Real-time analysis of e-cigarette aerosol constituents using PTR-MS

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SRNT-USA
26 February 2015

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1. Introduction

E-cigarettes are gaining acceptance as potential alternatives to traditional tobacco products. When an e-cigarette user takes a puff, the e-liquid solution is heated and the aerosol, consisting of propylene glycol and/or glycerol, water, flavorings and nicotine, is inhaled. From both a regulatory and sensory point of view it is important to determine the transfer of e-liquid compounds – especially nicotine - into the aerosol, their intake during inhalation and their release following exhalation.

We use Proton Transfer Reaction Mass Spectrometry (PTR-MS; Fig. 1) for the direct sampling and analysis of volatile organic compounds (VOCs) in both the e-cigarette mainstream and exhaled breath following the use of e-cigarettes. PTR-MS is a rapid and highly sensitive tool allowing the simultaneous monitoring of VOCs without sample preparation and compound separation [1]. This is achieved by combining soft ionization techniques (proton transfer from H_3O^+ which mainly yields protonated parent molecules [MH^+]) with a high resolution time-of-flight (TOF) mass spectrometer.

Here we show for the first time the application of PTR-MS to measure the influence of vaping behaviour (e.g. wether the aerosol is inhaled into the lungs or not) on the release of e-cigarette aerosol compounds via the exhaled breath.

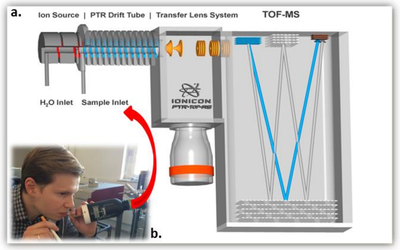


Fig. 1: (a) Schematic of a PTR-MS instrument, where the mass spectrometer is a time-of-flight (TOF) device; ionization of volatile organic compounds is based on proton transfer from H_3O^+ to yield protonated parent ions (MH^+); (b) the exhaled breath after taking a puff from an e-cigarette is sampled via a heated transfer line for immediate ionization and analysis by PTR-MS.

2. Experimental set-up

Instrument: PTR-TOF-MS 8000 with a detection limit of 10 parts per billion per volume (ppbv) and mass resolution of ca. 5000; sensitivity was 120 compounds/ppbv for benzene (standard calibration gas compound); the PTR settings were as follows: p (drift): 2.2 mbar, U (drift): 600 V, T (drift): 120°C. Mass spectra were recorded in the mass-to-charge (m/z) range of 0–310 atomic mass units with a time resolution of one second.

MH^+ of selected aerosol compounds: $H_3{}^{18}O^+$ (*m/z*: 21.02), nicotine (*m/z*: 163.12), 1,2-propylene glycol (*m/z*: 77.06), glycerol (*m/z*: 93,09), benzaldehyde (*m/z*: 107.05), isovaleraldehyde (*m/z*: 87,13), cis-3-hexenol (*m/z*: 101.1); m/z values were confirmed by calibration of PTR-MS with high purity standards (>99%) of said compounds (see below).

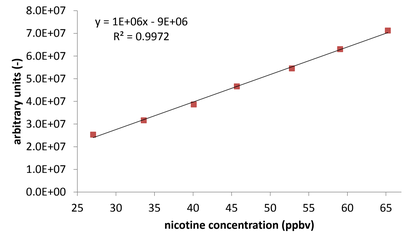
Calibration: a liquid calibration unit (LCU, [2]) was used to evaporate aqueous standards of the aerosol compounds into a gas stream, resulting in a gas flow containing compounds at defined concentration (ppbv-ppmv level).

Volunteer measurements: *Samples*: rechargeable "Original Flavour" Puritane e-cigarettes (nicotine 0, 8, 16 or 20mg/g) were used (manufacturer Fontem Ventures B.V.), the Netherlands; *Subjects*: 3 experienced e-cigarette users (closed systems/ cigalikes) age 26-41 (1 female); *Puffing regime*: subjects were instructed to draw for 3 s at the e-cigarette and keep the aerosol for 3 s in-mouth before I. immeditate exhalation („puffing" mode) or II. deep lung inhalation („inhalation" mode) prior to exhalation into the PTR-MS inlet (Fig. 1b). For each sample, the exhaled breath of 5 individual puffs were recorded from each subject.

Data analysis: The maximum intensities (Imax) of all peaks, after subtraction of the background, in the individual mass spectra of the target compounds shown (see "MH^+ of selected aerosol compounds") were determined; the respective intensities were normalized to the primary ion intensity ($H_3{}^{18}O^+$). Absolute concentrations were determined from the respective regression functions (see "Calibration"). For each volunteer and compound the arithmetic mean Imax and error (standard deviation) of 5 exhaled breaths after use of an e-cigarette were determined.

3. PTR-MS calibration

Calibration of nicotine and benzaldehyde



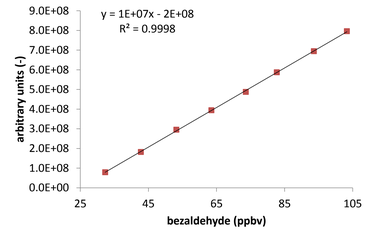


Figure 2 shows typical calibration plots for nicotine and benzaldehyde, two representative aroma compounds originating from the Virginia flavouring. Linear regression analysis revealed a fit with R^2>0,997 (r>0,998).

