at higher potentials all found to contain an additional electroactive functional group in the form of naphthalene or quinoline.[35] What's more despite their preliminary stage they were able to actively identify SC from seized street samples demonstrating promise from the initial application of electrochemical analysis to these species.

Yet despite this promise further investigations into the potential opportunity to employ these techniques for SC screening, it wasn't until 3 years later that new research on the electrochemical detection of these species appeared.[36, 37] However, these focused on the employment of biorecognition elements to alter the resistance of the electrode surface for their identification. Sensors such as these are highly specific, however they are also incredibly costly, difficult to construct and complex to run and as such do not fit in the scope for forensic screening methods, although do show strength in clinical environment where one specific species need be identified. As such, there clearly remains a large gap in the knowledge surrounding the possibility to employ electrochemical methods for the screening of SC actively. Indeed, the same assessment as for synthetic cathinone's would be required before the same conclusion could be brought for these NPS species. To aid this, work currently investigating the potential expansion of electrochemical sensors for this end is on-going. Our recent publication acts a preliminary study for the employment of differential pulse voltammetry (DPV) for SC screening with a focus upon BB-22 and its corresponding metabolite.[38] We successfully demonstrated the ability to readily detect both species under ideal conditions, thus providing a concept proof for sized sample analysis, where powders would be dissolved in the required electrolyte. However, when employed within a biological matrix of

human serum sensitivity was dramatically hindered, as demonstrated in Figure 3 and thus it is readily apparent further enhancements are necessary.[38] Particularly, for the screening of drug use where direct analysis within biological matrices such as saliva or urine would be required. However, although this represents an initial step forward in the employment of basic electrochemical techniques for SC screening, it is meant as an initial stepping stone upon which future research and collaborations will begin to provide the necessary knowledge needed in order for SC screening to be readily performed out with these type of sensing systems.

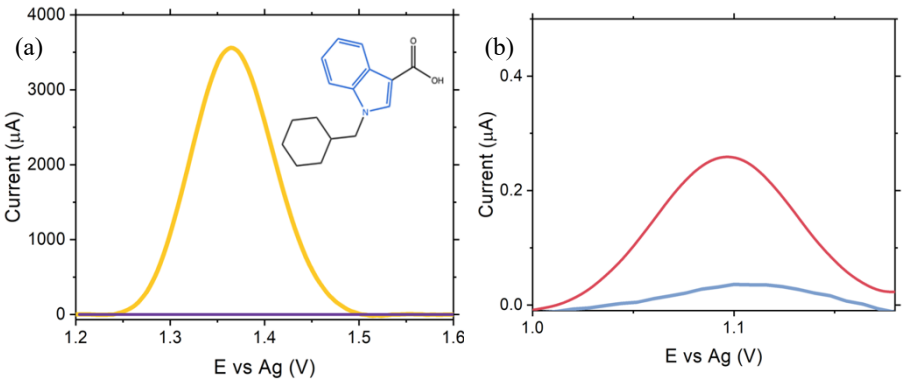

Figure 3: (a) DPV of SC BB-22 metabolite upon a carbon working electrode surface under ideal cell conditions, at a concentration of 1 mM (yellow) and (b) DPV of 0.2 mM BB-22 metabolite in human pooled serum (pink) and serum intrinsic signal shown in blue collected upon carbon working electrode surface. Reproduced from Ref. [38] with permission from IOP Publishing Ltd.

Electrochemiluminescence for NPS Screening

With the basic electrochemical techniques offering promise in regard to screening technologies, it becomes a fair assumption that employment of these alongside a secondary electrochemical method may be able to offer the increased sensitivity desired. Electrochemiluminescence (ECL) is one such technique. ECL combines the advantages of electrochemical techniques with those from photoluminescence.[39-47] Unlike its spectroscopy counterparts however ECL does not require an external light source to be incorporated within its instrumentation, with luminescence generated through the electro-initiated chemical reactions at the electrode surface ECL produces its own light source. As such, this negates the drawbacks of external light sources avoiding fluorescent interferents and vastly simplifies the necessary instrumentation dramatically

