Voltammetry as a rapid Screening method for NPS identification

A Ameen, H Russell, L Dennany*
[a]WESTChem, Department of Pure and Applied Chemistry, University of Strathclyde, Technology and Innovation Centre, 99 George Street, Glasgow, G1 1RD, UK
*lynn.dennany@strath.ac.uk; phone +44 141 548 4322

ABSTRACT

Designer drugs, also commonly known as new psychoactive substances (NPS), are increasingly in their prevalence and a challenge to toxicologists and forensic chemists. Synthetic cannabinoids (SCs) are among the largest group of NPS that have emerged in the illicit drug market all over the world. SCs may consist of different chemicals prepared in laboratories and herbal mixtures that said to be incense and not-for-human-consumption. The main aim of this paper is to investigate the use of electrochemical based methods for screening some of the emerging types of SC. More specifically, the paper takes electrochemistry approach called voltammetry to perform the detection and analysis of SCs whereby the main subjects for screening include STS-135 and 5F-ADB-PINACA. The expected result is that those compounds that belong to the same class should indicate almost similar behaviour to help achieve its objective, the paper reviews a number of recent publications relating to forensic drug analysis and much attention to electrochemical sensor methods.

Keywords: NPS; synthetic cannabinoids; GC-MS; electrochemistry; compounds; STS-135; 5F-ADB-PINACA; voltammetry

1. INTRODUCTION

SCs are a group of 'designer drugs' taken by users to mimic the effects of Δ^9-tetrahydrocannabinol (Δ^9-THC), the known psychoactive ingredient in natural cannabis (shown in figure 2.1).[1-5] SCs act as cannabinoid receptor agonists as their structure is often similar to Δ^9-THC (exemplar in figure 2.2), which enables them to bind to the same cannabinoid receptors in the body, namely CB_1 and CB_2.[1-4,6,7] Generally, this binding is greater than that of Δ^9-THC, although individual affinities can waver, which may explain the increased potency of SCs compared to Δ^9-THC itself.[2-4,8]

SCs often exist as solid crystalline material and are generally prepared for consumption by immersing plant material in a solvent containing the dissolved crystal.[2,8] This can lead to varied concentrations and combinations of SCs in each product which can contribute to the increased potency of SCs, as well as the observed worsened withdrawal symptoms from SCs compared to natural Δ^9-THC.[2,4,8] The reported increased potency of SCs highlights the need for a screening method for their detection.[2] Without proper substance identification, it is hard to predict the extent of the risk to the user. As well as having varied concentrations and compositions, SC products on the illicit market frequently contain impurities.[9] If no such identification methods are known, advancements in overdose remedies could conceivably be hindered as there is no reliable way of predicting what the products may contain.[8]

Major challenges are faced by analytical chemists in the quantification and qualification of SCs and as a result, current testing methods for SCs are limited. This includes the fact that standard screening methods do not facilitate the detection of SCs and for some SCs, confirmatory analysis is complicated by the fact that standards are not available. This means that standard forensic identification procedures, often based on chromatographic analysis where comparison with a standard is done, cannot be undertaken. On 21st October 2019, new drug-driving laws were introduced in Scotland, which saw the employment of roadside drug tests with a 'zero tolerance' policy towards the most common drugs of abuse, including 'natural' cannabis.[10,11] The gap in current forensic procedures must be addressed in order to make further progress in the employment of portable drug testing to include SCs and other synthetic substances.

Going by the growing challenges caused by SC variety in the drug market and forensic field, there is a need reference standard material to compare with drug spectral libraries for detection. Unfortunately, the available techniques are unable to identify some of the SCs because of their varying composition. Shaw and Dennany emphasized that the way to deal with these cases is by having a powerful technique that can analyze specific sample matrices, and with high sensitivity.[9]

This is a peer reviewed, accepted author manuscript of the following research output: Ameen, A., Russell, H., & Dennany, L. (2020). Voltammetry as a rapid screening method for NPS identification. Proceedings of SPIE, 11540, [115400X]. https://doi.org/10.1117/12.2573507

The urgent need for an alternative screening method makes electrochemistry as the best way to go. Electrochemical analysis now shows significant advantages - high sensitivity, can be used in crime scenes, cheap, portable, and fast. Recent laboratory tests proved that electrochemical analysis could determine the presence of subgroups of SC, including the indole and indazole based compounds.[12] STS-135 and 5F-ADB-PINACA (structures shown in Figure 1) are among those compounds that can be detected through electrochemistry. For this contribution we evaluate the use of voltammetric methods as a screening method for these compounds.

