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Comparison of Different Sample Introduction Techniques for the Analysis and Characterisation of e-Liquids Using GC-MS

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First Published: 2016

Introduction

The last decades have seen an exponential increase in the consumption of electronic cigarettes (EC) amongst smokers. EC use a heated element to disperse a solution of propylene glycol, glycerine, water, flavouring and usually nicotine known as e-liquid. The heating of the e-liquid results ultimately in an aerosol that can be inhaled by the user.

Initially, EC were governed by general product safety regulations which did not require products to be tested before being put on the market. However, since the 20th May 2016, a new European Legislation known as Tobacco Products Directive (TPD) came into force for the EC market as well. In fact, the TPD covers e-liquids and devices containing nicotine up to 20mg.

Product registrations for products on sale before 20th May 2016 must be completed by 20th November 2016 while existing stocks (non-registered products) may not be sold after 19th May 2017. Each formulation will require individual registration with submission of analytical data and toxicological risk assessment of components.

The Medicines & Healthcare Products Regulatory Agency (MHRA) has been selected as the relevant regulatory body in the UK. MHRA guidelines on testing currently require the following to be tested:

- Glycols (ethylene glycol, diethylene glycol, dipropylene glycol) present in the Propylene Glycol (PG) or Vegetable Glycerin (VG)
- Carbonyls (acetaldehyde, formaldehyde, acrolein, diacetyl, pentane-2,3-dione)
- Metals (Al, Cr, Fe, Ni, Sn)
- Flavours (>0.1% in flavour, typically 0.04% in product)
- Nicotine and related alkaloids
- Full toxicological risk assessment of all flavour components in e-liquids, in device and in emissions

Hence, the urgent need to develop testing methods to comply with the directive requirements.

From an analytical point of view, the analysis of e-liquids can be challenging at different levels. Firstly, the TPD will require characterisation of both e-liquids and emissions. Secondly, although e-liquids are composed mainly by only few ingredients, they represent a complex analytical matrix which can lead to instrumental system contamination, and consequently poor and irreproducible data. Last but not least, the directive covers a quite diverse array of target analytes, having not only quite different physical chemical properties but also ranging broadly in terms of concentration in the final sample.

It must therefore appear clear how the use of a selection of different sample introduction techniques can offer more flexibility to the analyst and consequently higher chances of success to tackle this complex analytical challenge.

This application note describes the comparison between different sample introduction techniques in order to identify the most suitable analytical approach to tackle the comprehensive investigation of e-liquids as required by the latest TPD. E-liquids with diverse PG/VG compositions were analysed and performances of the investigated techniques were compared for the analysis of TPD target compounds and flavour profiling.

Different techniques will be covered within this work and the reader will require previous basic knowledge of the above to fully understand the data. For additional information please check our website www.anatune.co.uk or email: enquiries@anatune.co.uk.

Instrumentation

Optimised sample handling and introduction for the analysis of the investigated e-liquids was developed on a GERSTEL MultiPurpose Sampler (MPS) 2 XL Dual head (Figure 1) equipped with the following features:

- Thermal Desorption Unit (TDU)
- Cool Injection System (CIS 4)
- Automated Tube Exchange (ATEX)
- Twister
- Dynamic Headspace (DHS)

GC-MS analysis was performed using the Agilent 7890B Gas Chromatograph coupled to the Agilent 7010 Triple Quadrupole QQQ-MS.

Figure 1 – GERSTEL Dual Head MPS for the GC-MS analysis and characterisation of e-liquids

Method

Sample Preparation

E-liquids covering a range of different PG/VG compositions (10/90 to 80/20) from different suppliers were analysed by means of four main sample introduction techniques:

- ATEX
- Twister Headspace
- Twister Liquid
- DHS as Fully Evaporative Technique (FET)

These techniques all share the same main setup using the TDU in combination with the CIS. However, they differ in the TDU liner configuration for sample introduction. In ATEX the sample is spiked directly into a microvial within the TDU liner.

Twister requires the use of PDMS coated stir bars to perform sorptive extraction of the sample which are then transferred to the TDU liner for analysis.

On the other hand, DHS uses a TDU liner packed with Tenax as absorbent for the headspace which is then directly desorbed in the TDU.

For both ATEX and DHS we used 1 uL neat sample while for the Twister sample prep, 1 mL of neat sample in 10 mL vial was either sampled in headspace mode for 2 hr at 40°C or diluted in 9 mL milli-Q water and then stirred for 2 hr at room temperature.

Figure 2 summarised the analytical workflow applied to e-liquids analysis.

