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E-cigarettes generate high levels of aldehydes only in 'dry puff' conditions

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ABSTRACT

Background and aims Aldehydes are emitted by electronic cigarettes due to thermal decomposition of liquid components. Although elevated levels have been reported with new-generation high-power devices, it is unclear whether they are relevant to true exposure of users (vapers) because overheating produces an unpleasant taste, called a dry puff, which vapers learn to avoid. The aim was to evaluate aldehyde emissions at different power levels associated with normal and dry puff conditions. **Design** Two customizable atomizers were prepared so that one (A1) had a double wick, resulting in high liquid supply and lower chance of overheating at high power levels, while the other (A2) was a conventional setup (single wick). Experienced vapers took 4-s puffs at 6.5 watts (W), 7.5 W, 9 W and 10 W power levels with both atomizers and were asked to report whether dry puffs were generated. The atomizers were then attached to a smoking machine and aerosol was trapped. **Setting** Clinic office and analytical chemistry laboratory in Greece. **Participants** Seven experienced vapers. **Measurements** Aldehyde levels were measured in the aerosol. **Findings** All vapers identified dry puff conditions at 9 W and 10 W with A2. A1 did not lead to dry puffs at any power level. Minimal amounts of aldehydes per 10 puffs were found at all power levels with A1 (up to 11.3 µg for formaldehyde, 4.5 µg for acetaldehyde and 1.0 µg for acrolein) and at 6.5 W and 7.5 W with A2 (up to 3.7 µg for formaldehyde, 0.8 µg for acetaldehyde and 1.3 µg for acrolein). The levels were increased by 30 to 250 times in dry puff conditions (up to 344.6 µg for formaldehyde, 206.3 µg for acetaldehyde and 210.4 µg for acrolein, $P < 0.001$), while acetone was detected only in dry puff conditions (up to 22.5 µg). **Conclusions** Electronic cigarettes produce high levels of aldehyde only in dry puff conditions, in which the liquid overheats, causing a strong unpleasant taste that e-cigarette users detect and avoid. Under normal vaping conditions aldehyde emissions are minimal, even in new-generation high-power e-cigarettes.

Keywords Acetaldehyde, acetone, acrolein, aerosol, aldehydes, dry puff, Electronic cigarette, formaldehyde.

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INTRODUCTION

One of the main concerns related to electronic cigarette (EC) use is the exposure to aldehydes emitted to the aerosol. Aldehydes are formed due to the heating and oxidation of the main EC liquid components, glycerol and propylene glycol [1]. Studies evaluating first-generation (cigarette-like) devices found that formaldehyde, acetaldehyde and acrolein are released to the aerosol at levels by far lower compared to tobacco cigarette smoke [2,3]. However, more recent studies examining aerosol generated from new-generation devices at high power levels found that the levels of aldehydes could approach or even exceed the levels found in cigarette smoke [4,5]. These studies generated a great deal of publicity, along with concerns that EC use at high power levels is associated with significant exposure to toxic chemicals which may have adverse health effects. This can have important implications, as a substantial proportion of vapers are using new-generation devices [6] which characteristically have the ability to generate high power levels.

