Influence of vaping topography on the retention rate of nicotine following use of e-cigarettes

Grant O'Connell[1], Stéphane Colard[2], Kostiantyn Breiev[3], Philipp Sulzer[3], Stefan S. Biel[1], Xavier Cahours[2], John D. Pritchard[4] and Kerstin M. M. Burseg[1]

[1] Fontem Ventures B.V., Amsterdam, The Netherlands; [2] SEITA – Imperial Tobacco Group, Fleury-les-Aubrais, France; [3] IONICON Analytik GmbH, Innsbruck, Austria; [4] Imperial Tobacco Ltd, Bristol, UK

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1. Introduction

Electronic cigarettes (e-cigarettes) are battery-powered devices that deliver aerosolised nicotine, propylene glycol and/or glycerol and flavourings to users from an e-liquid. As they do not contain tobacco or require combustion, they are gaining acceptance with smokers as alternatives to traditional tobacco products [1].

Regulators and the public health community are keen to understand whether the aerosol exhaled following use of e-cigarette products has implications for the quality of air breathed by bystanders. An indoor air quality model was recently published which evaluated potential bystander exposures to exhaled e-cigarette constituents, in particular to exhaled nicotine [2]. The authors identified 'quantity of chemical constituent exhaled' as potentially the most important factor influencing indoor air quality and bystander exposures.

To understand the potential impact of exhaled nicotine on indoor air quality and bystander exposures, it is essential that measurements are made regarding the quantity of nicotine retained by e-cigarette users (*i.e.* the fraction not exhaled). Here an experimental method is presented that allows the concentration of nicotine exhaled following e-cigarette use to be measured and the retention rate by the user estimated [3]. The influence that vaping topography (*i.e.* mouth-hold versus inhaling) has upon the retention of nicotine following e-cigarette use was studied in experienced volunteers.

2. Study design

PRODUCTS USED

Puritane™ rechargeable e-cigarette (battery capacity: 260 mAh) manufactured by Fontem Ventures B.V. Base e-liquid composition: propylene glycol (67%, w/w) and glycerol (30%, w/w) with 8 mg/g, 16 mg/g and 20 mg/g of pharmaceutical grade nicotine.

DETERMINATION OF CONCENTRATION OF NICOTINE INHALED PER PUFF

Using a linear smoking machine and vaping regimes reported in *Table 1*, two e-cigarettes from each nicotine strength were first machine-vaped and evaluated by GC-FID to determine the average concentration of nicotine delivered during a puff versus puff duration. This allowed a calibration curve to be generated (*Figure 1*).

Three experienced male e-cigarette users followed a series of specified vaping topographies (*Table 2*) for each e-cigarette. Test e-cigarettes evaluated by GC-FID above were vaped through a cigarette holder attached to a smoking puff analyser mobile device (SPA-M; SODIM, France) equipped with a specific e-cigarette adapter. As the device records time, puff duration, volume inhaled and pressure drop, it was used in this study to record the vaping topography of the e-cigarette users. From the participant's recorded vaping topography, the concentration of nicotine inhaled per puff was determined using the calibration curves obtained with the smoking machine for the corresponding e-cigarette device (*Figure 1*).

DETERMINATION OF CONCENTRATION OF NICOTINE EXHALED PER PUFF BY PTR-MS

To determine the concentration of nicotine exhaled following e-cigarette use for the different topographies, participants exhaled directly into a PTR-MS instrument. A high-sensitivity and high-resolution time-of-flight (TOF) mass spectrometry based PTR-TOF 8000 (IONICON Analytik GmbH, Austria) was utilized in this study and is reviewed elsewhere [4]. The concentration of nicotine exhaled by each participant was calculated from the ion yield for protonated nicotine (*m/z* 163).

NICOTINE RETENTION

By calculating the inhaled and exhaled nicotine concentrations per puff the nicotine retention rate can be estimated.

$$\text{Nicotine retention rate (\%)} = \frac{\text{Concentration inhaled (ppbv)} - \text{Concentration exhaled (ppbv)}}{\text{Concentration inhaled (ppbv)}} \times 100$$

Vaping regime	Puff number	Puff frequency (min^{-1})	Puff duration (s)	Puff volume (mL)	Total volume (mL)
1	15	1	3	40	600
2	15	1	4	55	825
3	15	1	5	70	1050

***Table 1**: Smoking machine parameters used to determine the relationship between e-cigarette nicotine delivery per puff and puff duration by GC-FID (puff volume was adjusted to keep airflow constant).*

Vaping topography instructions	Puff duration (s)	Mouth-hold or inhalation	Breath-hold duration (s)	Replicate
1	3	Mouth-hold	1	5
2	3	Mouth-hold	2	5
3	3	Mouth-hold	3	5
4	3	Mouth-hold	4	5
5	3	Inhalation	1	5
6	3	Inhalation	2	5
7	3	Inhalation	3	5
8	3	Inhalation	4	5

***Table 2**: Vaping topographies applied to assess retention of nicotine under various conditions.*

3. Summary of findings

Figure 1 shows the relationship between puff duration and nicotine delivery when the e-cigarettes were machine-vaped. At each nicotine strength, nicotine aerosol concentration increases with puff duration which corresponds to the time the atomiser coil is heated.

