A rapid method for the chromatographic analysis of volatile organic compounds in exhaled breath of tobacco cigarette and electronic cigarette smokers

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Abstract

A method for the rapid analysis of volatile organic compounds (VOCs) in smoke from tobacco and electronic cigarettes and in exhaled breath of users of these smoking systems has been developed. Both disposable and rechargeable e-cigarettes were considered. Smoke or breath were collected in Bio-VOCs. VOCs were then desorbed in Tenax cartridges which were subsequently analyzed by thermal desorption coupled to gas chromatography-mass spectrometry. The method provides consistent results when comparing the VOC compositions from cigarette smoke and the equivalent exhaled breath of the smokers. The differences in composition of these two sample types are useful to ascertain which compounds are retained in the respiratory system after tobacco cigarette or e-cigarette smoking.

Strong differences were observed in the VOC composition of tobacco cigarette smoke and exhaled breath when comparing with those of e-cigarette smoking. The former involved transfers of a much larger burden of organic compounds into smokers, including benzene, toluene, naphthalene and other pollutants of general concern. e-Cigarettes led to strong absorptions of propylene glycol and glycerin in the users of these systems. Tobacco cigarettes were also those showing highest concentration differences between nicotine concentrations in smoke and exhaled breath. The results from disposable e-cigarettes were very similar to those from rechargeable e-cigarettes.

1. Introduction

Electronic cigarettes (e-cigarettes) are designed to transfer mixtures of air and vapors into the respiratory system [1-3]. They use plastic or metal cylinders that contain electronic vaporization systems, a battery, in some cases, a charger, electronic controls and, optionally, replaceable cartridges. Different humectants, e.g. propylene glycol or glycerin, flavorings and nicotine at various concentrations are generally contained in the cartridges. They can be disposable (Type 1 e-cigarette) or rechargeable (Type 2 e-cigarette). Concern has been raised for the compounds incorporated into smokers as consequence of e-cigarette vaping.

Exhaled breath, namely the alveolar breath [4], may provide significant clues on the compounds that are retained in humans as consequence of this activity. Studies on VOCs in exhaled breath from e-cigarette smokers have been developed using solid phase microextraction inside a breath collection device [5] or exposure chambers which are subsequently sampled by absorption into solid phase sorption tubes. These tubes are then analyzed by desorption into gas chromatography coupled to mass spectrometry (GC-MS) [6]. In other cases, the absorption cartridge has been installed at the outlet of a smoking machine and the retained compounds are eluted with CS_2 and methanol for subsequent analysis by GC-MS [7].

In the present study, we describe a simplified method using a Bio-VOCs exhaled air sampler developed by the UK Health and Safety Laboratory (Markes International Ltd, Llantrisant, UK) for the comparison of the smoke generated by Type 1 and Type 2 e-cigarettes, tobacco cigarettes and the exhaled breath after vaping or smoking. This device has been used in the analysis of both exhaled alveolar air and mouth air [8-15]. Now, we are using BIO-VOCs for a rapid method of characterization of the volatile organic constituents in tobacco cigarettes and e-cigarettes. Blend type American tobacco cigarettes with filters (length 83 mm, length of filter 23 mm, diameter 8 mm) were used as test examples. Cigarettes with low nicotine content (0.6 mg), low tar (8 mg) and low carbon monoxide (9 mg) were chosen. The compounds analyzed in the present study were mostly in the gas phase. The results add to the current knowledge of exposure of smokers to organic compounds that so far have been mostly characterized in particulate phase transfer processes [16-23].

2. Experimental section

2.1. Sampling cartridges

Volatile organic compounds were concentrated by sorption into stainless steel sorbent cartridges (89 mm long 0.64 cm outer diameter) packed with 200 mg of Tenax TA 35/60 mesh (Markes International Ltd, Pontyclun, UK). The sorbent cartridges were preconditioned using helium (5N grade; 100 ml/min) at 320°C for 2 hours and then at 335°C for 30 min. In later conditioning cycles these cartridges were reconditioned at 335°C for 20 minutes with the same flow carrier gas. Once cleaned, the cartridges were sealed with brass Swagelock storage endcaps fitted with PTFE ferrules and stored in solvent-free clean environments.