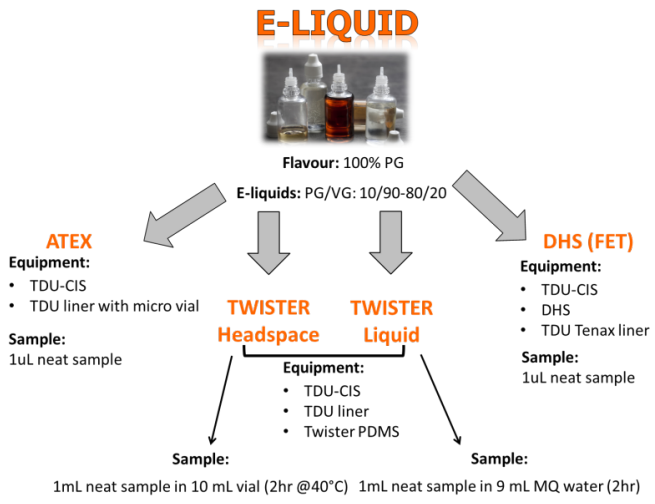

Figure 2 – Analytical workflow for the analysis of e-liquids

GC/MS Conditions:

GC:

- Column: HP 5MS UI 30mx0.25mmx0.25 µm
- TDU: Splitless mode
- TDU Ramp: 40°C held for 0.1 min, 600 °C/s min to 250°C held for 5 min
- CIS: Solvent Vent, Split 100:1.
- CIS Ramp: 10°C held for 0.1 min, 12 °C/s to 250°C held for 3 min
- Flow: 1 mL/min
- GC ramp: 40°C held for 2 min, 10°C/min to 250°C held for 5 min
- Auxiliary temperature: 260°C

MS:

- High efficiency Ion Source in Electron impact (EI) mode at 250°C
- MS Mode: MS1 Scan

Results and Discussion

Figure 3 shows the comparison of the total ion current chromatograms obtained for one of the tested e-liquid (20%PG 80%VG) using standard liquid injection with an Agilent Split Splitless (SSL) injector, ATEX, Twister Headspace, Twister Liquid, and DHS as FET.

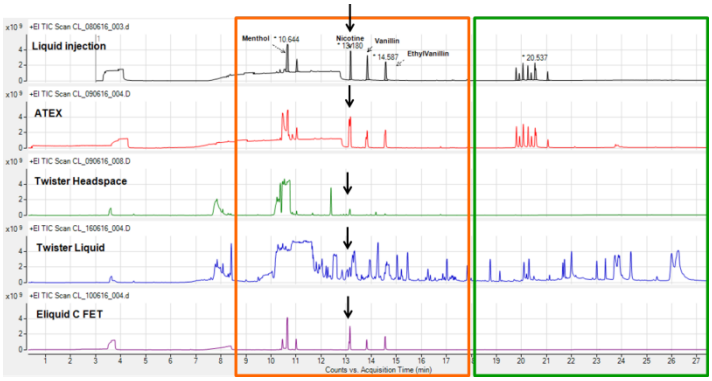

Figure 3 – Total Ion Chromatograms (TICs) comparison for different sample introduction techniques. From the top: standard liquid injection, ATEX, Twister Headspace, Twister Liquid, and DHS as FET

The investigated techniques showed similar pattern in the first part of the chromatogram as highlighted by the orange rectangle and differences mainly in the last part of the chromatogram (green rectangle). The nicotine peak is pointed out by the black arrows.

Figure 4 focuses on the comparison between standard liquid injection and ATEX. The two TIC chromatograms looked very comparable, despite having used two different inlets, the Agilent SSL for the liquid injection and the CIS for the ATEX.

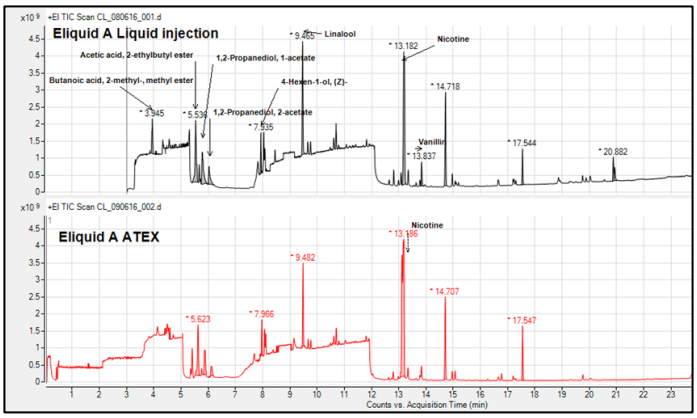

Figure 4 – Total Ion Chromatograms (TICs) for e-liquid A (60% PG 40% VG) using standard SSL liquid injection (top) and ATEX (bottom)

This match was confirmed for all tested e-liquids regardless the particular PG and VG composition. ATEX therefore guaranteed the same chromatography achievable using a standard SSL but giving the advantage of eliminating the risk of inlet cross-contamination and consequently increasing the robustness of the system and the reproducibility of the data.

However, both liquid injection and ATEX were heavily affected by the predominant presence of PG and VG as shown by the high baseline noise in the first half of the chromatogram.

The comparison of standard liquid injection and ATEX to DHS as FET (Figure 5), showed an improvement in the baseline noise and still quite good match between chromatograms, suggesting DHS FET as a better option than the previous two.

