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Wellbrook Court I Girton Road I Cambridge I CB3 0NA I
I tel: +44 (0) 1223 279210 I fax: +44 (0) 1223 279253
I email: enquiries@anatune.co.uk I anatune.co.uk

HIGH-THROUGHPUT RESIDUAL SOLVENT AND RESIDUAL MONOMER ANALYSIS USING SELECTED ION FLOW TUBE MASS SPECTROMETRY

Mark J. Perkins,[1] Diandree Padayachee,[2] Vaughan S. Langford,[2] Murray J. McEwan[2,3]

[1]Anatune Limited, Girton Road, Cambridge, CB3 0NA, United Kingdom

[2]Syft Technologies Limited, 3 Craft Place, Christchurch 8024, New Zealand

[3]Department of Chemistry, University of Canterbury, Christchurch 8000, New Zealand

Conventional chromatographic analytical methods for volatile organic compounds (VOCs) and inorganic gases are being challenged by faster and more direct analytical techniques. Selected ion flow tube mass spectrometry (SIFT-MS) is a leading contender among the real-time analysis techniques, because of its high selectivity and broad-spectrum analysis. When coupled with automated sampling systems, SIFT-MS provides significant throughput increases for both testing laboratories and quality assurance/quality control (QA/QC) in a process environment. In this paper, we illustrate these benefits for the specific applications of residual solvent analysis and residual monomer analysis, using formaldehyde emissions from polyoxymethylene (POM) polymer to illustrate.When coupled with automation, samples can be run 24 hours/day, speeding up research and development or QA testing. The data shown here were obtained using a Syft Technologies Voice200ultra SIFT-MS instrument integrated with a GERSTEL Multipurpose Sampler (MPS) (GERSTEL, Mülheim an der Ruhr, Germany) equipped with a GERSTEL purge tool. Samples were analyzed in 20-mL sample vials.

INTRODUCTION

One of the major drawbacks of the chromatographic techniques that form the backbone of volatile organic compound (VOC) analysis in the modern laboratory, is the time required to achieve the necessary separation. Slow analysis time is a major impediment to improving quality assurance, with typical sample throughputs of only 20 to 60 samples in 24 hours. While method optimisation using narrow-bore columns can yield analysis times of 10 minutes, it still remains impractical to increase testing frequency using traditional techniques. Direct headspace analysis, although faster than most GC analyses, can still take around 2 minutes to detect a compound such as ethanol. Another consideration is that the analysis time is often extended when multiple preparation steps, such as sample pre-concentration, drying and derivatisation, have to be carried out before the start of analysis.

Clearly, analytical techniques that directly analyse whole air – whether continuously or in headspace – without resorting to sample derivatisation, preconcentration or drying, have potential to greatly simplify laboratory processes and increase sample throughput. Introduced in the mid-1990s by Smith and Spanel [1,2], selected ion flow tube mass spectrometry (SIFT-MS) addresses this need. SIFT-MS instruments analyse gas samples directly, providing quantitative results within seconds, while comparing well with established chromatographic methods for monitoring VOCs, such as gas chromatography-mass spectrometry (GC/ MS) [3,4,5].

SIFT-MS (Figure 1) uses ultra-soft chemical ionisation (CI) to generate mass-selected reagent ions that can rapidly quantify VOCs to low parts-per-trillion concentrations (by volume, pptv). Eight reagent ions (H_3O^+, NO^+, O_2^+, O^-, OH^-, O_2^-, NO_2^- and NO_3^-) obtained from a microwave discharge of moist or dry air, are now applied in commercial SIFT-MS instruments. These eight reagent ions react with VOCs and other trace analytes in well-controlled ionmolecule reactions, but they do not react with the major components of air (N_2, O_2 and Ar). This allows for real-time analysis of air samples at trace and ultra-trace levels without pre-concentration.

Rapid switching between reagent ions provides high selectivity, because the multiple reaction mechanisms provide additional independent measurements of each analyte. The multiple

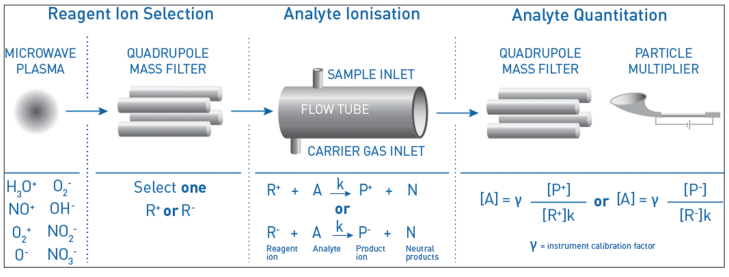

Figure 1. Schematic diagram of SIFT-MS – a direct, chemical-ionisation analytical technique.

