ANALYSIS OF DRUG-INFUSED PAPERS BY ASAP-MS

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INTRODUCTION

- **Drug misuse within UK secure institutions is prevalent and a major concern.**
  - → **It contributes to increased levels of aggression and violence.**
  - → **The emergence of novel psychoactive substances (NPS) have exacerbated the issue.**
- **In prisons it has been reported that an estimated 60% to 90% of the prison population in England and Wales use NPS.[1]**
- **It has been reported that paper and other materials infused with drugs have been smuggled into UK secure institutions.[2,3]**
- **Reducing access to drugs in secure institutions is a key consideration in the overall strategy to reduce drug use.**
- **An effective method of testing materials received by individuals may assist in this process.**
- **The aim of this study was to assess the potential of RADIAN™ ASAP Mass Detector (Figure 1), a compact device based on Atmospheric Solids Analysis Probe-Mass Spectrometry (ASAP-MS), as a simple yet rapid, screening tool for suspect papers that had been confiscated.**

SAMPLE EXTRACTION

- Duplicate samples ('A' and 'B') from twenty papers that were suspected to contain drug substances were provided for analysis. Each anonymised sample measured approximately 2x2 cm.
- 1x1cm squares were cut from the supplied paper samples.
- Samples were placed into individual screw cap vials with 500 µL of methanol and sonicated for 5 minutes (Figure 2).
- After sonication, the solvent was transferred to a clean screw cap vial ready for ASAP-MS analysis or further diluted for QTof analysis.

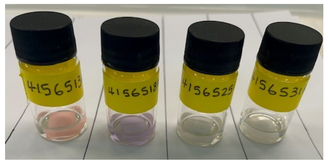

Figure 2. Suspect paper samples following sonication in methanol.

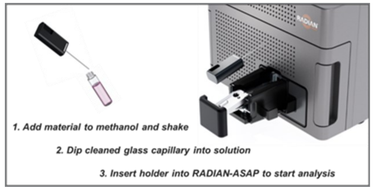

Figure 1. Data acquisition using the RADIAN ASAP (Waters)

ASAP-MS ANALYSIS

The system comprised a RADIAN™ ASAP with LiveID™ software (Waters Corp.) for data processing. Samples were using the workflow shown in Figure 1. Each sample extract was sampled in triplicate i.e., the same glass capillary used for three cycles of 'dip and detect' to make triplicate measurements of one sample extract. The analysis is summarized as follows:

- Direct MS analysis (separation without chromatography), is performed by the process of ASAP ionization (Figure 3).[4] The process involves the volatilization of the sample with the use of a heated desolvation gas and a corona discharge for ionization, resulting in the generation of the protonated species (in positive ionization mode).
- The application of four cone voltages (15, 25, 35, 50 V) generates fragmentation by in-source collision-induced dissociation (CID).
- LiveID software compares by the acquired spectral data against a reference library prepared using certified reference material (CRM) for 70 common drug compounds, using a reverse fit model; this matching can be performed in near real-time with a result provided in seconds (Figure 4). A match score of ≥ 850 (from a maximum of 1000) was used to indicate a positive identification.

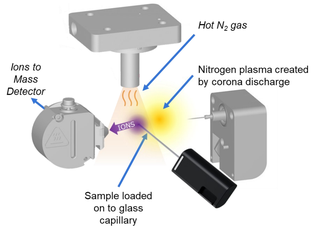

Figure 3. ASAP-MS ionization process

QTOF ANALYSIS

- The extracts were also analysed using an established QTof-based screening method.[5]
- Sample extracts were diluted 1:2000 in 5mM ammonium formate, pH 3.
- Analysis was performed using ACQUITY™ UPLC I-Class coupled with Xevo™ G2-XS QTof mass spectrometer.
- The screening method comprised of acquisition of accurate mass data using electrospray positive (ESI+), followed by comparison of the data to a reference library containing data for >2000 compounds, comprising retention time and exact mass data for the precursor and specific fragments.

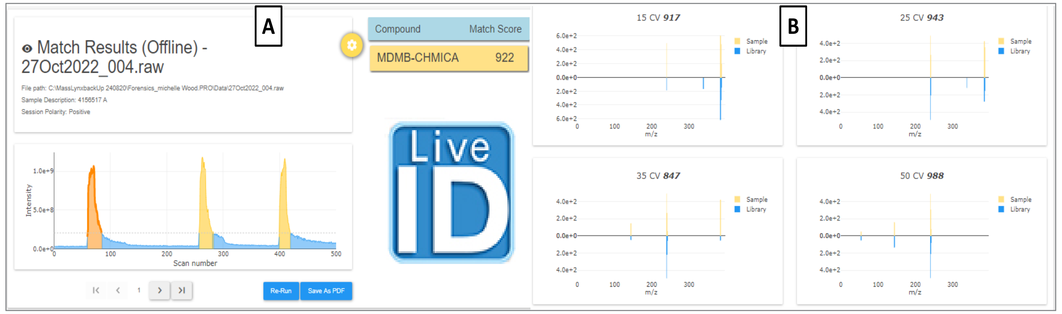

Figure 4. LiveID analysis of a suspected paper sample. Panel A shows three "dip and detect" replicates for the sample and the match score 922 (maximum 1000) obtained for the first replicate. Panel B displays the detail for this spectral match; all four cone voltages are used in the identification process with a weighted mean (lowest cone voltage with the highest weighting) used.