Calibrations were also performed for 1,2-propylene glycol, glycerol, and additional aroma compounds selected to represent a wide range of different physico-chemical properties (data not shown). In order to accommodate the wide range of compound concentrations (ppb to ppm level) found in this study additional calibration plots covering all levels detected were constructed (data not shown). Again, linear regression analysis revealed a fit with R^2>0,99 (r>0,995).

Fig. 2: Calibration plots for nicotine and a benzaldehyde derived from PTR-MS measurements of the protonated molecule (MH^+); the calibration was performed using liquid standards; the signal intensity of the protonated compounds are expressed in arbitrary units (-).

4. Quantification of nicotine and propylene glycol in exhaled breath

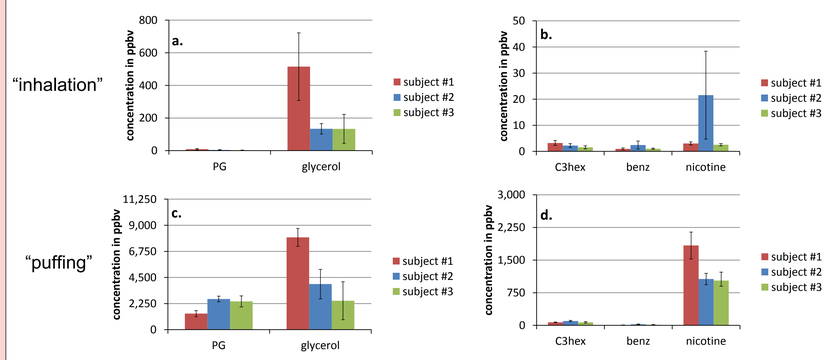


Fig. 3: Results of e-cigarette aerosol PTR-TOF-MS analysis for e-liquid excipients (1,2 propylene glycol, glycerol), nicotine and selected aroma compounds (cis-3-hexenol, benzaldehyde) detected in the exhaled breath after the use of a Puritane e-cigarette ("Original Flavour", 20mg nicotine); data represent the averages of 5 puffs of a subject (n= 3; error: standard deviation) following the use of the e-cigarette either in the "puffing" (3.a, b) or "inhalation" (3.c, d) mode; concentrations of compounds are given in ppbv.

The calibration plots were used for the quantification of specific compounds in the exhaled breath of 3 subjects after the use of a Puritane e-cigarette in the "puffing" (Figures 3a, b) or "inhalation" mode (Figures 3c, d). Across subjects, for each compound a lower breath concentration was detected for the "inhalation" mode indicating a higher retention of compounds by the body. This is of particular interest for the uptake efficiency of nicotine as a higher level of nicotine (on average about 1400ppbv) was released via the breath in the "puffing" mode. In contrast, hardly any nicotine (on average less than 10ppbv) was released in the "inhalation" mode where compounds were able to enter the lungs (Figures 3b, d).

Breath concentrations of 1,2 propylene glycol were clearly lower compared to glycerol for both e-cigarette vaping modes (Figures 3 a, c). This is surprising given that the e-liquid mainly consists of 1,2 propylene glycol which also makes up most of the aerosol (puff analysis of smoking machine operated devices; data not shown). The PTR-MS breath analysis then suggests a much higher retention of 1,2 propylene glycol versus glycerol upon vaping ("human interaction"). This was less pronounced when comparing the two aroma compounds cis-3-hexenol and benzaldehyde (Figures 3b, d) further indicating the distinctive retention behaviour of 1,2 propylene glycol.

Figure 3 also reveals large inter-subject variations (Figure 3). Similar variations were observed when analysing the exhaled breath after the consumption of foods or beverages [3]. Next to differences in the vaping topography this may be explained by differences in human physiology (e.g. lung volume, saliva composition).

5. Conclusions & future work

In this study we show for the first time the application of PTR-MS to analyse the exhaled breath of a person after the use of an e-cigarette.

Data showed that both "aerosol compound" and "subject" have an effect on the composition of the exhaled breath and therefore on the fraction of aerosol compounds retained and/or released into the environment. As a result, the e-liquid composition may not be a good predictor for a person´s exposure to e-cigarette aerosol compounds.

"Subject" effects can be explained by physiological differences as well as different e-cigarette user topographies. "Puffers" exhaled a large proportion of the aerosol compounds in this study whereas "inhalers" retained the majority of compounds they inhaled. This may have consequences for nicotine availability and uptake. User topography may also influence the aroma composition available at the olfactory receptors and explain differences in consumer perception and preference.

As regulators and public health organization are beginning to examine potential implications that exposure to exhaled e-cigarette aerosol constituents may have on the e-cigarette user as well as bystanders and non-users, our approach may also be useful for investigating these concerns.

Please see **poster session 2; poster number 82** for our work applying PTR-MS to examine the exhaled breath following use of a range of different nicotine delivery products

References

1. A. Jordan et al., Int.J. Mass Spectrom. 286 (2/3) (2009) 122–128
2. http://www.ionicon.com/product/trace-calibration-systems/liquid-calibration-unit-lcu
3. F. Biasioli et al., *Trends Anal. Chem.* **30**, (2011) 968.

Declaration

This project was supported by Imperial Tobacco Group. The e-cigarette used in this study was manufactured by Fontem Ventures, a fully owned subsidiary of Imperial Tobacco Group.