DIRECT MASS DETECTION AS A RAPID, AT-POINT-OF-SAMPLING, SCREENING TOOL

Ben MacCreath[1], *Chris Henry*[1], *Rachel Sanig*[1], *Michael Jones*[1], *Michelle Wood*[1], *Emily Lee*[1], *Li Yan Chan*[2], *Adabelle Ong*[2]

[1]*Waters Corporation, Wilmslow, UK;* [2]*International Food and Water Research Centre, Waters Pacific Pte Ltd, Singapore*

INTRODUCTION

Modern analysts are constantly challenged with finding more information from complex samples. The result is a plethora of analytical techniques and tools necessary to characterize sample components, often requiring high levels of expertise to operate.

Mass spectrometers are a common detector used for such tasks due to their excellent sensitivity, precision, accuracy, and ability to screen and differentiate several chemical species simultaneously, frequently being paired with chromatography systems to further deconvolute complex chemistry. However, it can be the case that the indepth analysis involved is too cumbersome, too expensive, or takes too long to achieve. Speed-to-decision could be improved through a rapid screening method to directly provide the level of information required, or to triage the sample set for further analysis, significantly improving costs and time efficiency.

With the introduction of the RADIAN™ ASAP mass detector, samples can be taken directly from reaction vessels and introduced directly into the instrument with little or no sample preparation required. This gives the user near instant access to information-rich mass spectral data for rapid decision making.

DIRECT MASS CONFIRMATION

Here, a simulated reaction workflow is used, the synthesis of atenolol from intermediate 4-hydroxyphenyacetamide (4-HPA).[1] Samples were analysed at 5 different "time points" (n=5) by dipping the glass rod into each solution and introducing directly to the RADIAN. The spectra for each simulated timepoint clearly shows the reduction in 4 HPA (*m/z* 152) and the increase in atenolol (*m/z* 267), *Figure 1*.

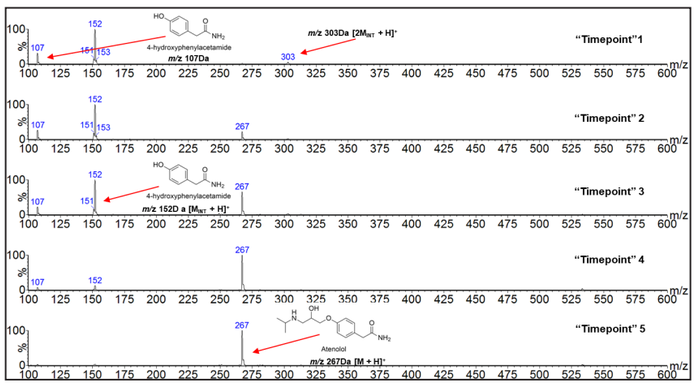

Figure 1. Extracted spectra of each simulated timepoint showing Increase of atenolol (m/z 267) concomitant with the reduction of the intermediate 4-HPA (m/z 152).

As reaction monitoring is defined by the correlation of the reactant(s) and the product(s), it is possible for semi-quantitative monitoring to be carried out by measuring ratios between the mean responses with the mean response ratio of both analytes, *Figure 2*. This provides a visualization of the changing intensities in each analyte with the line in red showing a clear upward trend in atenolol relative intensity.

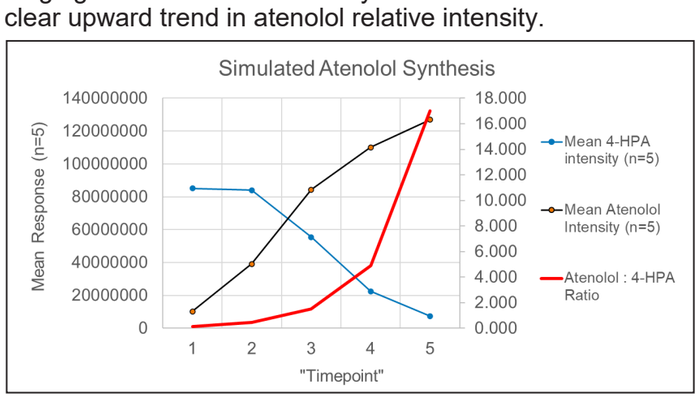

Figure 2. Graphical representation of the response reduction in 4-HPA (blue) concomitant with the increase in atenolol (black). The ratio of atenolol:4-HPA is represented in red.

