FOOD TESTING & AGRICULTURE

RAPID PROFILING OF VOCS AND SVOCS IN E-CIGARETTE VAPOURS FOR REGULATORY COMPLIANCE AND QUALITY CONTROL

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Markets and Applications Programs

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ABSTRACT

This Application Note describes a simple, quick Thermal Desorption-based approach for the sampling and analysis of target compounds (such as nicotine, impurities and flavour compounds) in vapours from flavoured e-cigarettes. Used in conjunction with GC–MS analysis, the result is a versatile screening method for tackling the challenge of regulatory compliance and quality control in this rapidly expanding industry.

INTRODUCTION

E-Cigarettes have seen a massive growth in popularity in recent years, fuelled by a widespread understanding that their health impacts are lower compared to tobacco products, and by their appeal to users due to their similarity in the way they are consumed. The widespread use of e-cigarettes has resulted in a high degree of scrutiny into the chemical components of the 'e-liquids' that are vaporised – namely aqueous propylene glycol and/or glycerol (as carrier fluids), nicotine and added flavourings. However, studies of the formulations themselves are of limited relevance in the context of user exposure to chemicals, because (like cigarettes), chemical transformations take place during the vaporisation process, and this may generate potential toxins.

Such factors have led agencies in the European Union and the USA to issue regulations on e-cigarettes, namely:

• EU Tobacco Products Directive:[1] This became applicable in EU Member States in May 2016, and sets out rules governing the manufacture, presentation and sale of tobacco and related products. Article 20(2) places an obligation on the manufacturers and importers of e-cigarettes to notify the Member States of any 'nicotine-containing e-liquid products' they intend to market, including details of emissions of formaldehyde, acetaldehyde and acrolein, and (depending upon the device, liquid and toxicological assessment) diethylene glycol, ethylene glycol, butanedione (diacetyl) and pentane-2,3-dione (acetylpropionyl).

• US Food and Drug Administration: Also in May 2016, the US FDA extended its authority over regulation of tobacco products to include electronic nicotine delivery systems (ENDS) such as e-cigarettes.[2a,b] This will place a requirement on manufacturers to submit (amongst other information) an ingredients listing and information on 93 "harmful and potentially harmful constituents (HPHCs)"[2c] that might be present in either the liquid or the resulting vapour.

As well as regulatory compliance, VOC-profiling of e-liquids or e-cigarette vapour is valuable for quality control and product improvement – for example, by checking the consistency of levels of nicotine and flavour chemicals, or checking for the presence of contaminants.

Whatever the ultimate aim of VOC analysis, gas chromatography coupled with mass spectrometry (GC–MS) is an ideal choice to ascertain the presence or absence of volatile and semi-volatile organic compounds (VOCs and SVOCs) from a targeted list.[3,†] In the specific case of e-cigarette vapour, thermal desorption (TD) has been used[4,5] to maximise sensitivity for trace-level target compounds.

In this Application Note, we show how a simple, inexpensive approach employing sorbent tubes to sample organic vapours from e-cigarettes can be interfaced with TD–GC–MS for the rapid analysis of target VOCs and SVOCs. The result is a protocol that incorporates simple sampling, robust and automated analysis, flexibility in setting method parameters, and comprehensive data analysis, making it a simple solution to the challenge of regulatory compliance and quality control.