ECs have a unique mode of function which is significantly different from tobacco cigarettes. Unlike tobacco cigarettes, which are burned continuously at similar temperatures during the whole time of use, ECs undergo repeated thermal cycles of heating and cooling. The resistance and wick are impregnated with liquid, so the energy delivered when the EC device is activated is used to raise the liquid temperature to the point of evaporation. After completing the puff, no energy is delivered to the resistance and wick, so the temperature is progressively decreasing; at the same time, liquid is re-supplied to the wick encircled by the resistance, further decreasing its temperature. When there is insufficient supply of liquid to the wick, it is possible that high temperatures are generated. However, liquid overheating results in the development of a strong unpleasant taste that the users (vapers) detect and avoid by reducing power levels and puff duration or by increasing interpuff interval. This phenomenon has been described previously, and was named 'dry puff phenomenon' [7]. It actually represents a natural defence mechanism against exposure to overheated liquid emissions. The dry puff phenomenon is dependent upon power levels; however, the difference between atomizers' design and characteristics means that each atomizer can be used at different power levels before generating dry puffs. Thus, there is no specific power level at which the dry puff phenomenon is generated with all available atomizers. Because there is no method of detecting dry puffs other than the taste, it is possible that some of the findings from laboratory studies do not translate into the risk of e-cigarette use by humans. In fact, two clinical studies evaluating aldehydes exposure to EC users found that the levels were lower than in smokers [8,9]. Lower concentrations of acrolein metabolites were also observed in dual users of tobacco cigarettes and ECs than in cigarette smokers [9]. Moreover, the conclusion from previous studies that power levels alone are responsible for generation of very high levels of aldehydes may be misleading.

The purpose of the study was to examine the amount of aldehyde emissions at different power levels associated with both normal and dry puff conditions.

MATERIALS AND METHODS

Two customizable atomizers (Kayfun Lite plus; SMtec GmbH, Everswinkel, Germany) with different setups were prepared. In one of them (A1) we used a double 3 mm-thickness wick made of silica, which was expected to result in a high liquid supply rate to the wick and resistance head. This would prevent liquid overheating and generation of the dry puff taste at high power levels. The second atomizer (A2) was prepared with a single 3 mm-thickness wick made of silica, which was expected to have lower liquid supply rate to the wick and resistance head compared to A1 and, thus, would be more prone to development of the dry puff phenomenon at high power levels. A2 represents a setup used commonly in commercial atomizers, and was similar to the setup used in atomizers of previous studies [4,5]. The airflow rate and the amount of liquid were similar in both atomizers.

The atomizers were filled with EC liquid composed of 45% glycerol, 45% propylene glycol, 8% water and 2% nicotine (20 mg/ml nicotine concentration). The choice was based on a study by Kosmider *et al.* [4], which showed that this liquid generated the highest levels of aldehydes in the aerosol compared to propylene glycol-based or glycerol-based liquids. Seven vapers were recruited through an online forum. The reason for recruiting seven vapers was to assess the interindividual differences in detecting dry puffs. They were invited to the clinic and took four puffs of 4 s duration and 30 s interpuff interval with both atomizers, using a variable-wattage EC battery device (Hana Modz DNA 40; Hana Modz, Woodridge, Illinois, USA), at four power levels: 6.5 Watts (W), 7.5 W, 9 W and 10 W. Vapers were blinded to the setup of each atomizer. The puff durations were chosen to match the conditions used by Jensen *et al.* [5]. The reason for asking participants to take four puffs is that measurements of evaporation temperature (anecdotal) have shown that the first puff has a lower temperature level because the atomizer is initially at room temperature. The 30-s interpuff interval is not enough to bring the atomizer temperature down to environmental level, so the temperatures at the initiation and the end of the second puff are higher. Therefore, it is likely that the dry puff taste is not detected on the first puff but could be detected on subsequent puffs. Vapers were asked to report if dry puff conditions were generated. The dry puff phenomenon is detected easily and avoided by vapers; all participating vapers verified that they had experienced and were able to detect dry puffs.

The protocol was approved by the ethics committee of our institution and written informed consent was provided by every vaper before participating to the study.

CHEMICAL ANALYSIS

The EC device and atomizers were attached to a smoking machine. The aerosol from 60 puffs was collected in two impingers (connected in series) containing a solution of 2,4-dinitrophenylhydrazine (2,4-DNPH) and acetonitrile. Three samples per atomizer and power level were examined. The DNPH derivatives of formaldehyde, acetaldehyde acrolein and acetone were measured by high-performance liquid chromatography, with a previously validated protocol [10]. Blank air samples were collected simultaneously in different impingers to measure environmental levels of aldehydes. Environmental levels were subtracted from the levels found in the aerosol. The levels of aldehyde in the aerosol were reported per 10 puffs and were compared with the levels found in tobacco cigarette smoke generated under Health Canada Intense puffing regime (2-s puffs, 30-s interpuff interval), as reported by Counts *et al.* [11]. The limits of detection (LOD) with the method used were 0.25 μg/10 puffs for formaldehyde, 0.75 μg/10 puffs for acetaldehyde, 0.92 μg/10 puffs for acetone and 0.17 μg/10 puffs for acrolein.