THERMAL DESORPTION

When dealing with complex samples, a degree of separation is beneficial. The RADIAN can apply a temperature ramp, or thermal gradient, which separates components based on their different boiling points.

To model polymer (de)formulation, PEG600 was combined with a polymer additives standard mix and diluted in methanol.

A temperature ramp method (to 600 °C) was set on the RADIAN to thermally separate out the additives and polymer for a less complex spectra.[2] *Figure 3* highlights the thermal desorption profile and how the profile of ions changes across the run. Some examples of identified substances are highlighted.

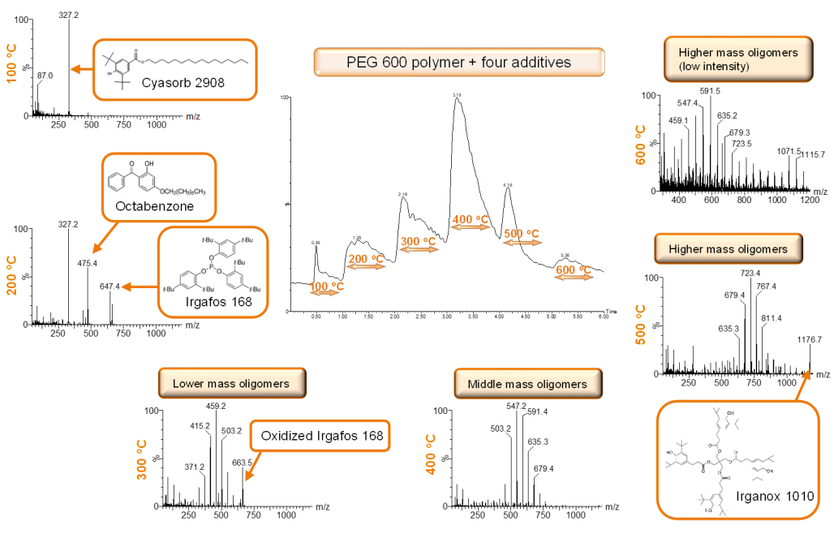

Figure 3. A thermal ramp to 600 °C with a hold at each 100 °C adds an extra dimension of separation to complex mixtures. Additives and oligomers can then be assigned.

HOW DOES RADIAN ASAP WORK?