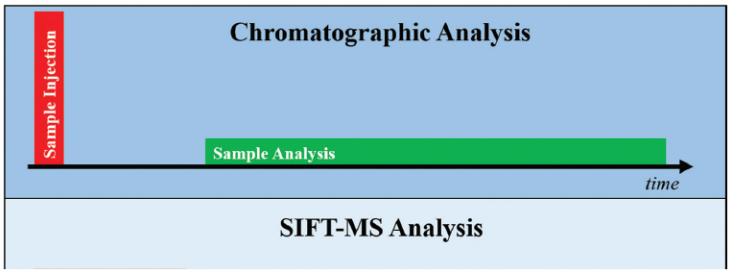

Figure 2. Graphical representation of the different sample-injection and analysis requirements of chromatographic techniques and SIFT-MS.

reagent ions also help to remove uncertainty from isobaric overlaps in mixtures containing multiple analytes.

In SIFT-MS, the ability for rapid direct analysis of a sample provides unique opportunities for high-throughput headspace and gas analysis, irrespective of whether the task is routine VOC monitoring or the analysis of chromatographically challenging species, such as ammonia, formaldehyde, hydrogen chloride and hydrogen sulphide. In contrast to GC-based techniques that require rapid injection to achieve good chromatographic separation, SIFT-MS only needs steady sample injection for the duration of the analysis – that is, sample injection and analysis occur simultaneously (Figure 2).

The recent coupling of SIFT-MS with autosamplers provides new opportunities for both contract and R&D laboratories serving various industries (from environmental analysis, to food testing, to pharma), as well as for process monitoring. In this paper, we describe the application of automated SIFT-MS to residual solvent and residual monomer analysis, which are relevant to the pharmaceutical and food industries, in particular. Of particular significance is the simplicity and speed with which formaldehyde is analysed using SIFT-MS, compared to traditional chromatographic methods.

EXPERIMENTAL

Automated VOC analysis was carried out with a Voice200ultra (Syft Technologies, Christchurch, New Zealand) coupled with a Gerstel MPS2 autosampler (Gerstel, Mülheim an der Ruhr, Germany). Headspace measurements were carried out on all samples. Where appropriate, samples were first incubated in a Gerstel Agitator prior to injection of the sample into the Voice200ultra through a Gerstel septumless sampling head. The sample inlet temperature on the Voice200ultra was maintained at 150°C. The reagent ions used for analysis were H_3O^+, NO^+ and O_2^+, and the carrier gas was helium.

Analyses were run in Selected Ion Mode (SIM) for the compounds of interest. Analytical methods were created using the Method Editor module in the LabSyft software package (Syft Technologies, Christchurch, New Zealand).

The Gerstel MPS2 autosampler is controlled using Gerstel's Maestro software. In addition to controlling the injection into the SIFT-MS, the Maestro software's PrepAhead function allows for optimal scheduling of preinjection preparation steps, such as syringe flush or incubation. This ensures that the highest sample throughput is achieved.

RESULTS AND DISCUSSION

Rapid analysis of residual solvents

While solvents are frequently used in the manufacture of pharmaceuticals, the presence of these (often toxic) solvents in the end products is of concern. Rapid, mass-screening of products for residual solvents would significantly improve QA/QC processes in the pharmaceutical industry. Because SIFT-MS analysis is direct, it can even be implemented on an existing conveyor system without impacting on the manufacturing time.

Figure 3 shows the simultaneous analysis of a multicomponent mixture of solvents, including benzene and toluene, as well as chromatographically challenging species such as ammonia and formaldehyde. All 13 compounds were monitored within 90 seconds.

Rapid analysis of packaging materials

Many food and pharmaceutical products are packaged in some form of polymer-based material. Residual monomers in packaging can interact with the drug formulations in pharmaceutical products or affect the aroma or safety of food products [6]. SIFT-MS is ideally suited to residual monomer analysis, because these compounds tend to be volatile and are readily released into the packaging headspace.