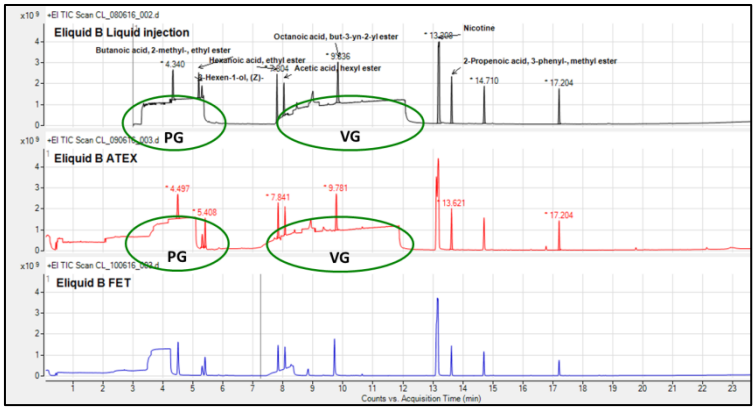

Figure 5 – Total Ion Chromatograms (TICs) for e-liquid B (60% PG 40% VG) using standard SSL liquid injection (top), ATEX (middle) and DHS as FET (bottom)

Furthermore, Figure 6 shows the obtained TICs for Twister Headspace and Twister Liquid in comparison to the standard SSL liquid injection for the analysis of e-liquid C (20% PG 80% VG).

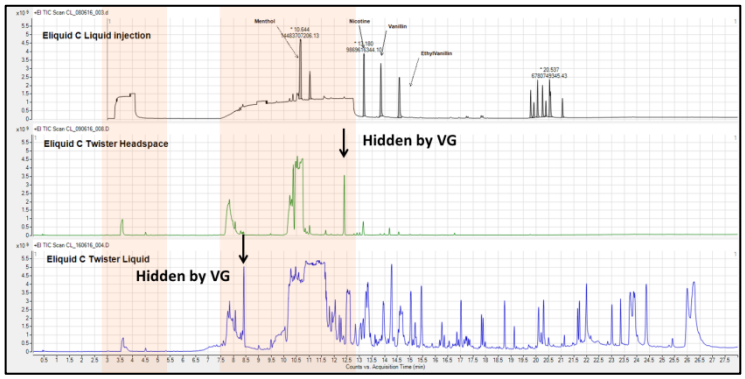

Figure 6 – Total Ion Chromatograms (TICs) for e-liquid C (20% PG 80% VG) using standard SSL liquid injection (top), Twister Headspace (middle) and Twister Liquid (bottom)

Chromatogram baseline was significantly improved when compared to the direct liquid injection thanks to the selectivity of the stir bar sorptive phase, as shown by the areas highlighted in orange. This could unmask some peaks previously hidden by the noise as pointed out by the black arrows.

Focusing specifically on the comparison between Twister Headspace and Twister Liquid for e-liquid D (Figure 7), high similarity could be observed in the first part of the chromatograms which captures the more volatile component as highlighted by the orange arrows.

As predictable, the Twister liquid could sample the non-volatile component which was missed by the Twister Headspace as shown by the area highlighted in orange.

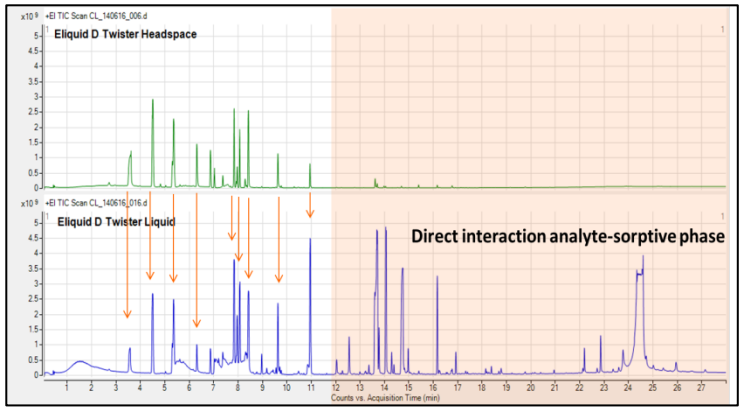

Figure 7 – Total Ion Chromatograms (TICs) for e-liquid D (50% PG 50% VG) using Twister Headspace (top) and Twister Liquid (bottom)

Conclusions

Five main sample introduction techniques were compared for the analysis of e-liquids with different PG/VG composition: standard SSL liquid injection, Automated Tube Exchange (ATEX), Dynamic Headspace (DHS) as Fully Evaporative Technique (FET), Twister Headspace and Twister Liquid.

Liquid injection via SSL, ATEX and FET DHS were fully comparable. The use of ATEX however will prevent inlet matrix contamination while DHS as FET can give reduction of the PG/VG background.

Twister result looked extremely promising: detection of target compounds (e.g. nicotine) could be achieved and the improvement in the baseline and elimination of PG/VG background allowed the detection of peaks previously hidden by the noise.

Acknowledgements

Nathan Hawkins, Account Manager, East of England, Metabolomics Market Specialist

Sean O'Connor, Account Manager, South East of England and Ireland, Food and Flavour Market Specialist

Max Bullock, VAPE Direct, Milton Keynes