ANALYSIS OF DRUG-INFUSED PAPERS BY ASAP-MS

Emily Lee *and Michelle Wood*
Toxicology & Forensics R&D, Waters Corporation, UK

Waters™

INTRODUCTION

Drug misuse within UK prisons is prevalent and a major concern; it contributes to increased levels of aggression and violence amongst inmates, and puts a strain on valuable medical resources. Misuse has a negative effect on the stability, security and overall effectiveness of the penal system. Whilst traditional drug substances such as opiates, cocaine and cannabis continue to be widespread in prisons, the emergence of potent novel psychoactive substances (NPS) have significantly exacerbated the issue. It has been reported that the use of NPS, particularly synthetic cannabinoids, is widespread with estimates from 60% to 90% of the prison population in England and Wales.[1]

Recently paper and other materials infused with drugs have been smuggled into UK prisons, including letters to inmates impregnated with drugs including NPS such as etizolam and synthetic cannabinoids receptor agonists.[2,3] Reducing inmates access to drugs is a key consideration in the overall strategy to reduce drug use in prisons by tackling supply and demand. An effective method of testing materials which have been received by inmates, may greatly assist in this process.

The aim of this study was to assess the potential of RADIAN™ ASAP Mass Detector, a compact device based on Atomospheric Solids Analysis Probe-Mass Spectrometry (ASAP-MS), as a simple, yet rapid, screening tool for drug infused paper.

SAMPLE PREPARATION

Paper samples used in the study were: 80gsm white paper, newspaper, greetings card, envelope and "glossy" magazine and included samples that were free from ink and that included ink.

Two alternative methods were used to infuse the papers (1 minute) with common drug substances:

Pipetting method:

- A 50µL aliquot of certified reference material (0.2mg/mL and 1mg/mL in methanol) was pipetted onto 1x1cm pre-cut paper squares, which were then placed on a glass tile for 30 minutes to dry.

Soaking method:

- Paper samples cut into 4x4cm sections were placed in a beaker with diluted certified reference material (1mg/mL in methanol), which were then placed on a glass tile for 30 minutes to dry. Once dry, a 6mm hole-punch was used to take samples from the larger square.

Drug-free papers were prepared by the same methods using methanol in place of reference material.

Extraction:

Samples prepared using both preparation methods were extracted using the same method.

- Pre-cut square samples or hole-punched samples were placed into individual screw cap glass vials with 500µL of methanol (Figure 1) and sonicated. Following sonication the solvent was transferred to a clean screw cap vial.

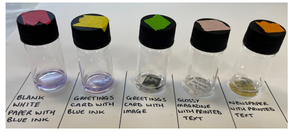

Figure 1. Different paper types following sonication in methanol

ASAP-MS ANALYSIS

Following the sample extraction the samples were analysed by RADIAN ASAP, as shown in Figure 2.

The system comprises a RADIAN™ ASAP with LiveID™ (Waters Corp.) for data processing.

- Direct MS analysis (separation without chromatography), is performed by the process of ASAP ionisation (Figure 3).[4] The process involves the volatilisation of the sample with the use of a heated desolvation gas and a corona discharge for ionisation, resulting in the generation of the protonated species (in positive ionisation).
- The application of four cone voltages (15, 25, 35, 50 V), generates fragmentation by in-source collision–induced dissociation (CID). The combination of the precursor and the generated fragment ions provide a spectral fingerprint for each analyte, thus increasing specificity (Figure 4).
- LiveID software compares the acquired spectral data against a prepared reference library (reverse fit model); this matching can be performed in near real-time with a result provided in seconds. A match score of 800 (from a maximum of 1000) was used to indicate a positive identification.

Figure 2. Data acquisition using the RADIAN-ASAP (Waters)

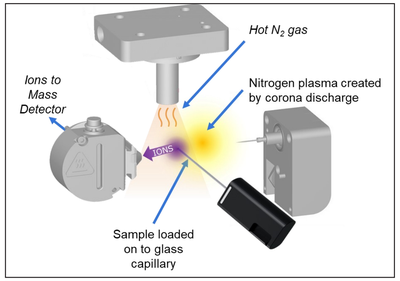

Figure 3. ASAP-MS ionisation process

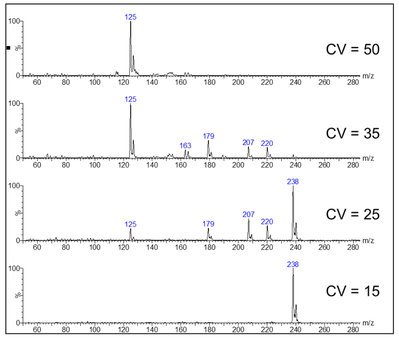

Figure 4. Spectral fingerprint generated by ASAP-MS for Ketamine CRM

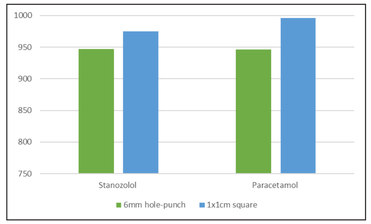

Figure 7. Match scores for hole-punch and pre-cut squares. Average match scores for 80gsm paper samples infused with 1mg/mL of reference standard

RESULTS AND DISCUSSION

ASAP-MS provides a direct analysis technique yielding mass spectrometry data without chromatographic separation. For all substances evaluated in this study, ionisation resulted in protonation ($M+H^+$) of the analyte. The application of increasing cone voltages (15, 25, 35, 50 V) led to the generation of characteristic product ions which improved accuracy of drug identification.

