Emissions of Toxic Carbonyls in an Electronic Cigarette*

by

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SUMMARY

Electronic cigarettes (e-cigs) provide a smoke-free alternative for inhalation of nicotine without the vast array of toxic and carcinogenic combustion products produced by tobacco smoke. Elevated levels of toxic carbonyls may be generated during vaporisation; however, it is unclear whether that is indicative of a fault with the device or is due to the applied conditions of the test. A device, designed and built at this facility, was tested to determine the levels of selected toxic carbonyls. The reservoir was filled with approximately 960 mg of an e-liquid formulation containing 1.8% (w/v) nicotine. Devices were puffed 200 times in blocks of 40 using a standardised regime consisting of a 55 mL puff volume; 3 s puff duration; 30 s puff interval; square wave puff profile. Confirmatory testing for nicotine and total aerosol delivery resulted in mean ($n = 8$) values of 10 mg (RSD 12.3%) and 716 mg (RSD 11.2%), respectively. Emissions of toxic carbonyls were highly variable yet were between $< 0.1\%$ and 22.9% of expected levels from a Kentucky Reference Cigarette (K3R4F) puffed 200 times under Health Canada Intense smoking conditions. It has been shown that a device built to a high specification with relatively consistent nicotine and aerosol delivery emits inconsistent levels of carbonyls. The exposure is greatly reduced when compared with lit tobacco products. However, it was observed that as the reservoirs neared depletion then emission levels were significantly higher. [Beitr. Tabakforsch. Int. 27 (2016) 30–37]

ZUSAMMENFASSUNG

Elektronische Zigaretten (E-Zigaretten) bieten eine rauchfreie Alternative für die Inhalation von Nikotin ohne die breite Palette an toxischen und kanzerogenen

Verbrennungsprodukten des Tabakrauchs. Während der Verdampfung können erhöhte Mengen toxischer Carbonyle entstehen; es ist jedoch unklar, ob dies auf einen Fehler des Geräts hinweist oder auf die angewendeten Testbedingungen zurückzuführen ist. Ein in dieser Einrichtung konstruiertes und gebautes Gerät wurde für die Bestimmung der Mengen ausgewählter toxischer Carbonyle getestet. Der Behälter wurde mit ca. 960 mg eines E-Liquids befüllt, das in seiner Formulierung 1,8% (Volumengewicht) Nikotin enthielt. Mit den Geräten wurden 200 Züge in Blöcken von je 40 nach einem standardisierten Protokoll vorgenommen: Zugvolumen von je 55 mL; 3 s Zugdauer; 30 s Abstand zwischen den Zügen; rechteckförmiges Zugprofil. In Bestätigungstests für den Nikotin- und Gesamtaerosolgehalt ergaben sich mittlere ($n = 8$) Werte von 10 mg (RSD 12,3%) bzw. 716 mg (RSD 11,2%). Die Emissionen toxischer Carbonyle waren stark variabel und lagen zwischen $< 0,1\%$ und $22,9\%$ der erwarteten Mengen einer Kentucky-Referenzzigarette (K3R4F) bei 200 Zügen unter den Bedingungen des Health-Canada-Intense-Rauchprotokolls. Es wurde gezeigt, dass ein nach höchsten Anforderungen gebautes Gerät mit einer relativ konstanten Nikotin- und Aerosolemission ungleichmäßige Mengen an Carbonylen abgibt. Die Exposition ist im Vergleich zu angezündeten Tabakerzeugnissen stark reduziert. Jedoch wurde beobachtet, dass die Emissionsmengen signifikant höher waren, wenn das Liquid im Behälter fast aufgebraucht war. [Beitr. Tabakforsch. Int. 27 (2016) 30–37]

RESUME

Les cigarettes électroniques proposent une alternative d'inhalation de la nicotine sans fumée et sans ingestion de la vaste gamme des produits de combustion cancérigènes et

toxiques présents dans la fumée du tabac. Des niveaux élevés de carbonyles toxiques peuvent être générés durant la vaporisation; toutefois, rien ne permet de déterminer avec clarté si ce phénomène est révélateur d'un défaut au niveau du dispositif ou s'il est dû aux conditions appliquées durant l'essai. Un dispositif, conçu et fabriqué en interne, a été testé afin de déterminer les niveaux des carbonyles toxiques sélectionnés. Le réservoir a été rempli d'environ 960 mg d'une formule liquide pour cigarette électronique contenant 1,8% (poids/volume) de nicotine. Les dispositifs ont été aspirés en 200 bouffées par blocs de 40 bouffées selon un régime normalisé reposant sur un volume de bouffée de 55 mL, une durée de bouffée de 3 s, un intervalle de 30 s entre les bouffées et un profil de bouffée à onde carrée. Les essais de confirmation relatifs à l'administration de nicotine et d'aérosols totaux ont indiqué des valeurs médianes ($n = 8$) de respectivement 10 mg (écart-type résiduel 12,3%) et 716 mg (écart-type résiduel 11,2%). Les émissions de carbonyles toxiques se sont révélées hautement variables et ont toutefois oscillé entre < 0,1% et 22,9% des niveaux attendus pour une cigarette de référence composée de tabac du Kentucky (K3R4F) et consommée en 200 bouffées dans les conditions de fumage édictées par Health Canada Intense. Il a été démontré qu'un dispositif construit selon des normes élevées et administrant des aérosols et de la nicotine de façon relativement constante émettait des niveaux inconstants de carbonyles. L'exposition est grandement réduite en comparaison des produits de tabac allumés. Cependant, nous avons observé que lorsque les réservoirs étaient presque vides, les niveaux d'émission étaient significativement plus élevés. [Beitr. Tabakforsch. Int. 27 (2016) 30–37]