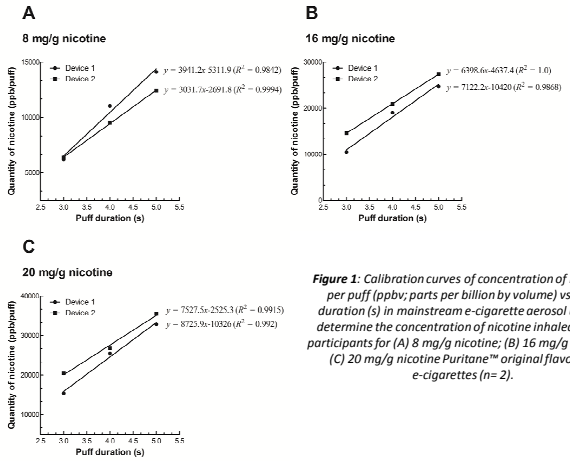

***Figure 1**: Calibration curves of concentration of nicotine per puff (ppbv; parts per billion by volume) vs. puff duration (s) in mainstream e-cigarette aerosol used to determine the concentration of nicotine inhaled by the participants for (A) 8 mg/g nicotine; (B) 16 mg/g nicotine; (C) 20 mg/g nicotine Puritane™ original flavoured e-cigarettes (n= 2).*

The mean values for the concentration of nicotine delivered and exhaled and therefore the concentration retained by the three e-cigarette participants across each e-cigarette for the mouth-hold and inhalation topographies is summarized in *Table 3*.

E-cigarette	E-cigarette use topography across all breath-hold durations	Mean concentration of nicotine inhaled across all e-cigarette users (ppbv)	Mean concentration of nicotine exhaled across all e-cigarette users (ppbv)	Mean nicotine retention rate across all e-cigarette users (%)
8 mg/g	Mouth-hold	6317	1514	**77**
	Inhalation	6671	1.76	**> 99**
16 mg/g	Mouth-hold	13703	1514	**89**
	Inhalation	11468	2.31	**> 99**
20 mg/g	Mouth-hold	20668	1786	**92**
	Inhalation	18485	1.76	**> 99**

***Table 3**. Mean concentration of nicotine delivered and exhaled and nicotine retained for each mouth-hold and inhalation topographies across all e-cigarette users for the different nicotine-containing e-cigarettes. Ppbv, parts per billion per volume.*

The retention rate of nicotine was found to be >99% on average when the e-cigarette aerosol was inhaled by the users. This finding is in good agreement with previously published values in smokers of conventional tobacco cigarettes [4]. A substantial fraction of nicotine (86% on average) was also retained when the aerosol is kept in the mouth only and not inhaled.

We hypothesise that the high nicotine retention rate following inhalation of the e-cigarette aerosol is likely due to the evaporation of nicotine out of the aerosol particles and/or diffusion to the surface where it is absorbed (pulmonary nicotine absorption). It is likely this evaporation/diffusion and absorption also occurs in the mouth (buccal nicotine absorption). Whether these retention rates correlate with an increase in nicotine intake into the systemic system was not determined in this study.

4. Conclusions & future work

The retention rate of nicotine following use of the commercially available 'closed' system e-cigarette was >99% on average following inhalation of e-cigarette aerosols and 86% on average following holding aerosols in the mouth-hold only (*i.e.* no inhalation), regardless of the nicotine concentration of the device.

In a recent assessment of indoor air quality during e-cigarette use there was no measurable increase in the airborne concentrations of nicotine when compared with no vaping control sessions or background measurements [6]. The authors suggested this may be attributable to the high retention rate of nicotine following e-cigarette use. The results from this present study support the suggestion that extremely low concentrations of nicotine are exhaled following inhalation of e-cigarette aerosols as a result of the high nicotine retention rate *i.e.* >99%.

The 2015 review of the scientific literature by Public Health England also noted that use of e-cigarettes "*release negligible levels of nicotine into ambient air with no identified health risks to bystanders*" [1], which can be attributed to the high retention rate of nicotine by e-cigarette users as reported in this study.

The results from this present study support the suggestion that extremely low concentrations of nicotine are exhaled following inhalation of e-cigarette aerosols as a result of the high nicotine retention rate in the user.

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