2.2. Sampling

Exhaled breath was sampled with a Bio-VOC system 30 min after tobacco cigarette or e-cigarette smoking. To avoid metabolic differences all volunteers were asked to smoke with the tobacco cigarettes and Type 1 and 2 e-cigarettes considered in this study. People inspired and expired deeply three times, then retained the breath for 20 s and blew into the Bio-VOC body through a disposable cardboard mouthpiece at their highest capacity. The air remaining in the Bio-VOC was transferred into the sorbent cartridge by pushing a screw-in plunger through the Bio-VOC body. This procedure was repeated five times in each smoking test and all exhaled VOCs were accumulated in the same cartridge. Thus, a total volume of 750 mL of exhaled breath was collected.

Tobacco cigarette and e-cigarette smoke were sampled by connecting the mouth outlets to the Bio-VOC outlet. The screw-in plunger was used to pull smoke into the Bio-VOC cylinder. Then, the tobacco cigarette or e-cigarettes were removed and the cartridge was connected to the Bio-VOC outlet and the screw-in pluger was used to push the smoke present in the Bio-VOC into the cartridge which sorbed the VOCs from the sample. The sampled volume with this procedure was 150 mL.

Indoor ambient air was also sampled for comparison using this device. The procedure was the same as that used for tobacco cigarette and e-cigarette smoke but without connecting any of those devices to the sorbent cartridge. In this case the procedure was repeated four times and a total volume of 600 mL was collected.

2.3. Transfer of the VOC into the GC-MS

VOCs trapped in the sorbent cartridges were transferred with helium (5N grade; no inlet split flow) to a thermal desorption (TD) instrument equipped with a Unity Series 2 Thermal Desorber and an Ultra 50:50 Multi-tube Auto-sampler (Markes International Ltd). The compounds were desorbed from the cartridges at 300ºC for 5 min (desorption flow 40 mL/min) and re-concentrated in a graphitized carbon sorbent cold trap (U-T11GPC-2S for General Purpose; Markes International Ltd) cooled at -20ºC. This cold trap was heated to 300°C over 5 min while passing a helium flow of 7.5 ml/min (split flow 6 ml/min) for VOC transfer to an uncoated and deactivated fused-silica capillary transfer line of 1 m length (internal and outer diameters 0.25 and 0.35 mm, respectively) heated at 200ºC. Total split ratio was 5:1.

For the Type 2 e-cigarette analyses, inlet split flow during cartridge desorption was 50 mL/min and desorption trap conditions operated at a carrier helium flow of 28.5 mL/min and an outlet split flow of 27 mL/min. Total split ratio was 95:1.

2.4. GC-MS operational conditions

The transfer line introduced the compounds into a Gas Chromatograph 7890 (GC; Agilent Technologies Inc., Santa Clara, CA) coupled to a Mass Spectrometer 5975C Inert XL MSD. The GC was equipped with a DB-5MS UI capillary column (length 60 m; internal diameter 0.32 mm; film thickness 1 m; Agilent J&W GC Columns). Helium (5N grade) was the carrier gas at a flow of 1.5 ml/min (constant flow mode). The GC oven temperature program started at 40°C (holding time 10 min) then it increased to 150ºC at 5°C/min and to 210°C at 15°C/min (final holding time 10 min).

A transfer line heated to 280ºC carried the compounds from the GC to the MS. The MS source and quadrupol temperatures were 230°C and 150°C, respectively. The MS operated in electron impact mode. The detector was full scanned between 30-380 amu.

2.5. Compound identification and quantification

VOCs were identified based on retention times and library identification of the mass spectrum from each chromatographic peak (NIST2009, Mass Spectral Search Program, version 2.0f). Quantification was performed by the external standard method.