INTRODUCTION

Electronic cigarettes (e-cigs) are the most widely recognised type of electronic nicotine delivery systems (ENDS) and may pose significant health risks due to the potential inhalation of large doses of toxins deep into the lung tissue (1). The United States Food and Drug Administration (FDA) has the authority under the Tobacco Control Act of 2009 to extend its regulatory control to other tobacco products not specifically enumerated in the statute (2). The proposal '*Deeming Tobacco Products to be Subject to the Food, Drug and Cosmetic Act...*' ('Deeming') was published in the Federal Register in 2014 (3). It has been proposed that e-cigs which are not marketed for 'therapeutic purposes' are to be classified as tobacco products. Therefore, a clear distinction has emerged between consumer tobacco products and therapeutic devices which would require a pharmaceutical licence. The rise in popularity of e-cigs has made them an important part of the strategy towards tobacco harm reduction (4). The revised European Union (EU) Tobacco Products Directive (TPD2) is due to be implemented in May 2016 (5). Member states are required to enact legislation to ensure compliance with the directive. Article 20 of the directive relates specifically to e-cigs. Manufacturers and importers of e-cig devices and refill containers will be subject to reporting obligations, restrictions on unit volumes, and nicotine concentrations with a maximum permissible limit in e-liquids of

20 mg/mL. Formulations with higher concentrations will be subject to Directive 2001/83/EC relating to medicinal products (6). A proposed standard method is currently under development by the International Organization for Standardization (ISO) Technical Committee 126; responsible for tobacco and tobacco products (7). Clearly e-cigs are not tobacco products in the conventional sense. Formulations may contain natural extracts of tobacco (NET) and, therefore, low levels of other tobacco-derived chemicals (8, 9). However, distilled nicotine is also commonly used.

The FDA has stated that insufficient data is currently available to determine what effects e-cigs have on the public health (3). Emissions vary considerably and a lack of uniformity in methods inhibits any useful comparison with lit tobacco products (10). The World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC) has stated that whilst average levels of certain toxic and carcinogenic compounds were 1–2 orders of magnitude lower than tobacco smoke (11); levels of formaldehyde and acrolein, as high as those found in tobacco smoke, have been reported (12). Proposed measures under TPD2 will require manufacturers to submit notifications including emission levels (5). However, the composition of the aerosol will depend on the ingredients used in the formulation and the thermal degradation products produced which will not be necessarily clear to either manufacturer or regulatory authority. Studies to date have tended to focus on known tobacco smoke constituents. The Health Canada list of 44 constituents (13) and the FDA list of 93 harmful and potentially harmful constituents (HPHC) in cigarette smoke and/or filler (14), were formulated to determine exposure risk in lit products. These constituents are tobacco-derived or combustion/pyrolysis products of tobacco and it can be foreseen that e-cigs will not contain many of the chemicals listed. This paper focuses on toxic carbonyl content in the e-cig aerosol and whether elevated levels might be indicative of a fault with the device by making a comparison with the nicotine and aerosol delivery or if it is symptomatic of the applied test conditions.

HARMFUL CONSTITUENTS IN E-CIGS

E-liquids

The bulk of the liquid contained within an e-cig (e-liquid or e-juice) usually consists of propylene glycol (PG) and glycerol (VG) although ratios vary greatly. Nicotine may be added either by direct extraction from the tobacco leaf into the bulk constituents to give a NET or by addition of distilled nicotine which is usually plant-derived although it can be synthesised. The specification for EP/USP (European Pharmacopoeia/United States Pharmacopoeia) pharma grade nicotine is > 99.0%. Formulations with 0% nicotine are also marketed. Water is usually also present. PG and VG are low toxicity compounds widely used in many products. Allergic reactions to PG have been documented in a minority of the population (15). For this reason VG only formulations are readily available. Nicotine is a highly addictive substance and can be extremely toxic if ingested especially e-liquids containing high concentration formulations (16).

Other chemicals may be added to facilitate the extraction process or to flavour or buffer the solution and are present at much lower concentrations. Certain chemicals have reportedly been used in formulations that are not toxic by ingestion but are respiratory toxins. Diacetyl and acetyl propionyl, used as flavours, have been detected in various formulations with many of them exposing users (or vapers) to higher than safe levels (17).