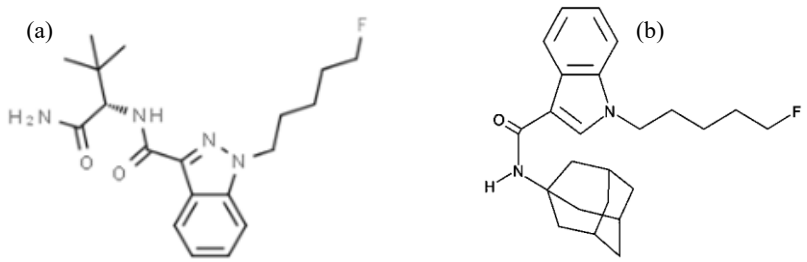

Figure 1: (a) 5F-ADB-PINACA (Molecular Formula: $C_{19}H_{27}FN_4O_2$) and (b) STS-135 (Molecular Formula: $C_{24}H_{31}FN_2O$).

2. EXPERIMENTAL

2.1 Materials and Reagents

Lithium perchlorate electrolyte ($LiClO_4$) was purchased from Sigma-Aldrich and prepared as an electrolyte solution using HPLC gradient grade acetonitrile (CH_3CN) from VWR. Standard of 5F-ADB-PINACA and STS-135 in crystalline powder form were purchased from LGC Ltd. Hannah pH 210 microprocessor pH meter is used to measure the electrolyte pH at 25 ^oC.

2.2 Instrumentation.

Voltammetric behaviour was recorded at room temperature, and the measurements were carried out using CHI 602E and PalmSens Version EM Stat 3 potentiostat for CV and DPV respectively. Experiments were performed in one-compartment glass electrochemical cell using a conventional three-electrode system; A silver wire (Ag) and platinum wire (Pt) electrode were used as a reference and counter electrode respectively. For a comparative study on a bare electrode, both a 3 mm glassy carbon (GC) and Pt electrode were used as a working electrode.
CV parameters were recorded in the potential range between 0 V to +2.0 V vs Ag wire at 100 mV^{-1} scan rate and 1x 10^{-5} scan sensitivity. The DPV measurements optimal conditions were as follow: 50 mV for the pulse amplitude; 50 ms pulse width and 4 mv increment potential. The potential scan range is $1.0 \leq E \leq 1.95$ vs Ag wire. The variation in the potential window depends on each analyte oxidation peak potential. All the working electrodes were manually cleaned before each run with a figure-eight formation on the 0.05 µM alumina slurry felt pad, then rinsed with deionised water and acetonitrile to remove the slurry and prevent being transfer into the solution.

3. RESULTS AND DISCUSSION

The electrochemical behaviour of 1 mM of 5F-ADB-PINACA was investigated utilising both glassy carbon (GC) and platinum (Pt) working electrodes over the potential range $0 \leq E$ vs Ag ≤ 2 V as illustrated in Figure 2. 5F-ADB-PINACA is an indazole-based SC from the indazole-3-carboxamide family, and as is expected, it undergoes oxidation at ~ 1.8 V vs Ag. This is likely because of the abstraction of an electron from the indole ring moiety.[13] SCs have the ability to undergo irreversible oxidation due to the presence of pyrrole and pyrazole ring moiety of indole and indazole respectively. [3] Oxidation in these compounds results when electrons are abstracted from the indole ring moiety. Two irreversible oxidation peaks are observed because the indole and indazole-based SCs also contain the quinoline or naphthalene moieties in addition to the indole ring moiety. These oxidations are more apparent on the GC electrode compared to that of the Pt working electrode.