decreasing instrument footprint and enhancing their portability. [39-47] ECL also benefits from the ability to (re)generate the required intermediates at the electrode surface enabling the production of large numbers of photons per measurement cycle, resulting in enhanced sensitivities over the more traditional electro-analytical techniques. [47-49] ECL has been employed the detection of a variety of illicit species although most prominently for the detection of amphetamine type substances [21, 50-53] and cocaine [54-57]. With the increase in electrochemical techniques for NPS detection, ECL has also expanded toward NPS identification in recent years. The detection of NPS via ECL largely see's a reliance upon those which contain amine functionality. The first reported detection of NPS via ECL dates back to 2013 when Lledo-Fernandez *et al*.[58] utilised the traditional ruthenium luminophore for detection of the widely known NPS ketamine. The secondary amine functionality of ketamine made it a primary candidate for detection via an ECL system. The authors constructed their system by including the ruthenium luminophore $[Ru(bpy)_3]^{2+}$ at an optimised concentration of 1 mM into the acetate buffer containing the ketamine sample.[58] The authors found the addition of ketamine increased the signal observed from the buffered ruthenium combination to a significant degree, thereby allowing for the positive identification of the target analyte. Utilising glassy carbon electrodes in a conventional cell set up, they were able to achieve a detection limit for the NPS down to 39 ng/mL.[58] Although this detection was in significant excess of the chromatographic techniques the authors used as a baseline, it remains a significant achievement for the first employment of ECL for ketamine detection and does lie within the expected range of criminal cases involving ketamine spiking.[59] Having established the suitability of their proposed method they then investigated the possibility of detection within alcoholic beverages without the need for sample pre-treatment to a great success.[58] Having spiked ketamine into gin and tonic the authors demonstrated detection down to 200 ng/mL, with a typical reported ketamine dosage of 400 ng/mL in spiking cases.[58] However, although this initially appears promising given the negation of any sample preparation strategies (which given this early stage was indeed a notable achievement for the authors) they failed to acknowledge the impact which the mixer tonic would have upon their system. As is evident from their presented calibration curve there is negligible difference in the signal observed from a blank matrix to that containing 200 ng/mL.[58] This is not surprising given that tonic contains the alkaloid species quinine, whose tertiary amine makes it an ideal co-reactant. As such there would be significant interference from the quinine species which the authors failed to considered. Nonetheless, this initial ECL sensing system for NPS demonstrated a promising avenue for the employment of the technique in NPS screening benefiting from many of the benefits of the traditional electrochemical approaches.

The detection of ketamine via ECL was further improved through the development of an immunosensing system which utilised carbon quantum dots (CDs) as the luminophore.[60] Rather than the anodic co-reactant system of Lledo-Fernandez *et al*.[58], here the authors relied upon a quenching mechanism via the cathodic co-reactant mechanism of potassium persulfate.[60] Rather than direct detection, Li *et al.[60]* methodology was an in-direct method where by the increasing concentration of ketamine, resulted in the decrease of the potassium persulfate signal. This sensing mechanism is quite common with ECL QD based systems, which largely operate in the cathodic region where $K_2S_2O_8$ is a standard co-reactant.[60-63] Employment of this method resulted in a an almost 1000-fold improvement in sensitivity with the authors reporting a detection limit of 0.067 ng/mL.[60] This is a remarkable improvement in sensitivity, and highlights the significant benefits of electrode modification with the luminophore film, alongside immunoreactions, which offer superior specificity, as demonstrated by the authors through both interference studies and analysis of spiked human plasma; a complex matrix known to cause interference with ruthenium-based sensors.[60] However, the main limitation of these types of sensing systems is their complexity of manufacture and use, alongside their high specificity which in this instance renders them ideal for ketamine detection but prevents their use for the screening of any alternative NPS. As such, sensor designs like these would require prior knowledge of the target analyte prior to construction. However, the ever-evolving market of NPS and constant structural modifications would result in the manufacture of such immuno-based sensors would be continually catching up to the clandestine NPS manufacturers.

These initial ECL detection strategies for NPS were amongst the primary reports which inspired our subsequent research into this area.[18-21] Focus was placed upon the criteria of portability, versatility and ease of use when developing ECL sensors toward NPS detection, where hallucinogenic tropane alkaloids atropine and scopolamine were used as model compounds.[18-21] The alkaloid functionalities of these species gifted them the ability to behave as suitable co-reactants to the traditional ruthenium luminophore. Building upon the method of Lledo-Fernandez *et al*.[58] and incorporating film electrode modification strategies similar to that of Li *et al.* [60] both atropine and scopolamine were detected within a variety of complex matrices; including herbal material, commercial beverages and biological fluids. [18-21] The driver for ease of use and portability seen methods focus upon the negation of any sample preparation of separation strategies. In the case of Lledo-Fernandez *et al*.[58] the impact of tonic water was not consider upon their sensing system. Assessment of this however was performed by ourselves in an attempt to establish the ability to determine atropine within spiked tonic, an attribute with direct relevance to a previous criminal case.[19, 64, 65] As expected the quinine functionality within tonic water does indeed produce a notable ECL signal, although significantly lower than that containing the target analyte, it does

highlight the need to establish a reliable threshold.[19] Indeed, it is likely that prior to the wider employment of ECL sensors as screening strategies toward NPS identification, any matrices likely to be encountered would need to be assessed. Each matrix intrinsic signal would need to be reliably established and then stored within an accessible database. Construction of such a database would be an onerous task, with standardisation required across electrode material, potentiostat and detection set up required, however it would be vital should transition of these sensors into active forensic deployment be made.