Certain impurities may also be present in the e-liquid. Nicotine that has been derived from the tobacco plant may contain carcinogenic tobacco-specific nitrosamines (TSNA) and phenols (9). A study by ETTER *et al.* of 10 commercial refill e-liquids detected various minor tobacco alkaloids and nicotine degradation products (18). The same study did not detect any ethylene glycol (EG) and diethylene glycol (DEG); however, an FDA commissioned study found trace levels of DEG in one commercial brand (19). Toxic aldehydes, formaldehyde and acetaldehyde, have been detected in e-liquids (20); however, these chemicals are far more likely to be generated in the aerosol.

E-cig aerosol

It is likely that the e-liquid is contained within a reservoir often called the ‘cartomiser’ and is vaporised using a heater coil wrapped around a wicking material. E-cigs are battery powered which can be activated either by a flow sensor or manually. Unlike a conventional lit tobacco product there is no combustion and although some thermal decomposition may occur due to high temperature and contact with solid surfaces, the composition of the vapour remains essentially unchanged. Aerosolised PG and VG are relatively benign; however, inhalation of large volumes of PG has been shown to cause acute ocular and upper airway irritation (21). Certain aldehyde compounds including formaldehyde, acetaldehyde, and acrolein have been found in e-cig aerosol (12). They are thermal decomposition products of PG and VG. This has been demonstrated experimentally using pyrolysis analysis (22, 23). Levels vary greatly from device to device and are affected by the amount of heat generated by the coil. Studies using ‘tank-style’ devices with adjustable voltage output have demonstrated that emissions of formaldehyde and other toxic aldehydes may even exceed that of conventional cigarettes when operated at the higher voltage setting (24, 25).

However, FARSALINOS *et al.* state that increasing the voltage to such a degree would cause excessive heat and subsequent drying of the wicking material (26). The elevated levels of aldehydes are caused by burning of the wicking material. The taste would be so unbearable that the vapor would cease puffing immediately. There is clearly a different set of criteria to what defines a cigarette performing normally to an e-cig.

Particles from the various components contained within the device can be transferred to the aerosol. The heater coil is typically made from a nickel chromium alloy (nichrome) wrapped around the wicking material which is typically made from silica based fibreglass although other materials such as cotton may be used. The soldered joints and the plastic coatings are another possible source of emissions. Various metals including cadmium, chromium, lead and nickel have been detected in e-cig aerosol (12, 27, 28). These metals are HPHCs cited by the FDA (14). Silicate beads originating from the fibreglass wicks have also been detected in the aerosol (27).

Sources of other toxic emissions may be derived from impurities in the e-liquid. Known tobacco carcinogens such as TSNA have been detected in the aerosol (12, 29). These compounds may be present in NET formulations; however, endogenous production (30), and formation during vaporisation may occur. Other tobacco-derived toxic chemicals such as phenols may be present.

Typical temperatures produced by the e-cig heater coil (~ 200–250 °C under dry conditions) would not be expected to produce significant levels of pyrolysis products; however, studies do suggest that spikes in temperature due to drying of the wicking material produce elevated levels of toxic aldehydes (28). Therefore, nicotine or additives could also decompose and produce toxic emissions.

METHODOLOGY

A standard method for determination of nicotine in e-liquids is currently under development by the ISO (7). A standard set of machine conditions for sampling e-cig aerosol has been developed by the Cooperation Centre for Scientific Research Relevant to Tobacco (CORESTA). It proposes a standard puffing regime: 55 mL puff volume; 3 s puff duration; 30 s puff interval; square wave puff

Figure 1. Cartomiser used in the experiment containing a mid-coil atomiser in contact with a polyester reservoir (not to scale).

Table 1. GC-FID conditions for nicotine analysis.

Column	J&W CP-WAX 52CB (25 m × 0.53 mm; 1 µm)
Inlet temperature	250 °C
Injection volume	1 mL
Flow rate	15 mL/min
Carrier gas	Hydrogen
Oven	150 °C isocratic
Detector	FID; 250 °C; 25 mL/min H ₂ ; 400 mL/min air; 1 mL/min He

profile (31). Standardised machine sampling of cigarettes is well established. The ISO 3308 standard method is used worldwide by the industry for the measurement of “tar”, nicotine and carbon monoxide (32). It provides a standard comparison across cigarette brands. It consists of a puffing regime of 35 mL puff volume; 2 s puff duration; 60 s puff interval; bell wave puff profile. The Health Canada Intense (HCI) smoking protocol consists of a puffing regime of 55 mL puff volume; 2 s puff duration; 30 s puff interval; bell wave puff profile with 100% ventilation blocking (33). The CORESTA e-cig method (CRM 81) (31) is very similar to the HCI regime except that it incorporates a 3 s puff duration and also the bell wave puff profile was deemed unsuitable for e-cigs because products activated by flow sensor must reach a certain pressure threshold and this can vary significantly from device to device. The square wave profile enables more reproducible puffs due to the rapid change in velocity at the commencement of the puff.