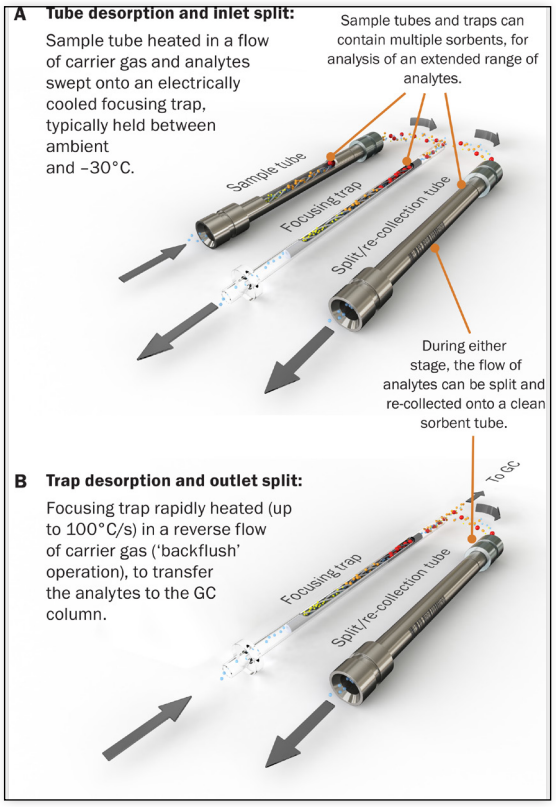

Figure 1: *How two-stage thermal desorption works.*

Background to the sampling and analysis technologies

Easy-VOC™ is a hand-held manually operated device that 'grab'-samples small volumes of air (typically 50–200 mL) directly onto sorbent tubes. Sorbent tubes push into the end of the Easy-VOC, and air/gas is drawn steadily and directly into the tube over a period of several seconds. Air can be sampled in accurate aliquots of 50 or 100 mL, and larger volumes are easily collected by pulling a series of samples onto the same tube in quick succession to reduce detection limits.

Thermal desorption (TD) is a versatile GC pre-concentration technology that is used to analyse volatile and semi-volatile organic compounds (VOCs and SVOCs) in a wide range of sample types. By concentrating organic vapours from a sample into a very small volume of carrier gas (Figure 1), TD maximises sensitivity for trace-level target compounds, helps to minimise interferences, and routinely allows analyte detection at the ppb level or below. It also greatly improves sample throughput, by allowing full automation of sample preparation, desorption/extraction, pre-concentration and GC injection.

† The only exception is formaldehyde, which is usually monitored by derivatisation followed by high-performance liquid chromatography (HPLC).

The new 'xr' range of TD instruments from Markes International enhance these capabilities, offering a wide analyte range (C_2–C_{44} including reactive species), automated re-collection and re-analysis of split portions for method validation and compliance with standard methods, optional internal standard addition for improved confidence in results, and electronic/manual options for control of carrier gas. In this study we use the TD100-xr (Figure 2) for fully automated analysis of up to 100 sorbent tube samples.

Figure 2: *Markes' TD100-xr automated thermal desorber with Agilent GC.*

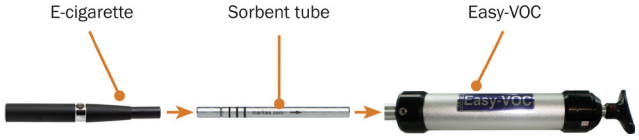

Figure 3: *Schematic showing assembly used to sample e-cigarette vapours. Note that sorbent tubes can also be used with standard 'smoking machines'.*

EXPERIMENTAL

Standard preparation:

A solution of butanedione, pentane-2,3-dione, acetoin and diethylene glycol, each at 6.25 µg/µL, was prepared in propylene glycol–glycerin–methanol mix (2 : 2 : 6 v/v). This was injected in a flow of gas onto a tube using a Calibration Solution Loading Rig (CSLR™, Markes International – see Application Note 007 for details).

Sampling:

An e-cigarette was connected to the sampling end of an industry-standard (3½" long × ¼" o.d.) 'Odour/Sulfur' inert-coated stainless steel sorbent tube suitable for sampling C3–C30 (Markes International part no. C2 CAXX-5314). This assembly was then connected to an Easy-VOC grab-sampler (Markes International), the e-cigarette activated, and 50 mL of vapour (representative of industry-standard puff volumes) collected over a period of 4 seconds (Figure 3). The tubes were then analysed by TD–GC–MS.

TD:	
Instrument:	TD100-xr™ (Markes International)
Pre-purge:	1 min at 100 mL/min
Desorption:	12 min at 320°C at 50 mL/min
Inlet split flow:	100 mL/min (6 : 1)
Trap:	Odour/Sulfur trap (Markes International part no. U-T6SUL-2S)
Pre-trap-fire purge:	1 min at 20 mL/min
Trap low:	25°C
Trap heating rate:	Max
Trap high:	320°C (3 min)
Outlet split flow:	100 mL/min (51 : 1) (tobacco-flavoured e-liquid), 10 mL/min (6 : 1) (menthol and blueberry-flavoured e-liquid)

GC:	
Instrument:	7890B and 5977A (Agilent Technologies)
Column:	VF-624ms™, 60 m × 0.25 mm × 1.4 µm
Carrier gas:	Helium, 2 mL/min constant flow
Oven:	40°C (5 min), 8°C/min to 240°C (5 min)

Quadrupole MS:	
Mode:	Scan
Mass range:	m/z 35–500
Source:	300°C
Quadrupole:	150°C
Transfer line:	320°C
Tune type:	e-tune
Compound identification:	Target compounds were identified by a search against NIST 14 (match factor >700).