Calibration curves encompassed nine calibration solutions in methanol (Merck KGaA, Darmstadt, Germany) at different concentration in the range between 0.5 and 200 µg/ml. They were prepared from commercial solutions: UST Modified Gasoline Range Organics (1000 µg/ml in methanol; Supelco, Inc. Bellefonte, PA, USA), FIA Paraffin Standard (Accustandard Inc., New Haven, CT), and the individual standards: 2-methylbutane, 1-pentene, cis-2-pentene, trans-2-pentene and 4-methyl-1-pentene, all grade GC Standard (Sigma-Aldrich Co., St. Louis, Mo).

A Calibration Solution Loading Ring (CSLR™, Markes International Ltd., Llantrisant, UK) was used to introduce the calibration solution into clean sorbent cartridges which allowed controlled vaporization and purging of the solvent (carrier gas flow at 50 ml/min during 3 min). The different standard solutions were directly introduced into the cartridges which were subsequently analyzed in the TD-GC-MS. This allowed the determination of linear concentration ranges and limits of detection. Recoveries were determined by introduction of standard solutions into the Bio-VOCs heated at 50ºC. Repetitivity was also determined by sequential analysis of standards introduced into the Bio-VOCs.

3. Results and discussion

3.1. Exhaled breath and air concentrations.

The gas chromatograms corresponding to indoor air from a building of Barcelona and exhaled breath of volunteers present in this indoor environment without smoking are compared in Fig. 1. Compound identification is reported in Table 1. Acetone and isoprene were the main compounds in exhaled breath. These are two endogenous compounds usually present in this type of sample. Both chromatograms also had some common peaks such as benzene, toluene, styrene, benzaldehyde, δ-limonene, decanal, nonanoic acid, and a siloxane series. Benzene and toluene may constitute trace amounts of vehicular exhaust in the area. The siloxane series may represent some background input of the analytical system.The other compounds may reflect a relationship between in-door atmospheric VOCs and exhaled breath of residents in this environment.

3.2. Smoke from tobacco cigarettes and e-cigarettes

Representative chromatograms of the VOC in the smoke composition of tobacco cigarettes and Type 1 and Type 2 e-cigarettes are shown in Fig. 2. As expected a strong contrast was observed between tobacco cigarette and e-cigarette smoke. The former contained a wealth of compounds including nicotine and related products such as nicotyrine, 7-methyl-1H-indole, myosmine, isonicoteine. The occurrence of myosmine, isonicoteine and nicotyrine together with nicotine in tobacco cigarette smoke has been reported in previous studies [24, 25]. 2,5-dimethylfuran is another compound characteristic of tobacco cigarette smoke that has been proposed as a specific marker [25-29]. In the present study, this compound was present in the chromatogram of the tobacco cigarette smoke and absent in those of the e-cigarette smoke (Fig. 2; Table 1).

Besides these specific compounds several aromatic compounds such as benzene, toluene, xylenes, ethylbenzene and styrene were also found in the chromatogram of tobacco cigarette smoke (Fig.2). These compounds are not specific for tobacco cigarette smoke, as several of them are found in the BTEX mixtures associated to traffic emissions. However, as documented elsewhere [25-27, 30-31], benzene, a known carcinogen, is common in tobacco cigarette smoke. In this respect, the relative proportion of benzene and toluene in the samples described in this study, 44% and 56%, respectively, is in agreement with the relative proportion of these compounds measured in other tobacco smoke cigarettes measured with other sampling methods, 43% and 57%, respectively [31].

Other compounds commonly related with traffic emissions were also present in the tobacco cigarette smoke chromatogram, e.g. n-heptane, n-octane, 1-ethyl-2-methylbenzene, 1-ethyl-3-methylbenzene and naphthalene. The occurrence of these compounds in tobacco cigarette smoke has also been reported [25, 27].

