

Cherry-flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde

Abstract Many non-cigarette tobacco products, including e-cigarettes, contain various flavourings, such as fruit flavours. Although many flavourings used in e-cigarettes are generally recognised as safe when used in food products, concerns have been raised about the potential inhalation toxicity of these chemicals. Benzaldehyde, which is a key ingredient in natural fruit flavours, has been shown to cause irritation of respiratory airways in animal and occupational exposure studies. Given the potential inhalation toxicity of this compound, we measured benzaldehyde in aerosol generated in a laboratory setting from flavoured e-cigarettes purchased online and detected benzaldehyde in 108 out of 145 products. The highest levels of benzaldehyde were detected in cherry-flavoured products. The benzaldehyde doses inhaled with 30 puffs from flavoured e-cigarettes were often higher than doses inhaled from a conventional cigarette. Levels in cherry-flavoured products were >1000 times lower than doses inhaled in the workplace. While e-cigarettes seem to be a promising harm reduction tool for smokers, findings indicate that using these products could result in repeated inhalation of benzaldehyde, with long-term users risking regular exposure to the substance. Given the uncertainty surrounding adverse health effects stemming from long-term inhalation of flavouring ingredients such as benzaldehyde, clinicians need to be aware of this emerging risk and ask their patients about use of flavoured e-cigarettes.

Current estimates show that 12.6% of US adults report ever use of electronic cigarettes (e-cigarettes), a number that continues to rise.¹ Recent studies confirm that e-cigarettes presumably pose lower health risks to the user due to the disparity in toxic compounds found in e-cigarettes relative to tobacco cigarettes.² While the 2009 Family Smoking Prevention and Tobacco Control Act gave rise to a US ban on added, non-menthol flavourings in cigarettes,³ currently, non-cigarette tobacco products, including e-cigarettes, are permitted to have added flavourings (eg, candy, fruit). Although many flavourings used in e-cigarettes are generally recognised as safe when used in food products, concerns have been raised about the potential inhalation toxicity of these chemicals.⁴ The potential effects flavour

compounds may have on the respiratory health of e-cigarette users are unclear. A recent report by Barrington-Trimis *et al*⁴ outlined the need for research on flavour additives used in e-cigarettes, noting the lack of safety data on long-term health effects from inhaling flavouring chemicals.

One such flavouring compound, benzaldehyde, is an aromatic aldehyde used in food and cosmetics.⁵ Although data suggest little to no toxicity from oral and dermal exposure to benzaldehyde, occupational exposure has been linked to irritation of the eyes and mucous membranes of the respiratory passages.⁵ Given the potential inhalation toxicity of benzaldehyde to e-cigarette users, we examined benzaldehyde levels generated from flavoured e-cigarettes. We hypothesised that aerosol generated from flavoured e-cigarettes would contain significant amounts of benzaldehyde.

METHODS

We measured benzaldehyde in aerosol generated from an e-cigarette refilled with 145 flavoured nicotine-containing solutions purchased from international online retailers. The solutions were classified into eight flavour groups according to labelled characteristics: berry/tropical fruit (n=40), tobacco (n=37), alcohol related/drink (n=15), chocolate/sweet flavour (n=11), coffee/tea (n=11), mint/menthol (n=10), cherry (n=10), and other, non-identifiable flavour varieties (eg, 'Indian Summer', 'Cosmopolitan') (n=11). A refillable eGo e-cigarette (heater resistance 2.4 ohm, battery 900 mAh, 3.4 V) was used for testing. Aerosol was generated using an automatic smoking simulator following protocols used in previous studies (inhalation time 1.8 s, puff volume 70 mL, interval between puffs 17 s).⁶ For each experiment, 30 puffs were taken from each e-cigarette in two series of 15 puffs, with a 5 min interval between series. Benzaldehyde from aerosol was trapped on sorbent tubes, extracted and analysed using a high-performance liquid chromatography method as recommended by the US Environmental Protection Agency.⁷ The lower limit of quantitation (LLOQ) was 0.025 µg/30 puffs. A Kruskal–Wallis test was performed to assess differences in the distributions of benzaldehyde levels according to flavour grouping. For each product tested, we calculated a daily inhaled dose of benzaldehyde, assuming that an experienced e-cigarette user puffs on an e-cigarette 163 times a day.⁸ We compared the inhaled dose using 30 puffs from a flavoured e-cigarette with an inhaled dose

from a single tobacco cigarette (0.5–4.5 µg/cigarette).⁹ We also compared the inhaled dose from flavoured e-cigarettes with a hypothetical dose inhaled by healthy workers who would be exposed during an 8 h work shift to the permissible exposure limit (PEL) of benzaldehyde as defined by the US Workplace Environmental Exposure Level Guides¹⁰ (90.5 mg=inhalation rate 1.3 4 m³/h×8 h×8.7 mg/m³ PEL).