It is reasonable to assume that other tobacco-specific methods will also be adapted for routine e-cig testing purposes. They include ISO 4387 (34) for determination of total particulate matter (TPM) and preparation for nicotine measurement, and CORESTA Recommended Method No. 74 (CRM 74) for determination of carbonyl compounds in cigarette mainstream smoke (MSS) (35). Under TPD2 (5) manufacturers will be required to ensure nicotine delivery is consistent and toxic emissions are reported; however, without standardised methods it is difficult to have regulation in place.

Table 2. UHPLC conditions for carbonyls analysis.

Column	Waters acuity BEH C18 (100 mm × 2.1 mm; 1.7 µm)
Temperature	35 °C
Injection volume	5 µL
Flow rate	0.4 mL/min
Mobile phase A	30% acetonitrile; 62% water; 7% THF; 1% IPA
Mobile phase B	65% acetonitrile; 27% water; 7% THF; 1% IPA
Gradient	Equilibration 3 min (90% A: 10% B); 0–2.5 min (90% A: 10% B); 2.5–5.0 min (47% A: 53% B); 5.0–6.0 min (100% B); 6.0–8.0 min (100% B); 8.0–10.0 min (90% A: 10% B)
Detector	UV (365 nm); 2.5 Hz

IN-HOUSE TESTING

The e-cig device tested in this study was designed and built at this facility. The cartomiser (Figure 1) contained a mid-coil atomiser consisting of a nichrome resistance wire wrapped around a fibreglass silica wick. The wick is in contact with a fibrous reservoir manufactured from polyester with a density of 0.13 g/cc. The heating coil operated at a resistance of 2.8 Ω. The applied voltage was a nominal output of 3.7 V which generated an output power of approximately 4.9 W. The type of battery was a rechargeable lithium ion.

The cartomiser was filled with 0.8 mL e-liquid (approximately 960 mg) containing 18 mg/mL nicotine (Pharmacopoeia Europaea Grade) and the following other ingredients: propylene glycol, glycerol, vanilla extract, linalool, vanillin, menthol, malic acid, acetylpyrazine, ethyl acetate, ethyl maltol, trimethylpyrazine, tabanone, beta-damascenone, and water.

Devices were puffed using a Cerulean SM450 20 Channel linear machine (Cerulean, Milton Keynes, U.K.) and

Table 3. Breakdown of nicotine delivery over 5 x 40 puff blocks, total nicotine delivery and trapped aerosol. Total puffs: 200.

Rep	Nicotine (mg)					Total nicotine delivery (mg)	Total aerosol trapped (mg)	Nicotine in aerosol (w/v) %	Total liquid trapped %
	Puffs 1–40	Puffs 41–80	Puffs 81–120	Puffs 121–160	Puffs 161–200				
1	2.4	2.2	2.1	1.9	1.6	10.3	728.0	1.72	75.8
2	2.9	2.5	2.4	2.0	1.8	11.6	818.0	1.72	85.2
3	2.8	2.4	2.2	2.0	1.8	11.1	791.3	1.72	82.4
4	2.6	2.1	2.1	1.8	1.6	10.2	722.8	1.73	75.3
5	2.2	2.1	1.9	1.7	1.6	9.5	679.4	1.70	70.8
6	1.9	1.8	1.7	1.6	1.5	8.5	610.1	1.70	63.6
7	2.9	2.3	2.1	1.9	1.7	10.9	774.9	1.71	80.7
8	2.0	1.7	1.6	1.5	1.3	8.1	601.9	1.65	62.7
Mean	2.5	2.1	2.0	1.8	1.6	10.0	715.8		
SD	0.4	0.3	0.3	0.2	0.1	1.2	80.5		
RSD %	15.8	12.8	13.8	10.2	9.1	12.3	11.2		

Table 4. Carbonyl content from 5 reps of the device puffed using a 55 mL puff volume / 3 s puff duration / 30 s puff interval / square wave puff profile.