In addition to these VOCs, many polar compounds were also represented in the tobacco cigarette smoke chromatogram, e.g. ethanol, acetone, acetic acid, butane-2,3-dione, methyl ethyl ketone, methylfuran, isovaleraldehyde, pyridine, methylpyridine, benzaldehyde, phenol, benzonitrile, acetophenone. These compounds have also been found in tobacco cigarette smoke in previous studies [7, 25-26, 30, 32]. Some aldehydes such as crotonaldehyde are also identified with this method. This compound has also

been found in tobacco cigarette smoke in analyses using the dinitrophenylhydrazine method [33].

Chromatographic peaks for several unsaturated compounds were also found in the tobacco cigarette smoke sample, such as buta-1,3-diene, isoprene, hex-1-ene, hep-1-ene and δ-limonene. Several of them are known natural products that can also be found in many plant species. Their presence in tobacco cigarette smoke is consistent with previous studies [7, 25, 27, 30].

The analytical approach of the present study has been designed for the identification and quantification of the volatile compounds. However, some compounds found in the present study (Table 1) have also been identified in the particulate phase in analytical methods specifically designed for the compounds present in this phase, e.g. acetic acid, crotonaldehyde, n-heptane, phenol, δ-limonene, benzoic acid, hydroquinone, nicotine, 7-methyl-1H-indole, myosmine and nicotine [23]. These compounds are generally polar and formed by pyrolysis or distillation of the tobacco components under the high temperature conditions of smoking. Condensation processes lead to their distribution between the gas and particulate phases.

In contrast, the smoke of the e-cigarettes was mainly composed of propylene glycol and glycerin which is consistent with the product description of the manufacturers (note that the chromatographic peaks are overloaded). In addition the smoke of the e-cigarettes contained nicotine and related products such as miosmine and nicotyrine. The smoke of Type 2 e-cigarette also contained vanillin and ethyl vanillin which were likely added as a flavor.

3.3 Exhaled breath from tobacco cigarette and e-cigarette users

Representative chromatograms of the VOCs in the exhaled breath of tobacco cigarette and Type 1 and Type 2 e-cigarette users are shown in Fig. 2. The chromatogram of exhaled breath of a tobacco cigarette smoker showed a simplified mixture of the compounds found in the previously described smoke of these cigarettes (Figure 2) indicating that most of the original smoke components were retained in the lungs. Thus, the relative intensity of most of the higher molecular weight VOCs, those of higher chromatographic retention time, decreased significantly. However, some compounds that are specific of tobacco cigarette smoke such as nicotine, nicotyrine and 2,5-dimethylfuran were found in the exhaled breath. Their occurrence in the VOC

composition can be used to indicate the exposure of the individuals to tobacco smoke compounds. Other VOCs such as benzene, toluene or δ-limonene were less specific of tobacco cigarette smoke but they still were dominant peaks in the exhaled breath chromatograms of the tobacco cigarette smokers. Isoprene was the most abundant exhaled breath peak. As mentioned above, this is an endogenous compound.

In the exhaled breath of the e-cigarette smokers the chromatographic peaks of propylene glycol and glycerin were absent indicating that they remained in the respiratory system of the smokers. Comparison of both original e-cigarette smoke and exhaled breath of the e-cigarette smokers also showed a strong decrease of the peaks corresponding to nicotine and related compounds. On the other hand, two main peaks in the chromatograms from exhaled breath were those corresponding to acetone and isoprene which likely represent endogenous sources. In addition, benzene, toluene and 2,5-dimethylfuran were also found. These peaks were below limit of detection in the e-cigarette smoke vapors. Their occurrence in exhaled breath could reflect past exposures of the volunteers.