RESULTS AND DISCUSSION

1. Analysis of impurities mix

To check the analytical capability of the system, a matrix-matched standard was loaded on to a sorbent tube using the CSLR, and analysed as described earlier. This standard contained four relevant e-cigarette impurities or additives – namely butanedione (diacetyl), pentane-2,3-dione (acetylpropionyl), acetoin and diethylene glycol – and two common e-liquid carrier compounds, propylene glycol (PG) and glycerin (VG).

The results (Figure 4) show that the key components of interest are well-separated from the matrix components, confirming the suitability of the analytical setup for this investigation.

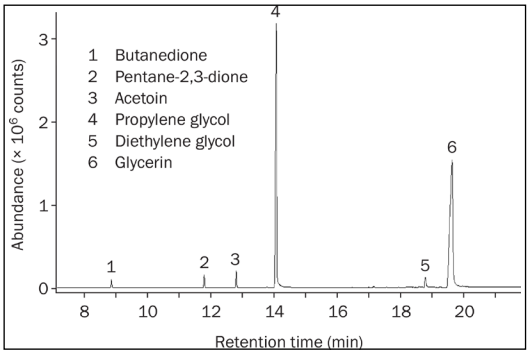

Figure 4: *Analysis of an e-cigarette impurities mix using TD–GC–MS, showing no co-elution of low-level compounds with matrix components (#4 and #6).*

2. Analysis of e-cigarette vapours

The vapours released from the e-cigarette were analysed in two separate studies using different-flavoured e-liquids, in both cases using an Easy-VOC grab-sampler to pull the vapours from the e-cigarette directly into a sorbent tube, avoiding the need for any sample preparation. Analysis of these tubes was then carried out using the TD–GC–MS conditions described earlier.

The first study used a 'tobacco-flavoured' e-liquid (Figure 5), and found a number of trace-level components despite the very high concentrations of propylene glycol (#2) and glycerin (#6). These components included acrolein (#1), which (as well as nicotine (#9)) is present on both the EU and FDA lists of compounds of concern, and flavour/aroma compounds that may be of relevance to the consumer experience, such as levomenthol (#5) and ethyl vanillin (#11).

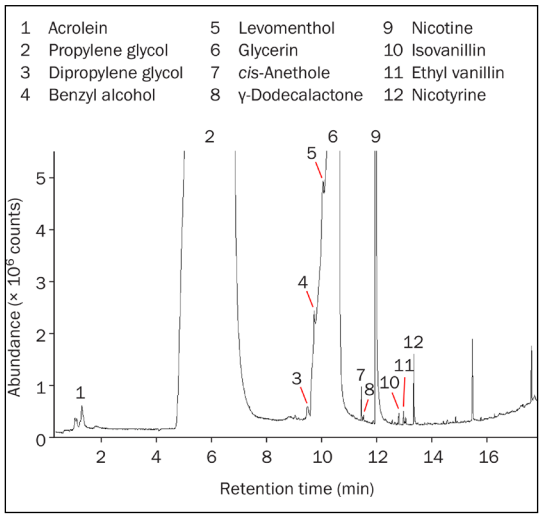

Figure 5: *TD–GC–MS analysis of vapour from an e-cigarette loaded with a 'tobacco-flavoured' e-liquid, indicating major components and some trace-level components with regulatory or organoleptic relevance.*

The second study used an e-liquid with a 'menthol and blueberry' flavour (Figure 6). Initially, a high outlet split (i.e. with a small proportion of the sample sent to the GC) was used to quantify the higher-loading compounds, including menthol (#31) and nicotine (#39), followed by a lower outlet split of the re-collected sample (shown). This ensured a strong response from the lower-level flavour compounds, increasing their intensity relative to the heavily overloaded peaks for propylene glycol and glycerin.

It is worth noting that the use of inert-coated stainless steel tubes, combined with the inertness of the flow-path in Markes' TD instruments, minimises the loss of thermally labile species, such as sulfur compounds and monoterpenes (e.g. α-pinene (#17), sabinene (#19) and β-pinene (#21) indicated in Figure 6).