Rep	Formaldehyde	Acetaldehyde	Acetone	Acrolein	Propionaldehyde	Weight loss from cartomiser (mg)
	µg/40 puffs					mg/40 puffs
Puffs 1–40						
1	4.44	2.29	< 2.96	0.53	0.38	187.6
2	9.57	9.50	< 2.96	2.34	0.90	179.8
3	3.05	2.10	< 2.96	0.57	nd	242.2
4	6.54	7.13	< 2.96	1.04	0.64	168.2
5	0.74	< 1.62	< 2.96	nd	nd	210.6
Puffs 41– 80						
1	5.02	3.59	3.51	0.60	0.46	165.1
2	15.68	16.18	3.81	3.33	1.19	156.8
3	21.13	13.91	3.70	3.07	1.03	206.8
4	16.02	17.47	3.84	2.68	1.26	143.1
5	2.75	2.17	3.26	< 0.31	nd	179.8
Puffs 81–120						
1	6.03	5.36	< 2.96	0.88	0.52	149.7
2	25.66	29.37	2.97	5.88	2.11	137.0
3	46.46	47.85	3.52	8.67	3.33	160.3
4	17.22	21.54	< 2.96	3.58	1.57	123.8
5	4.67	5.35	< 2.96	0.63	0.32	147.8
Puffs 121–160						
1	5.44	4.78	< 2.96	0.72	0.42	138.3
2	66.00	110.74	7.16	31.63	10.71	126.8
3	96.85	158.22	7.72	25.85	12.39	138.6
4	30.68	35.10	< 2.96	7.76	2.82	124.9
5	6.80	7.80	< 2.96	1.02	0.47	133.0
Puffs 161– 200						
1	5.64	4.69	2.99	0.74	0.37	117.9
2	231.17	511.70	49.92	160.31	104.49	51.4
3	142.58	336.51	17.16	52.67	29.92	124.4
4	122.93	271.73	20.10	59.34	35.00	75.5
5	9.25	12.59	3.18	1.81	0.93	112.7
LOD	0.20	0.48	0.89	0.09	0.09	
LOQ	0.67	1.62	2.96	0.31	0.29	

operated in accordance with CRM 81 (31). Devices were placed in holders containing labyrinth seals. Eight replicates of the device were tested for nicotine delivery and five replicates for carbonyl content. Each replicate was puffed 200 times and analysed in blocks of 40 puffs. The 200 puff cut-off ensured that none of the devices were empty by the end of the run. Nicotine delivery was determined based on ISO 4387 (34).

The aerosol was trapped onto Cambridge filter (CF) glass fibre pads and extracted in 20 mL propan-2-ol containing decanol as an internal standard. Analysis was performed using gas chromatography with flame ionisation detection (GC-FID) (Table 1).

The amount of aerosol trapped on the CF pads was determined gravimetrically. Carbonyl testing was based on CRM 74 (35). The whole aerosol was scrubbed using 30 mL of acidified 2,4-dinitrophenylhydrazine (DNPH) solution. Analysis was performed using ultra-high performance liquid chromatography (UHPLC) with UV detection (Table 2).

RESULTS

The delivery of nicotine and aerosol in 8 replicates of the device remained relatively consistent over 5×40 puff blocks (Table 3). A gradual decrease in trapped aerosol over the 5 puff blocks was observed. The amounts from each individual device ranged from 137.1–205.8 mg (Block 1); 123.8–175.2 mg (Block 2); 114.8–168.6 mg (Block 3); 109.6–144.0 mg (Block 4); and 108.7–125.8 mg (Block 5). After 200 puffs between 63% and 85% of the total fill volume had been trapped on the CF pad. The total nicotine to trapped aerosol ratio ranged from between 1.65–1.73% (w/v) after 200 puffs. The relative standard deviations (RSD) for trapped aerosol and nicotine delivery, over 200 puffs, were 11.2–12.3%, respectively.

The carbonyl content produced in the aerosol of this device is shown in Table 4.

Five out of the eight carbonyls tested were found in the aerosol of this device at significant levels. Some methyl

Table 5. Comparison of carbonyl yields with expected yields from a K3R4F Reference Cigarette under HCI conditions and UK HSE workplace exposure limits (WELs).

Rep	Formaldehyde	Acetaldehyde	Acetone	Acrolein	Propionaldehyde
	µg/200 puffs e-cigs				
1	26.57	20.70	6.50	3.47	2.16
2	348.07	677.50	63.86	203.50	119.39
3	310.06	558.59	32.10	90.83	46.68
4	193.38	352.97	23.94	74.39	41.29
5	24.22	27.91	6.44	3.46	1.73
	µg/200 puffs K3R4F Monitor Cigarette (expected values ^a)				
K3R4F	1520.00	32120.00	11940.00	3100.00	2460.00
	8-hr WELs (µg) equivalent to 200 x 55 mL volume of air (11,000 mL)				
Air	27.5	407	13310	2.53	522 ^b

^a Values based on in-house data validated for accuracy using CRM 74 (37);

^b Permissible Exposure Limit (PEL) defined by US Centers for Disease Control and Prevention;

ethyl ketone (MEK) was also detected but at levels close to or below the limit of quantification (LOQ). Crotonaldehyde and butyraldehyde were not detected by the method. Overall the results were highly variable.

Replicates 1 and 5 showed small increases over the course of the run whereas Replicates 2, 3, and 4 increased quite significantly with the largest increases observed in the last puff block.

Weight losses from each device ranged from 636 mg to 872 mg after 200 puffs. This accounted for between 66% and 91% of the total filled volume. A gradual decrease was observed over the 5 puff blocks ranging from 168.2–242.2 mg (Block 1); 143.1–206.8 mg (Block 2); 123.8–160.3 mg (Block 3); 124.9–138.6 mg (Block 4); and 51.4–124.4 mg (Block 5).