Figure 4 illustrates the rapid determination of monomer impurities in packaging using SIFT-MS. For illustrative purposes, all samples were analysed for all compounds in one scan, with a throughput of 60 seconds per sample.

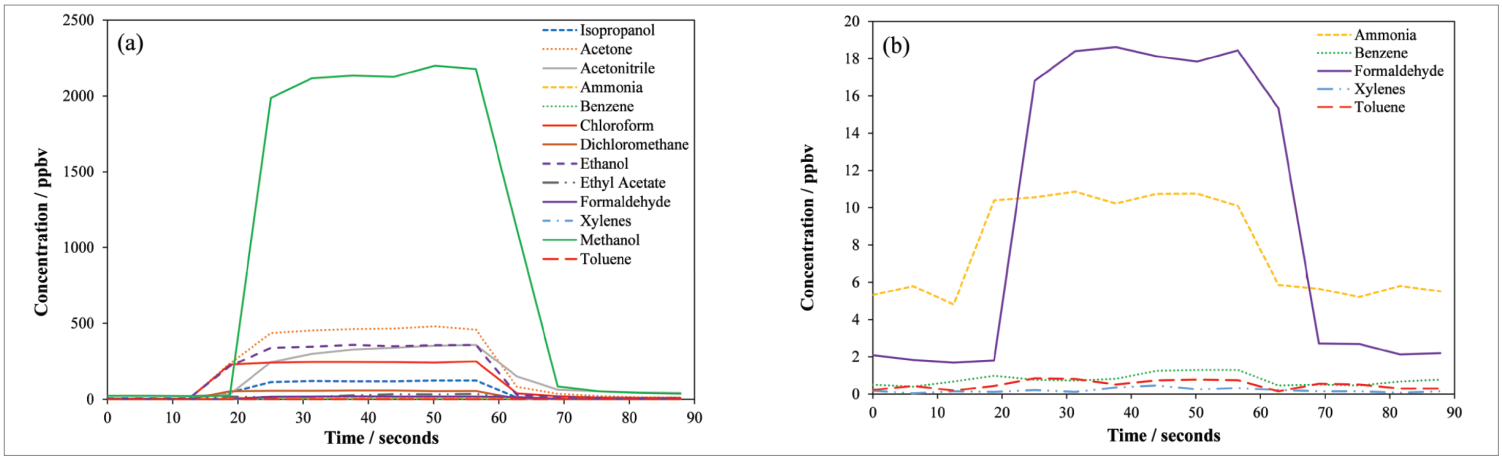

Figure 3. Rapid, simultaneous analysis of 13 solvents using SIFT-MS: (a) shows all compounds, and (b) is the expanded plot of the trace compounds. These data were obtained through direct analysis of ambient air in the Anatune Ltd laboratory (Cambridge, UK). Air was sampled continuously through the high-performance inlet for 40 seconds while the inlet was open (it was closed before and after the rise).

The residual monomer concentrations shown in Figure 4 represent the amount of monomer that has partitioned from the polymer material into the headspace, and it is possible that a significant amount of monomer remains within the bulk of the material. The ratio of monomer retained to monomer released into the headspace is related to the partition coefficient of these compounds. Without knowing these values for the analytes in these matrices, and under these experimental conditions, it is not possible to calculate the total amount of residual monomer in the sample. Additionally, complete equilibrium of the headspace may not have been reached, further complicating the measurement.

If multiple headspace measurements could be made and a total concentration calculated from all measurements, the actual concentration of residual monomer within the solid could be found. However, this would require a significant number of measurements to ensure total removal of all monomer within the polymer.

The multiple headspace extraction (MHE) technique [7] is a headspace technique that calculates the total concentration from a limited number of consecutive headspace analyses by recognising that the decrease in concentration over multiple headspace measurements is exponential. A headspace concentration is generated, the concentration measured and then flushed or vented and a new headspace generated (Figure 5). Figure 6 shows sequential MHE measurements of formaldehyde emitted from ground POM polymer. The concentration data are summarised in Table 1.