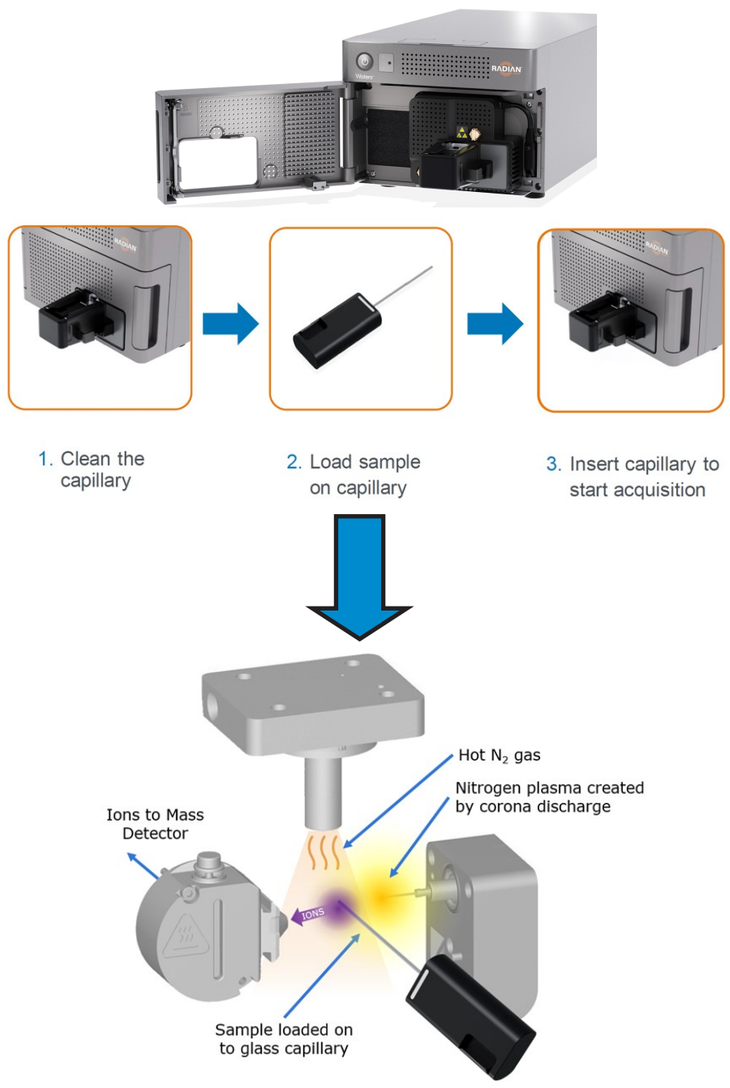

Figure 4. Sample introduction and source configuration of RADIAN ASAP.

LIBRARY MATCHING

With known targets, a library can be used for a simple, yet rapid, screen. To exemplify, this study uses a library of 69 drugs to identify drugs infused into paper. Drug infused paper has been a route to smuggle illicit substances into UK prisons.[3]

Nominal mass is not a robust single parameter for identification. Therefore, four cone voltages (15, 25, 35, 50 V) were applied to generate fragmentation by in-source Collision-Induced Dissociation (CID). The combination of precursor and the generated fragment ions provide a spectral fingerprint for each analyte, thus increasing specificity, *Figure 5*.

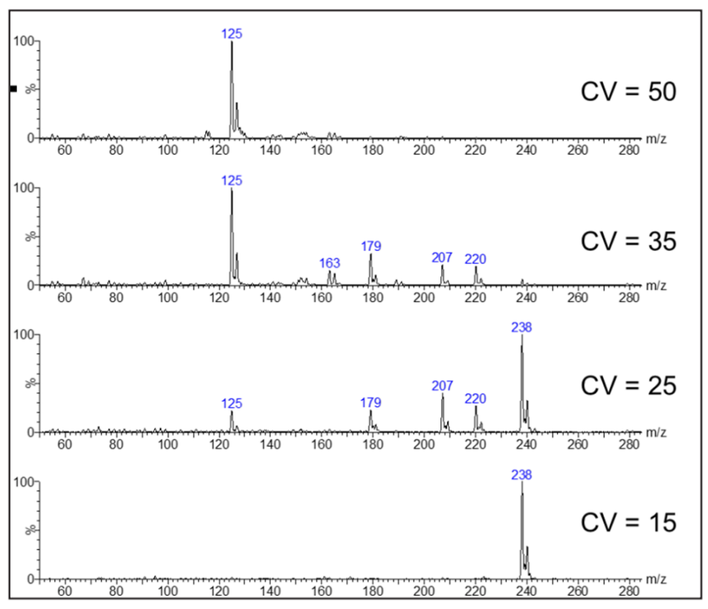

Figure 5. Spectral fingerprint generated by RADIAN ASAP for Ketamine CRM.

Using this methodology, seventeen common drug substances spiked onto a variety of paper types at 1 mg/mL were all correctly identified. The analysis and live spectral matching took less than 2 minutes per sample and results were unaffected by the presence of inks (for example in newspapers and glossy magazines).

MULTIVARIATE ANALYSIS

Ideally, downstream processes would have analytical tools that enable quick decisions at site. However, the experiments are likely performed by a non-analytical chemist. Identification of markers or 'fingerprinting' is a route often employed to simplify the interpretation. In this example, the RADIAN was employed to differentiate tea harvest seasons to avoid intentional mislabelling for financial gain (akin to counterfeiting).[4]

Triplicate extractions and analyses were recorded for samples of spring and autumn harvest oolong teas. Multivariate statistical analysis was then performed to identify markers unique to each set of samples, *Figure 6*.