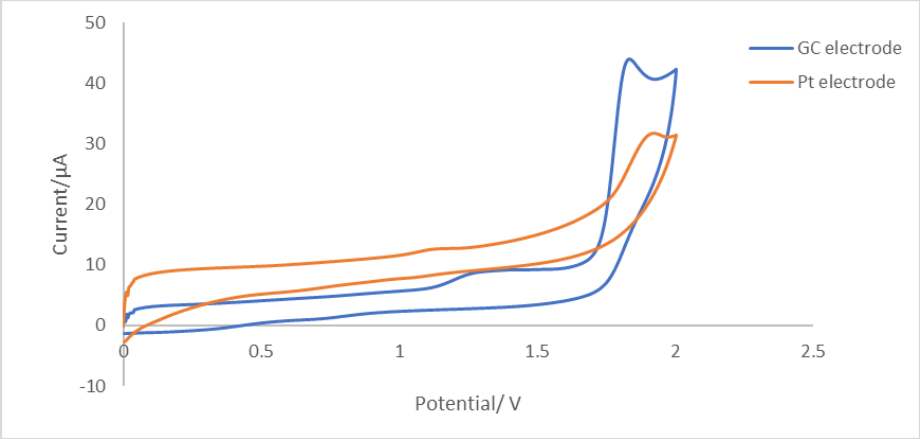

Figure 2: The comparison CV response of 1 mM 5F-ADB-PINACA stock solution using a GC electrode and Pt electrode, scanned over potential, $0 \leq E \leq 2$ vs Ag wire at a scan rate of 0.1 V s^{-1}.

The electrochemical behavior of 5F-ADB-PINACA, the indazole-based SC, for potential range $0 \leq E \leq 2$ V vs Ag wire is shown in figure 2. This indazole-based SC had only the irreversible oxidation using CV. 5F-ADB-PINACA had two irreversible oxidation peaks in the voltammogram at a scan rate of 0.1Vs^{-1}. The first peak was at E= ~1.28 V while the second and more prominent peak was at E= ~1.82 V. The first peak is due to the oxidation of the indole ring moiety of the indazole and the second peak is due to oxidation of functionalities of the naphthalene moiety.[14] The second peak is more stable than the first one because stability relates to the sluggishness in electron transfer and a positive potential is needed to observe an oxidation reaction.

The electrochemical behavior of STS-135, the indole-based SC, for potential range $1.0 \leq E \leq 1.75$ V vs Ag wire is shown in figure 3. Similar to 5F-ADB-PINACA, only irreversible oxidation was observed for STS-135. Also, STS-135 had two irreversible oxidation peaks observed in the voltammogram at a scan rate of 0.1 Vs^{-1}. The first peak was observed at E= ~ 1.26 V while the second more prominent peak was observed at E= ~ 1.40 V.