It was noted that a higher weight loss did not correlate with higher carbonyl yields. Replicate 2 produced the highest levels of carbonyls but also expelled the second lowest level of aerosol (652 mg). It would appear unlikely that this was due to drying of the wicking material because of insufficient liquid in the reservoir.

The emissions after 200 puffs were compared with expected levels from 200 puffs from Kentucky Reference Cigarettes (K3R4F) smoked under HCI conditions (equivalent to approximately 20 cigarettes) and recognised workplace exposure limits (WELs) defined by the United Kingdom Health and Safety Executive (HSE) in document EH40/2005 (36). Levels of formaldehyde were between 1.6% and 22.9% of expected K3R4F levels (Table 5). Other carbonyls were lower: acetaldehyde, < 0.1–2.1%; acetone, < 0.1–0.5%; acrolein, 0.1–6.6%; and propionaldehyde, < 0.1–4.9%. Formaldehyde, acetaldehyde and acrolein consistently exceeded 8-hr WELs by comparison of an equivalent volume of air in 200 × 55 mL puffs.

Various commercial e-cig brands have been tested by this laboratory and total carbonyls emissions found to range from < LOQ to > 1000 µg/puff block; however, the operating parameters between devices are so different that a reliable comparison was out of the scope of this study.

CONCLUSIONS

It has been shown that an e-cig device built to a high specification and which delivers relatively consistent quantities of nicotine and aerosol over 200 puffs emits inconsistent levels of carbonyls. The exposure is greatly reduced compared with lit tobacco products but levels of formaldehyde, acetaldehyde, and acrolein do exceed Workplace Exposure Limits defined by the UK Health and Safety Executive. It was observed that as the reservoirs neared depletion then emission levels were significantly higher. However, higher weight loss did not correlate with higher emissions. FARSALINOS *et al.* states that carbonyl emission levels are directly associated with ‘dry-puff’ conditions due to drying of the wicking material (26). If this is the case then it is more symptomatic of the test conditions rather than the device. In this study weight losses were attained in blocks of 40 puffs; however, this does not mean that the vapour generated was evenly distributed. Advances in vaping machine technology may enable the aerosol density at every puff to be determined and allow the operator to identify if a dry-puff has occurred. Other factors causing elevated carbonyl levels should also be considered. It is expected that the heating element and wicking material will deteriorate with use and could subsequently lead to more thermal degradation. Charring of the wicking material was observed in the devices tested. Under normal operating conditions the carbonyl emissions were very low compared with lit cigarettes; however, elevated levels were observed in some of the later puff blocks which is most likely due to drying out of the wicking material.

REFERENCES

1. Lerner, C.A., I.K. Sundar, H. Yao, J. Gerloff, D.J. Ossip, S. McIntosh, R. Robinson, and I. Rahman: Vapors Produced by Electronic Cigarettes and E-Juices with Flavorings Induce Toxicity, Oxidative Stress, and Inflammatory Response in Lung Epithelial Cells and in