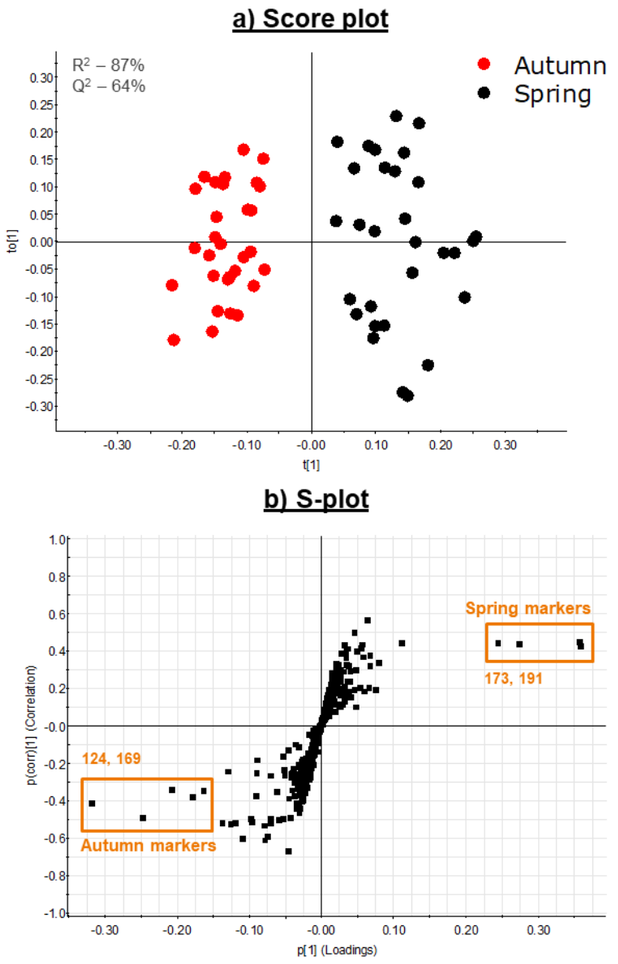

Figure 6. a) Score plot and b) S-plot obtained from OPLS-DA of the RADIAN ASAP mass spectra data of spring and autumn Tieguanyin samples

For identification of the markers High Resolution Mass Spectrometry (HRMS), would be required. In this same work it was shown there was no barrier when transferring a model from HRMS to the RADIAN.

CONCLUSION

- **Reaction progression is directly measured at-point-of-sampling**
- **Analysis of polymeric material is enabled without sample preparation. Chemical constituents such as base polymer and additives are easily detected and confirmed by m/z.**
- **Chemical markers responsible for sample group differences are isolated by the use of OPLS-Discriminant analysis.**
- **An in-house developed spectra library is used to achieve compound identification with a direct sampling method.**

The RADIAN's simplicity belies the multiple experiment types available, enabling rapid, at-point-of-sampling decisions to be made with low cost per sample analysis. The RADIAN can be used with solids or liquids across a broad chemical range.
With its small footprint and ease of use, the RADIAN ASAP could be deployed in a variety of settings for expert and non-expert users alike.

References

1. Direct Ionization Technique as a Rapid Screening Tool for Reaction Monitoring, Waters Application Note 720007111, January 2021
2. RADIAN ASAP for Simple Mass Spectral Screening of Polymer Formulations, Waters Application Note 720007270, May 2021
3. Analysis of Drug-infused papers by ASAP-MS, Waters Poster 135107567, 2022
4. H. R. Tan *et al*, Atmospheric solids analysis probe-mass spectrometry (ASAP-MS) as a rapid fingerprinting technique to differentiate the harvest seasons of Tieguanyin oolong teas, *Food Chemistry*, Vol. 408, 2023, 135135

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