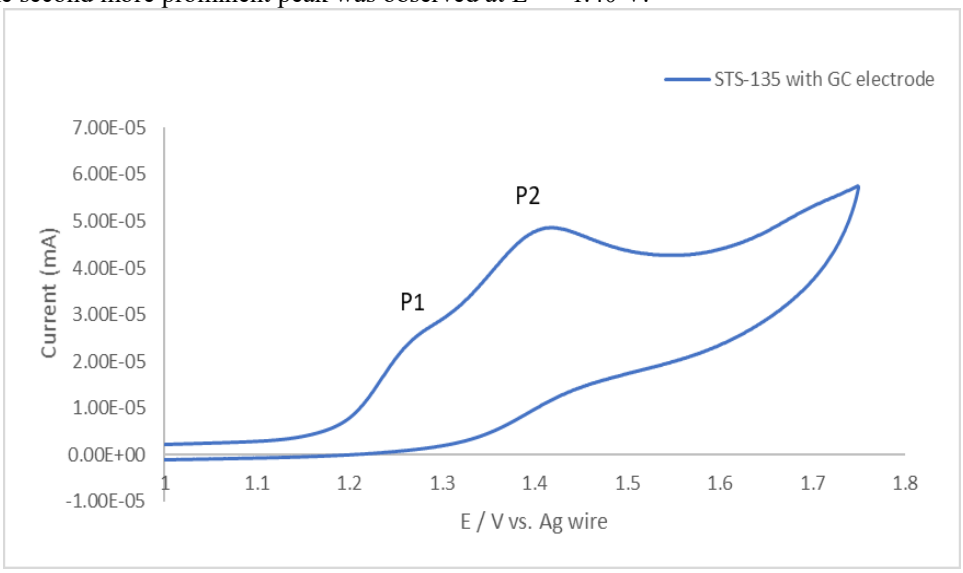

Figure 3: Typical CV of oxidation peak of STS-135, using GC electrode over the potential window, $1.0 \leq E \leq 1.75$ V vs Ag wire at a scan rate of 0.1 V s^{-1}.

In the case of the chosen SCs, both of them showed irreversible oxidation peaks. As indazole base exhibited one oxidation, while indole base Sc showed two oxidation peaks. The indole base SC oxidation potential appeared earlier than the indazole based SC which is expected, as Dronova *et al*. reported that indole had been oxidised at 1.15 V and indazole at 1.43 V. [14]

When both SC were analysed by DPV using GC electrode, a similar number of oxidation peaks that were seen in CV were observed. In figure 4, DPV of 5F-ADB-PINACA shows the same number of oxidation peaks on same working electrode but slightly reduced positive potential P1 at E= ~ 1.22 V due to oxidation with a substituent at C3 position of the pyrrole ring of the indole moiety and second peak P2 at E= ~ 1.77 due to a different substituent.[14] Both peaks are shifted to less positive for DPV in comparison to CV because DPV is a more sensitive technique than CV for this type of screening.[15]

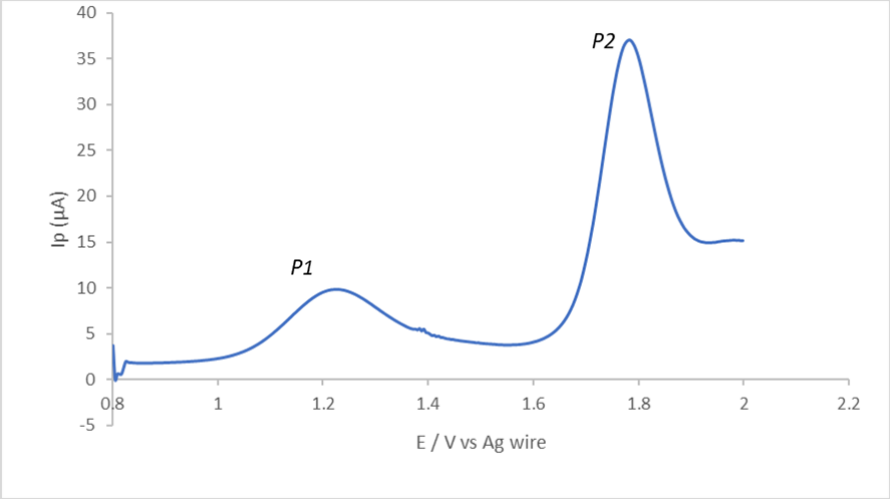

Figure 4: DPV response of 1mM of 5F-ADB-PINACA in 0.1M LiClO4 in CAN, scanned over potential 0.8 ≤ E ≤ 1.95 vs Ag wire.

For the STS-135, figure 5 shows two oxidation peaks with the first peak at E= ~ 1.24 V while the second more prominent peak at E= ~ 1.34 V. A similar trend was also observed for this SC.