- Mouse Lung; PLoS One 10 (2015) 1–26. DOI: 10.1371/journal.pone.0116732.
2. Congress of the United States of America: Family Smoking Prevention and Tobacco Control Act; Public Law 111–131, June 22, 2009. Available at: <http://www.gpo.gov/fdsys/pkg/PLAW-111publ31/pdf/PLAW-111publ31.pdf> (accessed December 18, 2015).
3. United States Food and Drug Administration: Deeming Tobacco Products to Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products; Federal Register, Vol. 79, No. 80, April 25, 2014. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2014-04-25/pdf/2014-09491.pdf> (accessed December 18, 2015).
4. Phillips, C.V.: Debunking the Claim that Abstinence is Usually Healthier for Smokers than Switching to a Low-Risk Alternative, and Other Observations about Anti-Tobacco-Harm-Reduction Arguments; Harm Reduct. J. 6 (2009) 1–10. DOI:10.1186/1477-7517-6-29.
5. European Commission: Directive 2014/40/EU of the European Parliament and of the Council of 3 April 2014 on the Approximation of the Laws, Regulations and Administrative Provisions of the Member States Concerning the Manufacture, Presentation and Sale of Tobacco and Related Products and Repealing Directive 2001/37/EC. Off. J. Eur. Commun. L127/1, 2014. Available at: http://ec.europa.eu/health/tobacco/docs/dir_201440_en.pdf (accessed August 20, 2015).
6. European Commission: Directive 2001/83/EC: Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code Relating to Medicinal Products for Human Use; Off. J. Eur. Commun. L311, 67–128, 2004. Annex to Directive 2001/83/EC: Off. J. Eur. Commun. L-159, 46–94, 2003. Available at: http://www.edctp.org/fileadmin/documents/ethics/DIRECTIVE_200183EC_OF_THE_EUROPEAN_PARLIAMENT.pdf (accessed December 18, 2015).
7. International Organization for Standardization (ISO): International Standard ISO/NP 20714. E-Cigarettes – Determination of Nicotine in Liquids Used in Electronic Nicotine Delivery Devices (E-Liquids); (Under development, Stage 10.99, 2015-05-04) ISO, Geneva, Switzerland, 2015. Available at: http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=68905 (accessed December 18, 2015).
8. Kim, H.J. and H.S. Shin: Determination of Tobacco-Specific Nitrosamines in Replacement Liquids of Electronic Cigarettes by Liquid Chromatography-Tandem Mass Spectrometry; J. Chrom. A 1291 (2013) 48–55. DOI: 10.1016/j.chroma.2013.03.035.
9. Farsalinos, K.E., I.G. Gillman, M.S. Melvin, A.R. Paolantonio, W.J. Gardow, K.E. Humphries, S.E. Brown, K. Poulas, and V. Voudris: Nicotine Levels and Presence of Selected Tobacco-Derived Toxins in Tobacco Flavoured Electronic Cigarette Refill Liquids; Int. J. Environ. Res. Public Health 12 (2015) 3439–3452. DOI:10.3390/ijerph120403439.
10. Cheng, T.: Chemical Evaluation of Electronic Cigarettes; Tob. Control 23 (2014) Suppl. 2 S11–S17. DOI:10.1136/tobaccocontrol-2013-051482.
11. World Health Organization (WHO): Framework Convention on Tobacco Control (FCTC) Electronic Nicotine Delivery Systems; Sixth Session. Moscow, Russian Federation. 13–18 October 2014. Available at: http://apps.who.int/gb/fctc/PDF/cop6/FCTC_COP6_10-en.pdf?ua=1 (accessed December 18, 2015).
12. Goniewicz, M.L., J. Knysak, M. Gawron, L. Kosmider, A. Sobczak, J. Kurek, A. Prokopowicz, M. Jablonska-Czapla, C. Rosik-Dulewska, C. Havel, P. Jacob III, and N. Benowitz: Levels of Selected Carcinogens and Toxicants in Vapor from Electronic Cigarettes; Tob. Control 23 (2014) 133–139. DOI:10.1136/tobaccocontrol-2012-050859.
13. Health Canada: Tobacco Reporting Regulations; Modified November 29, 2007. Available at: <http://www.hc-sc.gc.ca/hc-ps/tobac-tabac/legislation/reg/indust/method/index-eng.php#main> (accessed December 18, 2015).
14. United States Food and Drug Administration: Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke; Request for Comments; Federal Register Vol. 76, No. 156, August 12, 2011. Available at: <http://www.gpo.gov/fdsys/pkg/FR-2011-08-12/pdf/2011-20502.pdf> (accessed December 18, 2015).
15. Al Jasser, M., N. Mebuke, and G. de Gannes: Propylene Glycol: An Often Unrecognized Cause of Allergic Contact Dermatitis in Patients Using Topical Corticosteroids; Skin Therapy Lett. 16 (2011) 5–8. Available at: <http://www.skintherapyletter.com/2011/16.5/2.html> (accessed December 18, 2015).
16. Callahan-Lyon, P.: Electronic Cigarettes: Human Health Effects; Tob. Control 23 (2014) Suppl. 2 S36–S40. DOI:10.1136/tobaccocontrol-2013-051470.
17. Farsalinos, K.E., K.A. Kistler, G. Gillman, and V. Voudris: Evaluation of Electronic Cigarette Liquids and Aerosol for the Presence of Selected Inhalation Toxins; Nicotine Tob. Res. 17 (2015) 168–174. DOI: 10.1093/ntr/ntu176.
18. Etter, J.F., E. Zäther, and S. Svensson: Analysis of Refill Liquids for Electronic Cigarettes; Addiction 108 (2013) 1671–1679. DOI: 10.1111/add.12235.
19. Orr, M.S.: Electronic Cigarettes in the USA: A Summary of Available Toxicology Data and Suggestions for the Future; Tob. Control 23 (2014) Suppl. 2 S18–S22. DOI:10.1136/tobaccocontrol-2013-051474.
20. Farsalinos, K.E., A. Spyrou, K. Tsimopoulou, C. Stefopoulos, G. Romagna, and V. Voudris: Nicotine Absorption from Electronic Cigarette Use: Comparison Between First and New-Generation Devices; Sci. Rep. 4 (2014) 1–7. DOI:10.1038/srep04133.
21. Wieslander, G., D. Norbäck, and T. Lindgren: Experimental Exposure to Propylene Glycol Mist in Aviation Emergency Training: Acute Ocular and Respiratory Effects; Occup. Environ. Med. 58 (2001) 649–655. DOI:10.1136/oem.58.10.649.
22. Laino, T., C. Tuma, A. Curioni, E. Jochnowitz, and S. Stolz: A Revisited Picture of the Mechanism of Glycerol Dehydration; J. Phys. Chem. A 115 (2011)