STATISTICAL ANALYSIS

Values are reported as mean [standard deviation (SD)]. Differences in aldehyde levels were evaluated by using repeated measures analysis of variance (ANOVA), with four power levels as within-subject and two atomizers as between-subject factors for each compound. Comparison with tobacco cigarettes were performed by one-way ANOVA, comparing levels at 9 W and 10 W only, as the emissions from ECs at lower power levels were minimal. When chemicals were below the LOD, a value of LOD/2 was assigned for statistical comparisons. A *P*-value of 0.05 was considered statistically significant, and the analysis was performed by using commercially available software (SPSS version 22; SPSS Inc., Chicago, IL, USA).

RESULTS

All vapers reported that the unpleasant taste of the dry puff phenomenon was detected at 9 W and 10 W with A2, while A1 could be used at all power levels without generating the dry puff taste.

The results of the aldehyde measurements, reported per 10 puffs, are shown in Table 1. Significant differences were observed between different power levels for formaldehyde ($F = 107.9$, $P < 0.001$), acetaldehyde ($F = 106.8$, $P < 0.001$), acetone ($F = 24.5$, $P < 0.001$) and acrolein ($F = 55.2$, $P < 0.001$). Moreover, significant power × atomizer interactions were observed for formaldehyde ($F = 101.7$, $P < 0.001$), acetaldehyde ($F = 98.4$, $P < 0.001$), acetone ($F = 24.5$, $P < 0.001$) and acrolein ($F = 54.3$, $P < 0.001$). Minimal levels of aldehydes were found at all power levels with A1 and at 6.5 W and 7.5 W with A2. These levels were significantly lower compared to smoking [10]. In dry puff conditions (9 W and 10 W with A2), emissions were raised by 30–250 times for formaldehyde, acetaldehyde and acrolein. Acetone was detected only in the aerosol generated by A2 at power levels associated with dry puff conditions. At 9 W, atomizer A2 emitted higher levels of formaldehyde ($P = 0.005$) but lower levels of acetaldehyde, acetone and acrolein ($P < 0.001$) compared to tobacco cigarette smoke. At 10 W, A2 emitted higher levels of formaldehyde and acrolein ($P < 0.001$), but still lower levels of acetone and acrolein ($P < 0.001$) compared to tobacco cigarette smoke.

DISCUSSION

This is the first study, to our knowledge, that quantified aldehyde release to the aerosol of ECs at different power

Table 1 Aldehyde levels in e-cigarette aerosol under normal and 'dry puff' conditions. Levels approached or exceeded those in tobacco cigarette smoke only under dry puff conditions, which are detected and avoided by the consumers.