It has been suggested that the first point of any MHE measurement can be prone to experimental error [8]. Possible sources include the change in gas matrix from measurement 1 to 2 due to the flush cycle and excessively long standing time for the first headspace generation. It can clearly be seen in Figure 6 that the first concentration measured is significantly higher than the subsequent measurements. This is probably due to the relatively high extraction temperature (80°C) used in this experiment for this polymer type, which causes a significant release of formaldehyde from the top layers of the polymer particles compared to the slower release from the internal bulk. Further analysis also showed the second concentration measurement to be higher than expected. Since the MHE technique relies on adding all concentrations together, the total concentration is calculated from the sum of the first two injections and the extrapolated fi t to injection 3 onward (Figure 7). Equation 1 gives the fit equation [8] and Table 2 summarises the parameters, where 'Extrapolated injection 3' in the table refers to the injection 1 value recalculated from the linear fit.

Total HCHO concentration = Conc.(Inj. 1) + Conc.(Inj. 2) + Conc.(Extrapolated Inj. 3) / (1– e^{slope}) (1)

This gives a total residual monomer concentration of 13.8 ppmv formaldehyde in the headspace (as annotated on Figure 7). Conversion of this concentration to mg/ m^3 and accounting for vial volume, inlet dilution and injection temperature

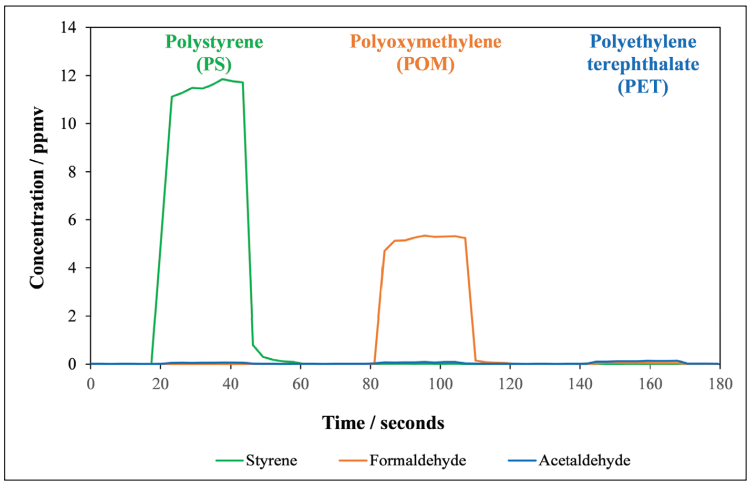

Figure 4. Rapid analysis of monomers present in the headspace of polystyrene (PS), polyoxymethylene (POM) and polyethylene (PET) polymers used for packaging. Ground samples of the polymers were incubated at 80˚C for 15 mins, followed by a 2.5 ml headspace injection into the Voice200ultra SIFT-MS instrument at 100 µL s-1.

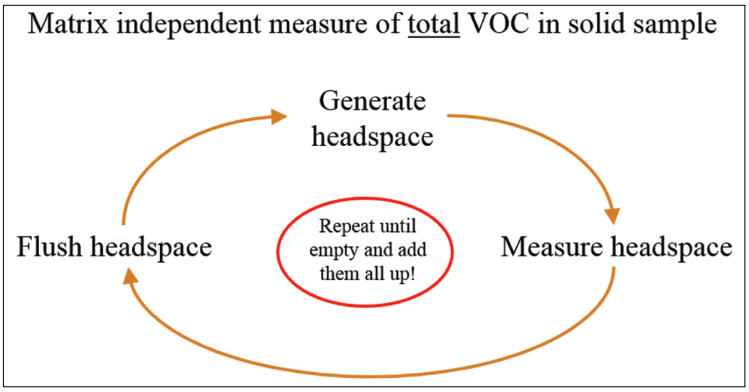

Figure 5. Schematic representation of the MHE technique.