- Paper samples (white paper, 80gsm) were initially prepared in triplicate, by spiking with 17 common drug substances at 1mg/mL, using the pipetting method. Samples were extracted for 5 minutes and analysed; the mean for the three replicate ASAP-MS analyses was calculated. All drugs were correctly identified with mean match scores ranging from 853 to 996 (Figure 5). Drug-free blank papers, which were treated with methanol only, did not result in any library matches >800 and therefore were deemed negative.
- In addition to the common drugs of abuse, several NPS were also included in this study; these substances are of particular interest as use of NPS in prison communities has reported to be endemic.[3] Figure 6 illustrates a typical result for a paper sample that was infused with the synthetic cannabinoid 5-Fluoro MDMB-PICA; for this sample a high match score of 979 was obtained using LiveID.
- Samples were also infused at a lower concentration of 0.2mg/mL for 6 drug substances. These samples resulted in slightly lower match scores than samples infused at 1mg/mL, however match scores still exceeded the threshold used for positive identification.
- For improved ease, and consistency of sampling, the use of a hole-punch (6mm diameter) was also evaluated (Figure 7). The match scores for hole-punched samples were lower than those obtained using the 1x1cm square sample, but still exceeded the minimum 800 threshold. The lower responses are likely to be reflective of the smaller area which was sampled.
- Extraction times of 5, 10 and 15 minutes were evaluated for the 80gsm white paper, prepared using both preparation methods. Increased sonication times showed no significant difference in library match scores obtained, therefore, to reduce overall analysis time a 5 minute sonication time was subsequently applied.
- As initial testing was based on in-house spiked paper samples which were free of ink, the study was extended to include evaluation of differing paper types/thickness and the potential effect on spectral data in the presence of inks. Paper samples that contained inks, included ballpoint pen (plain paper and greeting card), printed text (newspaper and a 'glossy' magazine) and printed image (greeting card) were tested (Figure 1). The 5 minute extraction method was confirmed to be suitable for all paper types tested with no significant difference in match factors compared to 80gsm white paper. Furthermore the presence of the inks did not have any significant effect on the match scores obtained. This is advantageous as materials received by inmates are likely to contain some form of ink.
- For most of the samples tested, a match against a single substance was returned. However, some exceptions were noted e.g. isotonitazene which was identified with a mean score of 964 but also resulted in a match score >800 for it's isomer protonitazene. This was not of great concern as the procedure detailed is intended for use as a preliminary fast screening technique, and differentiation may be achieved by use of a confirmatory method with MS detection such as LC-MS/MS. In our laboratory for example, isotonitazene and protonitazene can be differentiated by retention time using LC-MS/MS.

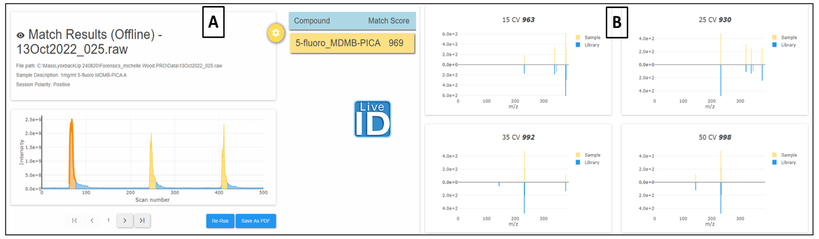

Figure 6. LiveID analysis of a sample infused, by the pipetting method, with 50µL of 1mg/mL 5-Fluoro MDMB-PICA. Panel A shows three "dip and detect" replicates for the infused sample and the match score 969 (maximum 1000) obtained for the first replicate. Panel B displays the detail for this spectral match; all four cone voltages are used in the identification process with a weighted mean (lowest cone voltage with the highest weighting) used.

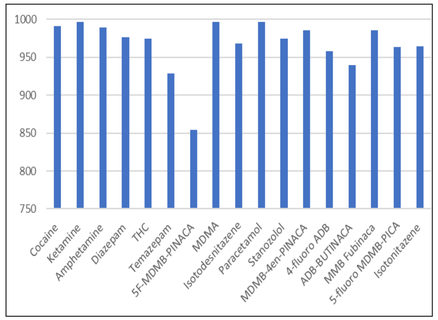

Figure 5. Average match scores for spiked paper samples (n=3) infused with 1mg/mL methanolic solutions of various reference materials, using a 5 minute extraction.

CONCLUSIONS

- **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 has shown promise as a simple screen for drugs and NPS (including synthetic cannabinoids and synthetic opioids) infused into paper samples.**
- **The extraction method is both quick and simple and has been demonstrated to be efficient for different paper-types, thicknesses and treatments. Sampling paper by use of a hole-punch further simplifies preparation.**
- **ASAP-MS analysis and spectral library matching takes less than two minutes for each sample. The presence of inks and other treatments did not appear to interfere with the detection of drug substances.**
- **The technique may be an effective tool to reduce access to drugs in prisons.**

References

1. Centre for Social Justice (2015). *Drugs in Prison*, London: Centre for Social Justice
2. Ford, L.T and Berg, J.D. Analytical evidence to show letters impregnated with novel psychoactive substances are a means of getting drugs to inmates within the UK prison service. *Annals of Clinical Biochemistry* 2018: 55(6): 673-678
3. Norman, C *et al.* Detection and quantitation of synthetic cannabinoid receptor agonists in infused papers from prisons in a constantly evolving illicit market. *Drug Test Anal.* 2020; 1-17
4. Wood, M; RADIAN ASAP with LiveID-Fast, Specific, and Easy Drug Screening. Waters Application Note Library Number, 720007125EN

TO DOWNLOAD A COPY OF THIS POSTER, VISIT WWW.WATERS.COM/POSTERS