	Formaldehyde (μg/10 puffs) n = 3	*Acetaldehyde (μg/10 puffs) n = 3*	*Acetone (μg/10 puffs) n = 3*	*Acrolein (μg/10 puffs) n = 3*
6.5 watts				
Atomizer 1	6.5 (1.7)	ND	ND	ND
Atomizer 2	3.7 (1.6)	0.8 (0.4)	ND	0.2 (0.1)
P-value[a]	NS	NS	NS	NS
7.5 watts				
Atomizer 1	6.1 (1.3)	ND	ND	ND
Atomizer 2	ND	0.8 (0.5)	ND	1.3 (0.8)
P-value[a]	0.001	NS	NS	0.045
9 watts				
Atomizer 1	9.5 (2.3)	3.5 (0.9)	ND	0.8 (0.6)
Atomizer 2[b]	119.2 (15.9)	58.9 (12.8)	4.6 (1.0)	48.4 (10.0)
P-value[a]	< 0.001	0.002	0.002	0.001
10 watts				
Atomizer 1	11.3 (2.6)	4.5 (1.2)	ND	1.0 (0.6)
Atomizer 2[b]	344.6 (56.0)	206.3 (33.3)	22.5 (7.1)	210.4 (48.8)
P-value[a]	0.001	< 0.001	0.006	0.002
	Formaldehyde (μg/cigarette) n = 50	*Acetaldehyde (μg/ cigarette) n = 50*	*Acetone (μg/ cigarette) n = 50*	*Acrolein (μg/ cigarette) n = 50*
Tobacco cigarette[c]	74.0 (23.7)	1240.3 (147.7)	641.9 (71.2)	120.4 (14.7)
P-value (9 W)[d]	< 0.001	< 0.001	< 0.001	< 0.001
P-value (10 W)[e]	< 0.001	< 0.001	< 0.001	< 0.001

[a]Repeated-measures analysis of variance (ANOVA). [b]Dry puff conditions, as detected by seven electronic cigarette users. [c]Data from Counts *et al*. (Health Canada Intense puffing regime) [10]. [d]One-way ANOVA, comparing data tobacco cigarettes with values from 9-W power setup. [e]One-way ANOVA, comparing data tobacco cigarettes with values from 9-W power setup. ND = not determined; NS = not significant.

levels which were characterized as normal and dry puff conditions by experienced vapers. Our results verify previous observations that it is possible for ECs to generate high levels of aldehydes; however, this is observed only under dry puff conditions. In contrast, minimal amounts of aldehydes were released to the aerosol at normal vaping conditions, even when high power levels were used. At those conditions, aldehyde emissions were far lower than tobacco cigarette smoke [10]. Aldehyde release was associated with the efficiency of the atomizer design to accommodate the high power levels through effective liquid supply to the wick. Thus, even at higher power settings, vapers are not expected to be exposed to significant levels of toxic aldehydes during normal EC use.

The issue of overheating and dry puff conditions has been neglected in most laboratory studies evaluating EC aerosol emissions. Heat is needed to generate aerosol from ECs, and new-generation devices have the ability to deliver elevated power levels, resulting in a high amount of energy applied to the atomizers. This energy, which depends upon power and time of activation (puff duration), is used to elevate the temperature of the liquid so that it evaporates. Under ideal conditions, the temperature should be raised to the point of evaporation of the liquid ingredients. However, if the amount of liquid in the wick is not enough, the excess energy is transformed into heat and the temperature can be increased significantly beyond the evaporation point. Schripp *et al*. used an infrared camera and found that temperatures can easily exceed 300°C when there is no liquid in the atomizer [12]. New-generation devices can be used to deliver high power levels and are very popular among dedicated vapers [6,13], but they are combined with appropriate atomizers which are designed to have a very efficient liquid supply to the wick. Thus, there is no absolute power level at which overheating conditions are generated with all available equipment; each atomizer has a different capacity to withstand high power levels. Unfortunately, there is no objective way to determine the dry puff conditions, raising the possibility that in laboratory studies aerosol is generated in conditions irrelevant to realistic use and exposure of vapers. In previous studies, we had to ask vapers to determine whether the laboratory conditions could generate dry puff conditions [14,15], and the puff duration was adjusted in one of them to avoid dry puffs [15]. In another study, we were forced to change the atomizer we originally selected due to complaints by participants that dry puffs were generated [7]. Herein, we have shown that determining the dry puff phenomenon is important in EC research, as it is associated with distinctively high levels of aldehyde release. Such levels were not observed under normal vaping conditions.