- 3592–3595. DOI: 10.1021/jp201078e.
23. Laino, T., C. Tuma, P. Moor, E. Martin, S. Stolz, and A. Curioni: Mechanisms of Propylene Glycol and Triacetin Pyrolysis; *J. Phys. Chem. A* 116 (2012) 4602–4609. DOI: 10.1021/jp300997d.
 24. Kosmider, L., A. Sobczak, M. Fik, J. Knysak, M. Zaciera, J. Kurek, and M. Goniewicz: Carbonyl Compounds in Electronic Cigarette Vapors: Effects of Nicotine Solvent and Battery Output Voltage; *Nicotine Tob. Res.* 16 (2014) 1319–1326. DOI:10.1093/ntr/ntu078.
 25. Jensen, R.P., L. Wentai, J.F. Pankow, R.M. Strongin, and D.H. Peyton: Hidden Formaldehyde in E-Cigarette Aerosols; *N. Engl. J. Med.* 372 (2015) 392–394. DOI: 10.1056/NEJMc1413069
 26. Farsalinos, K.E., V. Voudris, and K. Poulas: E-Cigarettes Generate High Levels of Aldehydes Only in ‘Dry Puff’ Conditions; *Addiction* 10 (2015) 1352–1356. DOI:10.1111/add.12942.
 27. Williams, M., A. Villarreal, K. Bozhilov, S. Lin, and P. Talbot: Metal and Silicate Particles Including Nanoparticles are Present in Electronic Cigarette Cartomizer Fluid and Aerosol; *PLoS One* 8 (2013). DOI:10.1371/journal.pone.0057987.
 28. Farsalinos, K.E., V. Voudris, and K. Poulas: Are Metals Emitted from Electronic Cigarettes a Reason for Health Concern? A Risk-Assessment Analysis of Currently Available Literature; *Int. J. Environ. Res. Public Health* 12 (2015) 5215–5232. DOI:10.3390/ijerph120505215.
 29. Westenberger, B.J.: Evaluation of E-Cigarettes; U.S. Food and Drug Administration. Washington DC. 2009. Available at: <http://www.fda.gov/downloads/drugs/scienceresearch/ucm173250.pdf> (accessed December 18, 2015).
 30. Stepanov, I., S.G. Carmella, S. Han, A. Pinto, A.A. Strasser, C. Lerman, and S.S. Hecht: Evidence for Endogenous Formation of *N*’-Nitrosornicotine in Some Long-Term Nicotine Patch Users; *Nicotine Tob. Res.* 11 (2009) 99–105. DOI:10.1093/ntr/ntn004.
 31. CORESTA Task Force E-cigarettes: CORESTA Recommended Method No. 81: Routine Analytical Machine for E-Cigarette Aerosol Generation and Collection – Definitions and Standard Conditions; June 2015, Cooperation Centre for Scientific Research Relative to Tobacco, Paris, France. Available at: http://www.coresta.org/Recommended_Methods/CRM_81.pdf (accessed December 18, 2015).
 32. International Organization for Standardization (ISO): ISO 3308:2012 Routine Analytical Cigarette-Smoking Machine – Definitions and Standard Conditions; ISO, Geneva, Switzerland, 2012. Available at: http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=60404 (accessed December 18, 2015)
 33. Health Canada: Health Canada Tobacco Reporting Regulations, Official Method T-115: Determination of "Tar", Nicotine and Carbon Dioxide in Mainstream Tobacco Smoke; Health Canada, Ottawa, Canada, 1999. Available at: <http://www.hc-sc.gc.ca/hc-ps/pubs/tobac-tabac/rc/index-eng.php> (accessed December 18, 2015).
 34. International Organization for Standardization (ISO): ISO 4387:2000. Determination of Total and Nicotine-Free Dry Particulate Matter using a Routine Analytical Cigarette Smoking Machine Determination of Total Particulate Matter and Preparation for Water and Nicotine Measurements; ISO, Geneva, Switzerland, 2000. Available at: http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=28323 (accessed December 18, 2015)
 35. CORESTA Smoke Science Study Group: CORESTA Recommended Method No. 74: Determination of Selected Carbonyls in Mainstream Smoke by HPLC; July 2014, Cooperation Centre for Scientific Research Relative to Tobacco, Paris, France. Available at: [http://www.coresta.org/Recommended_Methods/CRM_74-update\(July14\).pdf](http://www.coresta.org/Recommended_Methods/CRM_74-update(July14).pdf) (accessed August 21, 2015)
 36. United Kingdom Health and Safety Executive: EH40/2005 Workplace Exposure Limits; Second edition 2011. Available at: <http://www.hse.gov.uk/pUbns/priced/eh40.pdf> (accessed August 21, 2015). ISBN 978 0 7176 6446 7.

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