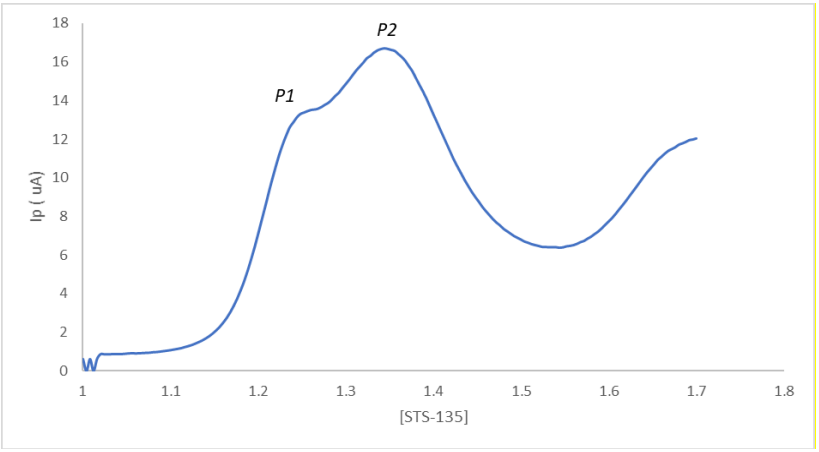

Figure5: typical DPV of 1 mM STS-13 5over the potential 1 ≤ E ≤ 1.75 vs Ag wire

Therefore, the optimized method was validated for these SC. DPV provided excellent sensitivity with limit of detection at 0.3 nM and 0.5 pM of indazole and indole- base respectively. Linearity was assessed with correlation coefficients $R^2 >$ 0.98 for indazole-bade SC and 0.99 for indole base SC as shown in figure 6. However, as with previous papers, the ability to discriminate between the different SCs still eludes this analysis. The major challenge, highlighted by this contribution is the need to discriminate between structurally similar compounds. This has been examined for other illicit substances[16-19] but research on SCs is still limited in this area. In addition, street samples of SCs are likely to contain other illicit substances, notably amphetamine type substances (ATS). However, previous studies have shown that ATS do not shown any electrochemical activity over the potential ranges explored in this study. The final challenge will be the detection of these SCs in biological matrices where there is likely to be many biological interferences. This contribution highlights the potential of electrochemical methods as a screening approach for these SC but also the many challenges that have still to be investigated.

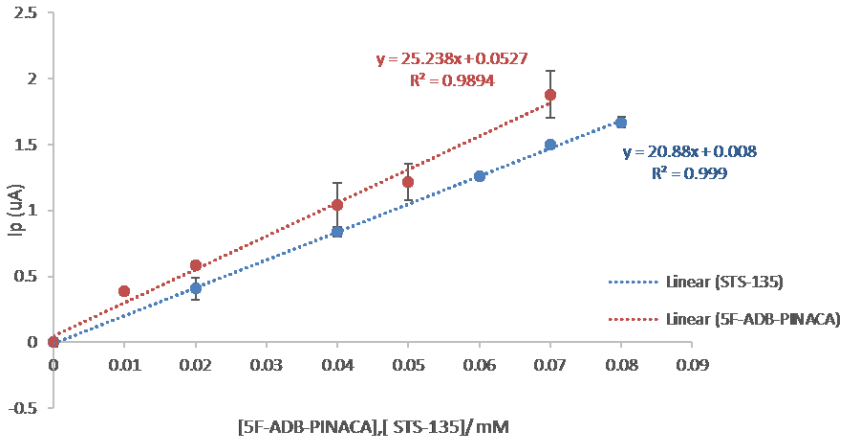

Figure 6: The calibration curve in the form peak heights vs [5F-ADB-PINACA] and [STS-135]

4. CONCLUSION

Synthetic cannabinoids belong to a group of NPS with various chemicals that are abused in place of marijuana. Besides, they are more dangerous than tetrahydrocannabinol (THC) that is found in natural cannabis plants. Not all the color tests that are currently available are able to detect and identify all the functional groups of synthetic cannabinoids; some have failed. The insufficiency or lack of reliable screening techniques is a major problem that makes it difficult to ensure effective regulation of the use of SCs. Fortunately, electrochemistry concept of voltammetry is a potential technique that will bring a solution to the screening difficulties in the forensic field and toxicology. This contribution illustrates the potential of electrochemistry to address this current gap in the field. Although in its infancy and with many other challenges to address before these methods can be implemented, it does highlight the need for rapid, fast, easy to use and cheap methods to screen for SCs and how electrochemistry can be utilized for this purpose.