RESULTS AND DISCUSSION

- For all substances detected in this study, ionization resulted in protonation of the analytes, $(M+H)^+$.
- The application of increasing cone voltages (15, 25, 35, 50 V) leads to the generation of characteristic product ions; the combination of the precursor and the generated fragment ions provide a spectral fingerprint for each analyte (Figure 5).
- Confiscated samples (n=20) were analysed and the mean for the three ASAP-MS replicates was calculated. The analysis of the paper samples led to a positive detection in 18 of the samples, with match scores ranging from 881 to 989 (summarized in Figure 6). Two samples did not result in any library matches and were deemed negative.
- There was good agreement between the QTof-based analysis and the ASAP-MS analysis. Some additional compounds were detected by the QTof, such as ethylphenidate, lidocaine and methiopropamine; likely due to the greater analytical sensitivity of QTof-MS when compared to ASAP-MS.
- Good agreement was shown between the analysis results for the supplied duplicate samples. There was one instance of discrepancy between sample duplicates (detected using both RADIAN ASAP and QTof analysis), this is likely to be due to the non-uniform distribution of the drug during the paper infusion.
- Following identification, the feasibility of a semi-quantitative analysis of drugs in paper using ASAP-MS was assessed. A calibration series for the two analytes identified, was prepared by infusing blank paper samples (1x1cm) with CRM and was extracted alongside 10 of the suspect papers. Molsodomine was used as an internal standard and was added to the methanol used for extraction of both the spiked papers and the confiscated papers (Figure 7 and 8).
  - → Suspect samples with positive detections for MDMB-CHMICA were found to contain approximate concentrations ranging from 0.05-3.08 mg/cm^2.
  - → Suspect samples with positive detections for 5F-AKB48 were found to contain approximate concentrations ranging from 1.34-3.04 mg/cm^2.

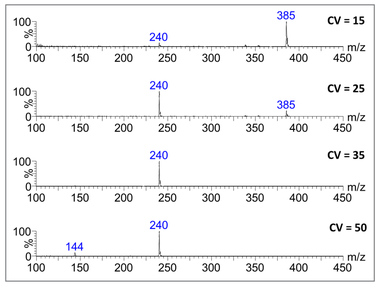

Figure 5. Spectral fingerprint generated by ASAP-MS for MDMB-CHMICA CRM

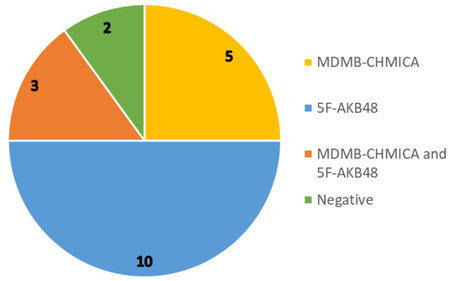

Figure 6. Analytes detected (match score >850) in a series of 20 suspect paper samples

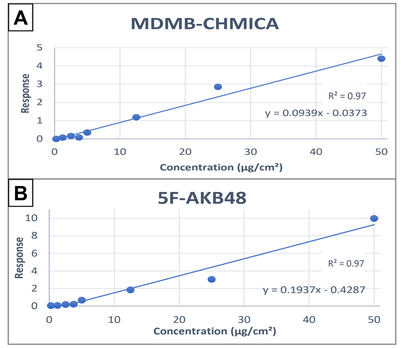

Figure 7. Calibration curves for ASAP-MS analysis of infused paper samples, 0.25-50 µg/cm². Panel A shows the linear calibration curve produced for MDMB-CHMICA and Panel B shows the linear calibration curve produced for 5F-AKB48.

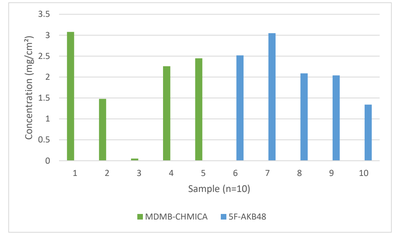

Figure 8. Concentrations obtained for confiscated papers (n=10) following semi-quantitative analysis using ASAP-MS

CONCLUSION

- **ASAP-MS is an easy-to-use, rapid and accurate direct MS screening technique; it provides MS data directly i.e., without the requirement for chromatographic separation.**
- **The technique shows promise as a simple screen for drugs and NPS which have been infused onto paper samples.**
- **The extraction method is both quick and simple and has been demonstrated to be effective for paper samples infused with drugs.**
- **ASAP-MS analysis and spectral library matching takes less than two minutes for each confiscated sample.**
- **Semi-quantitative analysis was shown to be promising approach with RADIAN ASAP, concentrations in confiscated samples were estimated at 0.05-3.08 mg/cm^2 for MDMB-CHMICA and at 1.34-3.04 mg/cm^2 for 5F-AKB48.**
- **The technique may be an effective tool to reduce access to drugs in prison.**

References

1. Centre for Social Justice (2015). *Drugs in Prison,* London: Centre for Social Justice
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