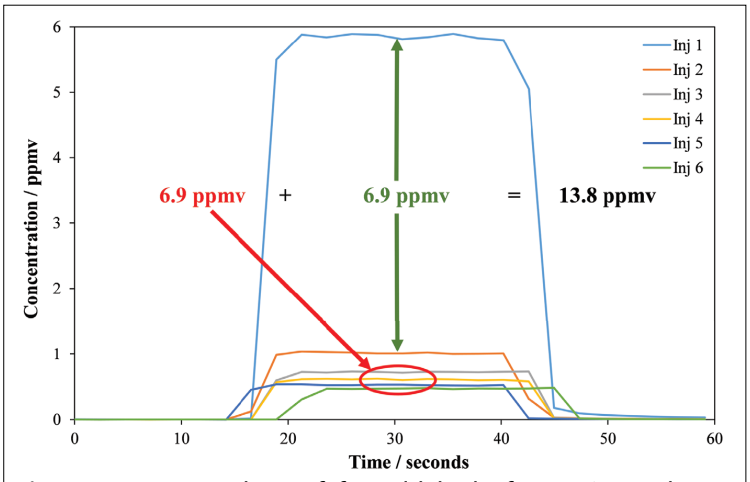

Figure 6. MHE analysis of formaldehyde from POM polymer using automated SIFT-MS. Ground samples of the polymers were incubated at 80˚C for 15 mins, followed by a 2.5-ml headspace injection into the SIFT-MS instrument at 100 µL s-1, followed by 3 minutes of vial fl ushing, repeated 6 times. See Table 1 for full data summary. Injections 1 and 2 are summed to give the value shown in green, while the red value is calculated from extrapolation of points 3 - 6 (Table 2).

temperature yields a formaldehyde concentration of 41 µg g ^{1} of POM polymer.

The speed of SIFT-MS analysis revolutionises the MHE technique – which is traditionally an expensive undertaking with slow chromatographic-based analytical techniques.

With SIFT-MS, each analysis takes less than one minute, enabling multiple concurrent analyses to be carried out, because the multiple samples can regenerate their headspace while the next sample is analysed. Using a standard Gerstel six-vial agitator designed for use with GC/MS, a 6.5-fold increase in throughput is achieved for SIFT-MS.

CONCLUSIONS

SIFT-MS is a direct analysis technique that utilises soft chemical ionisation to achieve highly sensitive, selective and non-discriminatory analysis without the need for chromatographic separation of analytes. By automating SIFT-MS with modern autosampler technology, sample analysis times are markedly decreased and throughput is increased compared to conventional chromatographic methods – even for chromatographically challenging species, such as formaldehyde.

Using SIFT-MS, samples can be comprehensively analysed for residual solvent content within 90 seconds. Residual monomer analysis of polymer and packaging samples can be achieved with markedly improved throughputs in both static and multiple headspace extraction applications.

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Injection Number	Concentration/ ppmv	ln (Concentration)
1	5.95	1.783
2	0.95	-0.0513
3	0.95	-0.364
4	0.584	-0.53785
5	0.515	-0.66359
6	0.454	-0.78966

Table 1. Concentration data for sequential injections of headspace during MHE analysis.

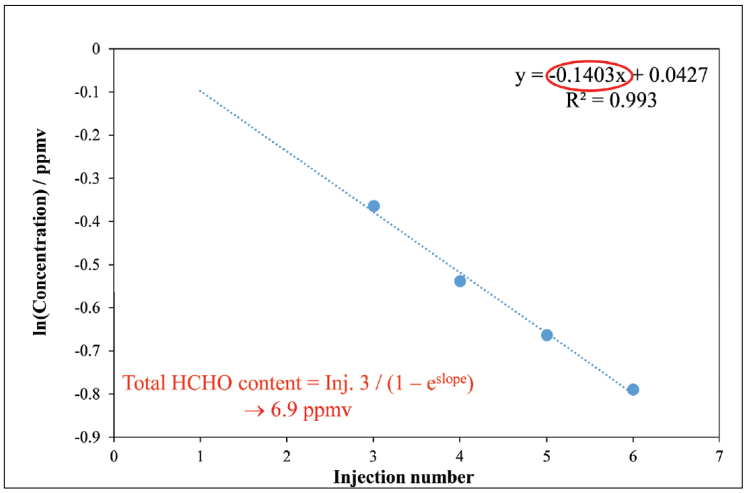

Figure 7. Residual monomer analysis of formaldehyde from a ground POM polymer using MHE.

Parameter	Value
Slope (injections 3 – 6)	-0.140
Intercept (injections 3 – 6)	0.0427
Extrapolated injection 3	0.907
Exp(slope)	0.869
Calculated HCHO from injection 3 onward / ppm v/v	6.93
Sum of injections 1 and 2 / ppmv	6.9
Total formaldehyde concentration / ppmv	13.8
Total formaldehyde concentration / µg g 1	41

Table 2. Parameters used for the MHE calculation.