Dry puffs are experienced by vapers infrequently and in specific situations. Most usually, they are associated with very low levels of liquid. New-generation atomizers have a clear window (plastic or glass), which gives vapers the ability to see the levels of liquid in the atomizer. Thus, such cases of dry puffs are uncommon. Other reasons for dry puffs include decaying coil and use of new equipment. When vapers are unacquainted with the new equipment (e.g. a new atomizer), it is possible that they may experience a dry puff during experimentation to find their preferable power levels and puff duration patterns. All cases combined, vapers are exposed to dry puff conditions on rare occasions (usually less than once daily); thus, it is not expected that exposure to high levels of aldehydes during dry puffs will have any long-term health effects.

It should be emphasized that heat generation is associated with the energy delivered to the atomizer. The energy unit is Joule (J), which is defined as power (W) multiplied by time (s). W is defined as voltage $(V)^2$ divided by resistance. Several studies on ECs report V rather than W levels [4,5]. This should be avoided because the energy (and thus heat generation) is related inversely to the resistance value of the atomizer. When using similar V levels to atomizers of different resistance values, there are large discrepancies in power and energy as well as heat generation. Therefore, in order to be able to compare different use conditions and equipment characteristics, it is appropriate to report power levels (W) and time of applying the power.

The levels of aldehyde emissions found herein were very low, but do not necessarily represent zero risk. A recent review concluded that a formaldehyde indoor air limit of 0.1 parts per million (p.p.m.) ($125\ \mu g/m^3$) should protect even particularly susceptible individuals from both irritation effects and any potential cancer hazard [16]. Considering a $20\ m^3$ average daily inhalation volume, that would represent approximately $2500\ \mu g$ total daily exposure, which is equivalent to taking > 2500 puffs per day. Thus, the findings from this study indicate that the risk associated with exposure to formaldehyde from ECs is minimal to non-existent. The World Health Organization has set an acceptable formaldehyde concentration in air of normal indoor conditions of 80 parts per billion (p.p.b.) ($100\ \mu g/ml$) [17], which results in a daily total exposure equivalent to > 2000 puffs. For other aldehydes, the safety limits are unclear and differ between organizations. Therefore, there may be a theoretical residual risk associated with exposure to aldehydes at the levels found in ECs aerosol; however, this risk is minute compared to smoking.

A limitation of this study is the evaluation of a single atomizer and a liquid with specific composition. Our results should be verified by further studies evaluating different atomizers, which will obviously generate dry puff conditions at different power levels. Herein, we have shown that even the same atomizer has different characteristics depending on the setup of the wick. Liquids of different composition should also be examined. A previous study has shown that aldehydes release was highest in a propylene glycol–glycerol mixture (similar to the liquid tested herein) [4], therefore it is possible to further reduce exposure to aldehydes by modifying the composition of the EC liquid. Finally, further studies are needed to quantify accurately the dry puff phenomenon in terms of aldehydes release, and to evaluate the interindividual differences in detecting the dry puffs. Herein, all vapers were able to identify dry puffs at the same puffing conditions.

CONCLUSION

Aldehyde emissions in EC aerosol are associated directly with dry puff conditions. In normal vaping conditions, the levels of aldehydes emissions are minimal and by far lower than the levels in tobacco cigarette smoke, despite the use of high power levels. In dry puff conditions, aldehyde emissions are significantly elevated to very high levels, but vapers are not expected to be exposed to such levels during normal EC use, even when they use new-generation high-power devices.