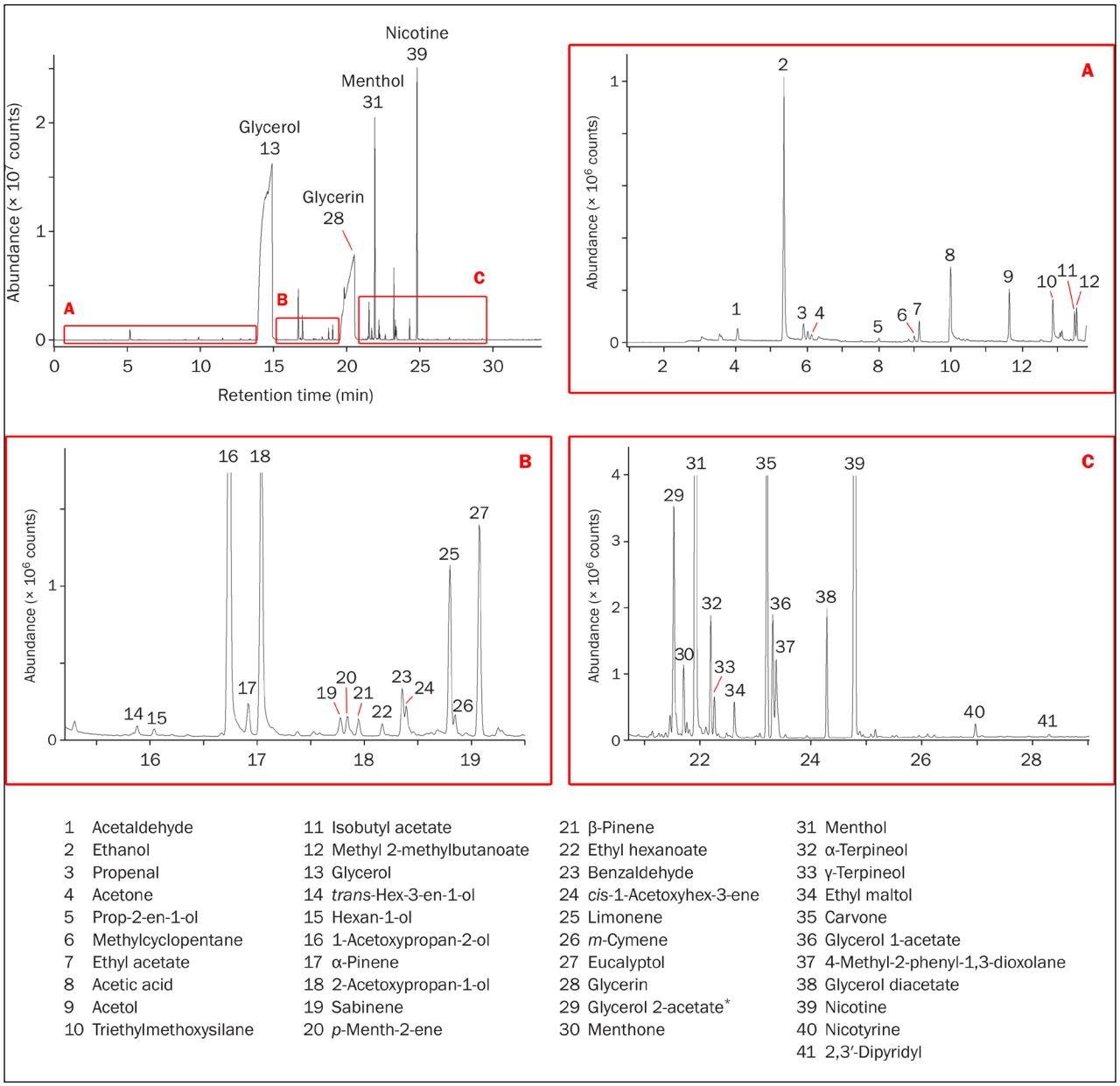

Figure 6: *TD–GC–MS analysis of vapour from an e-cigarette loaded with a 'menthol and blueberry' flavour e-liquid, indicating major components and a selection of lower-level components (some with regulatory or organoleptic relevance). * = Identity tentative.*

CONCLUSIONS

This study has shown that sampling of e-cigarette vapours onto sorbent tubes using the Easy-VOC, followed by TD–GC–MS analysis, is a simple and easy approach that is suitable for assisting compliance with e-cigarette regulations by allowing the detection of a wide range of target VOCs and SVOCs. The same approach, because of the speed of sampling and analysis, is also valuable for quality-control, as well as aroma profiling, competitive analysis and R&D in a number of other food and fragrance applications.

We have also shown the usefulness of the split-flow capability of Markes' instruments for simplifying the detection of compounds at high and trace levels – which is a particular challenge for e-cigarette vapour. This capability could be enhanced by using a modulator to heart-cut the high-loading glycols to a FID detector (for example), allowing a reduced split, and so greater sensitivity, for the trace-level components.

Another feature of the new 'xr' series of TD instruments that is valuable in such studies is the ability to automate re-collection of samples on the inlet and/or outlet splits. This can be used, for example, to analyse a single sample using multiple methods, which has obvious advantages for method development.

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