Consideration of the matrices likely encountered during NPS screening will likely influence the detection or sensing systems of choice. Electrochemistry lends itself well toward a variety of matrix types. Unlike its spectroscopic counterpart IR, samples can contain water with no detriment, whilst solids can be actively screened without sample burning, as is observed with Raman spectroscopy. Demonstration of this can be seen through the direct detection of the hallucinogenic tropane alkaloids within their native herbal plant material, *Datura*.[19] Through our coined abrasive ECL technique, plant material naturally containing the target species was identified. Detection was achieved through a simple method whereby herbal material was mechanically applied to the modified electrode surface.[19] Not only was the plant material found to show the predicted signals associated with atropine and scopolamine (with confirmation through mass spectrometry) differentiation was even made between mature and young plant material (see Figure 4).[19] Of course, again the question over matrix interference arose with the lack of specificity intrinsic to ECL plaguing the technique since its inception. Establishing where the possible matrix interference would lie becomes more challenging for natural plant material (with a vast array of species within), and often with NPS distributed on such material, it becomes a highly problematic challenge to tackle in the early stages of sensor development. One approach to begin establishing a threshold for samples distributed upon plant material would be to analyse a range of relevant species known to be contained with the same plant family as those used for NPS distribution. Such a system may take the shape proposed within our initial publication on this matter where *solanaceus* family members *tomatine* (tomato) and *solanine* (petunia) were used as a control group to facilitate *Datura* identification (Figure 4 (b)).[19] This revealed an ability to utilise plant family members as suitable controls, and could be a promising starting point for database construction.

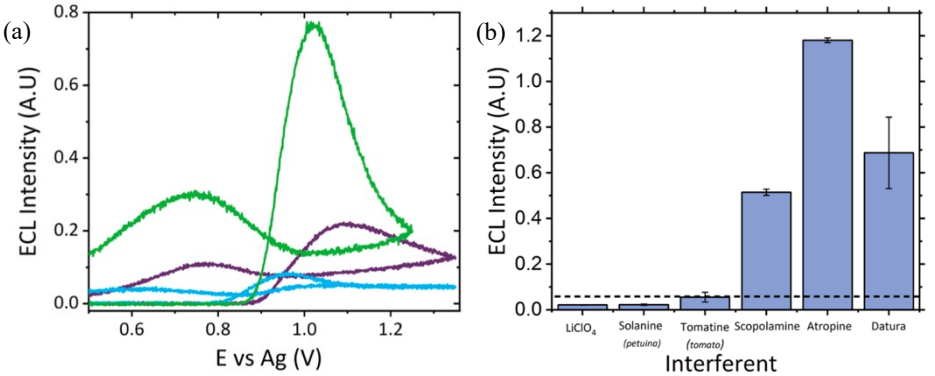

Figure 4: (a) ECL responses obtained after mechanical application of mature *Datura* leaf (green), young *Datura* leaf (purple), and tomato leaf (blue) onto $[Ru(bpy)_3]^{2+}$-modified electrode and (b) Maximum ECL responses observed from different species naturally found within the herbal material of the *solanaceous* plant family. The dotted line represents the established threshold signal. Adapted from ref. [19] with permission from American Chemical Society, Copyright 2019.

Of course, samples containing NPS will not only take the form of herbal material and commercial beverages, and thus consideration must be given to a wide range of alternative matrix. These may include but are not limited to biological fluids or solid samples. Biological fluids provide their own set of unique challenges, with the possibility for false negatives heightened. As such, a wide and varied study must be performed to establish potential interference from non-controlled substances (for example caffeine) or naturally occurring species (including urea) which may be present within a person's serum, blood, saliva, urine or sweat. Although we have made initial progress in this regard with simulated matrices or pooled serum[18, 21] it is inevitable before any screening could be performed upon biological samples that a controlled clinical study would be necessary. Particularly considering the known suitable co-reactants likely found within these matrices including caffeine[66], naturally occurring amino acids or similar biological components[67-70] and nicotine.[15, 71, 72]

Conclusion

Despite the clear challenges which remain the road toward employment of electrochemical sensors for NPS identification via screening methodologies has made

significant progress in the past decade. Indeed, a variety of NPS classes possess the necessary functionalities which make them compatible with electrochemical sensors, a trait only heightened by the flexibility offered by the versatile construction of these sensors. What's more unlike its more widely accepted counterparts, the systems required to perform at sight screening for substances are now commercially available at lower cost. Indeed, in house potentiostats and those based upon smart phone devices are rising in popularity amongst the academic community but a reliable and financially viable source will be needed should the transition into the forensic field take place, a criterion currently met by a number of commercial suppliers. Some even offer smart phone compatible instruments with in-app software which exploit the portability these academic smartphone devices offer. Electrochemistry, whether traditional or ECL does offer a viable solution to a number of the concerns when screening for NPS, in particular it stratifies the ability to specify between different NPS classes but can still handle the variation of structures within these that the colorimetric tests currently can't. However, this does not mean they are ready to be fully implemented to this end. Further research is required, particularly in regard to establishing a database of matrix effects, whether this be for ECL or traditional electrochemistry or indeed both. Establishing such a database is the greatest challenge restricting the mass employment of electrochemical sensors toward NPS screening but also once addressed has the potential to cement these sensors for this end within the forensic field.

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