Declaration of interests

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References

1. Uchiyama S., Ohta K., Inaba Y., Kunugita N. Determination of carbonyl compounds generated from the E-cigarette using coupled silica cartridges impregnated with hydroquinone and 2,4-dinitrophenylhydrazine, followed by high-performance liquid chromatography. *Anal Sci* 2013; **29**: 1219–22.
2. Bekki K., Uchiyama S., Ohta K., Inaba Y., Nakagome H., Kunugita N. Carbonyl compounds generated from electronic cigarettes. *Int J Environ Res Public Health* 2014; **11**: 11192–200.
3. Goniewicz M. L., Knysak J., Gawron M., Kosmider L., Sobczak A., Kurek J. *et al.* Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tob Control* 2014; **23**: 133–9.
4. Kosmider L., Sobczak A., Fik M., Knysak J., Zaciera M., Kurek J. *et al.* Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine Tob Res* 2014; **16**: 1319–26.
5. Jensen R. P., Luo W., Pankow J. F., Strongin R. M., Peyton D. H. Hidden formaldehyde in e-cigarette aerosols. *N Engl J Med* 2015; **372**: 392–4.
6. Farsalinos K. E., Romagna G., Tsiapras D., Kyrzopoulos S., Voudris V. Characteristics, perceived side effects and benefits of electronic cigarette use: a worldwide survey of more than 19,000 consumers. *Int J Environ Res Public Health* 2014; **11**: 4356–73.
7. Farsalinos K. E., Romagna G., Tsiapras D., Kyrzopoulos S., Voudris V. Evaluation of electronic cigarette use (vaping) topography and estimation of liquid consumption: implications for research protocol standards definition and for public health authorities' regulation. *Int J Environ Res Public Health* 2013; **10**: 2500–14.
8. Hecht S. S., Carmella S. G., Kotandeniya D., Pillsbury M. E., Chen M., Ransom B. W. *et al.* Evaluation of toxicant and carcinogen metabolites in the urine of e-cigarette users versus cigarette smokers. *Nicotine Tob Res* 2014 Oct 21 (online first). doi: 10.1093/ntr/ntu218
9. McRobbie H., Goniewicz M., Phillips A., Myers-Smith K., West O., Hajek P. Effects of the use of electronic cigarettes with and without concurrent smoking on acrolein delivery. Society for Research on Nicotine and Tobacco, 20th Annual Meeting, Seattle, Washington; 2014. Available at: https://srnt.org/conferences/2014/pdf/SRNT_2014_Rapids_C.pdf (accessed 25 April 2015).
10. Cooperation Centre for Scientific Research Relative to Tobacco. CORESTA Recommended Method no. 75: Determination of Selected Carbonyls in Mainstream Cigarette Smoke by HPLC; 2013. Available at: http://www.coresta.org/Recommended_Methods/CRM_75.pdf (accessed 19 February 2014).
11. Counts M. E., Morton M. J., Laffoon S. W., Cox R. H., Lipowicz P. J. Smoke composition and predicting relationships for international commercial cigarettes smoked with three machine-smoking conditions. *Regul Toxicol Pharmacol* 2005; **41**: 185–227.
12. Schripp T., Markewitz D., Uhde E., Salthammer T. Does e-cigarette consumption cause passive vaping? *Indoor Air* 2013; **23**: 25–31.
13. Farsalinos K. E., Romagna G., Tsiapras D., Kyrzopoulos S., Spyrou A., Voudris V. Impact of flavour variability on electronic cigarette use experience: an internet survey. *Int J Environ Res Public Health* 2013; **10**: 7272–82.
14. Romagna G., Allifranchini E., Bocchietto E., Todeschi S., Esposito M., Farsalinos K. E. Cytotoxicity evaluation of electronic cigarette vapor extract on cultured mammalian fibroblasts (ClearStream-LIFE): comparison with tobacco cigarette smoke extract. *Inhal Toxicol* 2013; **25**: 354–61.
15. Farsalinos K. E., Romagna G., Allifranchini E., Ripamonti E., Bocchietto E., Todeschi S. *et al.* Comparison of the cytotoxic potential of cigarette smoke and electronic cigarette vapour extract on cultured myocardial cells. *Int J Environ Res Public Health* 2013; **10**: 5146–62.
16. Golden R. Identifying an indoor air exposure limit for formaldehyde considering both irritation and cancer hazards. *Crit Rev Toxicol* 2011; **41**: 672–721.
17. Salthammer T., Mentese S., Marutzky R. Formaldehyde in the indoor environment. *Chem Rev* 2010; **110**: 2536–72.