3.4. Figures of merit

Linear concentration ranges over three magnitudes of concentration were found for most compounds analyzed (Table 2). In some cases, e.g. n-hexane, naphthalene, these ranges were about 200. The limits of detection ranged between 0.05 and 0.65 ng. The transformation of these limits into concentration values ($\mu g/m^3$) must be done by reference to the sampled volume that depends on the number of Bio-VOC replicates (N). Thus, amount detection limit (ng) is equivalent to concentration detection limit ($\mu g/m^3$) when multiplying the former by 1000/(150*N). The number of replicates in the analyses is indicated in section 2.2. The highest limits, e.g. toluene (0.65 ng), were due to background atmospheric levels by use of this compound in nearby labs. Repeatability (residual standard deviation of ten measurements) ranged between 5.9 and 23% which is consistent with previous measurements with Bio-VOCs in other studies [11]. Recoveries of standards introduced into the Bio-VOCs and analyzed as described in the experimental section ranged between 92 and 114% (Table 2).

3.4. Quantitative differences

The concentrations of some representative VOCs found in the tobacco cigarette and e-cigarette smoke and in the exhaled breath of the smokers are shown in Table 3. Concentrations of the same compounds in ambient indoor air and in volunteers breathing this air without smoking are shown for comparison. Tobacco cigarette smoke provided the samples containing highest concentrations of all compounds analyzed. Besides nicotine (1300 μg/m^3) it contained benzene, toluene, xylenes, ethylbenzene and naphthalene in high abundance (1100, 1400, 1500, 660 and 240 μg/m^3, respectively) as well as other compounds such as isoprene (2700 μg/m^3), pent-1-ene (700 μg/m^3), n-pentane (1200 μg/m^3), n-hexane (975 μg/m^3), n-heptane (1400 μg/m^3) and others. This composition was in strong contrast with that of smoke from the e-cigarettes in which all these compounds were virtually absent except nicotine (710-720 μg/m^3). Propylene glycol and glycerin were not found in the indoor air sample.

In principle, the compositions of exhaled breath reflected the differences of the cigarette smoke compositions (Table 3). Thus, tobacco cigarette smoke was the one with highest nicotine concentration and the highest content of this compound was found in the exhaled breath after tobacco cigarette smoking. In the cases shown in the present study, the differences in nicotine concentration between smoke and exhaled breath were highest for tobacco cigarettes, indicating that this was the smoking system with the highest nicotine transfer.

Isoprene is an endogenous compound and similar concentrations should be expected in all exhaled breath samples. However, it was found between 47-87 μg/m^3 in the e-cigarette smokers and 670 μg/m^3 in the tobacco cigarette smokers (Table 3). The high concentration of this compound in this volunteer may respond to a combination of non-absorbed compound from the tobacco cigarette smoke and generation of high yield of this compound after tobacco cigarette smoking. In fact, the exhaled breath of the tobacco cigarette smoker shows higher concentrations of all above mentioned compounds, including benzene, toluene, xylenes, ethylbenzene and naphthalene, than in the other exhaled breath samples.

4. Conclusions

The analysis of VOCs in smoke from tobacco cigarette and e-cigarettes and in the exhaled breath of users of these smoking systems can be performed by collection with

Bio-VOC, absorption in Tenax cartridges and analysis by TD-GC-MS. This method provides consistent results when comparing the composition of VOCs in cigarette smoke and exhaled breath of the smokers. It also allows the discrimination between endogenous and exogenous compounds and compounds reflecting past exposures to pollutants or tobacco smoke. Comparison of the concentrations between smoke and equivalent exhaled breath of the smokers illustrated the incorporation of higher burdens of VOCs in the tobacco cigarette smokers than in the e-cigarette smokers.

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FIGURE CAPTIONS

Figure 1. Chromatograms showing the composition of volatile organic compounds in air from an in-door environment and exhaled breath of a volunteer present in this environment without smoking.

Figure 2. Chromatograms showing the composition of volatile organic compounds in smoke from tobacco cigarettes, Type 1 and Type 2 e-cigarettes and in exhaled breath of smokers. To avoid metabolic differences all displayed exhaled breath chromatograms correspond to the same volunteer.