ACKNOWLEDGEMENTS

The authors would like to thank the State of Kuwait for financially supporting this research.

5. REFERENCES

[1] European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Perspectives on Drugs: Synthetic cannabinoids in Europe, http://www.emcdda.europa.eu/topics/pods/synthetic-cannabinoids, (accessed November 2019; last updated June 2017).

[2] UNODC Laboratory and Scientific Section Portals: Synthetic Cannabinoids, https://www.unodc.org/LSS/SubstanceGroup/Details/ae45ce06-6d33-4f5f-916a-e873f07bde02, (accessed January 2020; no update date available).

[3] EMCDDA Synthetic cannabinoids and 'Spice' drug profile, http://www.emcdda.europa.eu/publications/drug-profiles/synthetic-cannabinoids, (accessed January 2020; last updated January 2015).

[4] D. Debruyne and R. L. Boisselier, *Substance Abuse and Rehabilitation*, 2015, **6**, 113-129.

[5] United Nations Office on Drugs and Crime (UNODC), *Synthetic cannabinoids in herbal products*, United Nations Office, 2011.

[6] V. Shevyr, V. Melkozerov, G. W. Endres, Y. Shafran and Y. Morzherin, *Cannabis and Cannabinoid Research*, 2016, **1.1**, 186-194.

[7] V. A. Shevyrin and Yu. Yu. Morzherin, *Russian Chemical Bulletin International Edition*, 2015, **64**, 1249-1266.

[8] B. Mills, A. Yepes and K. Nugent, *The American Journal of the Medical Sciences*, 2015, **350**, 59-62.

[9] L. Shaw, L. Dennany, *Current Opinion in Electrochemistry* 2017, **3(1)**, 23-28.

[10] Scottish Government New Drug Driving Laws, https://www.gov.scot/news/new-drug-driving-laws-to-be-introduced/, (accessed January 2020; last updated 11th October 2019).
[11] The Drug Driving (Specified Limits) (Scotland) Regulations 2019, http://www.legislation.gov.uk/ssi/2019/83/contents/made, (accessed January 2020; last updated 2019 (No. 83)).
[12] L. Cumba, A. Kolliopoulos, J. Smith, P. Thompson, P. Evans, O. Sutcliffe, D. do Carmo, C. Banks, C., *Analyst,* 2015, **140(16)**, 5536-5545.
[13] J. Ammann, O. Drummer, D. Gerostamoulos, J. Beyer, J., *Victorian Institute of Forensic Medicine*, 2016, **41(3)**, 21-22.
[14] M. Dronova, E. Smolianitski, O. Lev, O., *Analytical Chemistry,* 2016, **88(8)**, 4487-4494.
[15] M. A. Balbino, L. S. de Oliveira, I. C. Eleoterio, E. N. Oiye, M. F. M. Ribeiro, B. R. McCord, A. J. Ipolito, M. F. de Oliveira, *Journal of Forensic Sciences*, 2016, **61**, 1067-1073.
[16] J. McGeehan and L. Dennany, *Forensic Science International*., 2016, **264**, 1-6.
[17] K. Brown, M. McMenemy, M. Palmer, M. J. Baker, D. W. Robinson, P. Allan and L. Dennany, *Analytical Chemistry*, 2019, **91**, 12396-12376.
[18] K. Brown, C. Jacquet, J. Biscay, P. Allan, L. Dennany, *Anal Chem*, 2020, **92 (2)**, 2216-2223.
[19] K. Brown, C. Jacquet, J. Biscay, P. Allan, L. Dennany, *Analyst*, 2020, **145**, 4295 – 4304.