RESULTS

Benzaldehyde was detected in 108 out of 145 examined products (levels above LLOQ). The highest yields of benzaldehyde were observed in cherry-flavoured products (5.129–141.2 µg/30 puffs). Benzaldehyde yields in aerosol generated from cherry-flavoured nicotine solutions were significantly higher than in other products ($\chi^2(7)=43.70$, $p<0.0001$; Kruskal–Wallis test). Benzaldehyde yields in non-cherry-flavoured products were within the range of 0.025–10.27 µg/30 puffs (table 1). The benzaldehyde doses inhaled using 30 puffs from flavoured e-cigarettes were often higher than doses inhaled from a conventional cigarette. The estimated median daily inhaled dose of benzaldehyde from cherry-flavoured e-cigarettes was 70.3 µg, which would be >1000 times lower than the PEL dose for benzaldehyde concentrations in the workplace (figure 1).

DISCUSSION

By examining benzaldehyde levels in aerosols generated from a wide range of flavoured nicotine solutions, our study demonstrated that elevated levels of benzaldehyde exist in cherry-flavoured products. Users of cherry-flavoured products may inhale significantly higher doses of benzaldehyde compared with users of other flavoured products. Although this study has several limitations, including an arbitrarily selected testing protocol that may not reflect actual product use, this study points out a potential risk associated with using flavoured e-cigarettes.

As e-cigarette popularity increases, respiratory clinicians need to be aware of potential risks that may result from use. Although e-cigarettes may be a promising harm reduction tool for smokers, findings indicate that using these products could result in repeated inhalation of benzaldehyde, with long-term users risking regular exposure to the substance. Given the uncertainty surrounding adverse health effects stemming from long-term inhalation of flavouring ingredients such as benzaldehyde, patients should be asked

Table 1 Yields of benzaldehyde in aerosol generated from flavoured e-cigarettes (n=145)

Flavour	Number of tested products	Proportion of products with positive benzaldehyde (>greater than limit of quantitation) (%)	Median benzaldehyde yield ($\mu\text{g}/30$ puffs)	Range of benzaldehyde yields ($\mu\text{g}/30$ puffs)
Fruit (other than cherry)	40	62.5	0.050	BLQ—2.041
Tobacco	37	78.4	0.219	BLQ—2.093
Alcohol related or drink	15	73.3	0.118	BLQ—4.499
Coffee or tea	11	81.8	0.143	BLQ—3.010
Chocolate or sweet flavour	11	90.9	0.130	BLQ—5.327
Mint or menthol	10	40.0	0.025	BLQ—0.237
Cherry	10	100	12.93	5.129—141.2
Other	11	90.9	0.321	BLQ—10.27

BLQ, below limit of quantitation (0.025 $\mu\text{g}/30$ puffs).

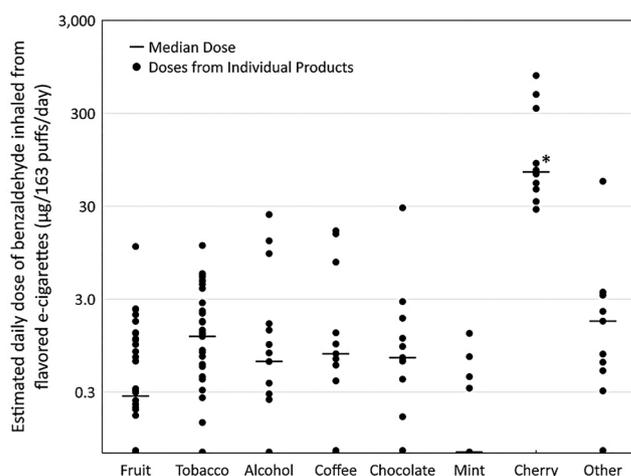


Figure 1 Estimated daily doses of benzaldehyde resulting from inhaling flavoured e-cigarette aerosol (163 puffs per day¹⁰) (n=145).

about use of flavoured products, particularly patients with respiratory diseases.

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Competing interests LK, AS, AP, JK and MZ are employees of the Institute of Occupational Medicine and Environmental Health. One of the institute's objectives is outsourcing for the industrial sector, including manufacturers of e-cigarettes. However, this has no influence on studies design, conducting studies, manuscript preparation, statistical analysis or other relevant scientific work conducted in the Institute of Occupational Medicine and Environmental Health. AS accepted personal fees from the eSmoking Institute in Poznan, Poland, and non-financial support from Chic Group LTD, a manufacturer of electronic cigarettes in Poland, outside of the submitted work. In 2011, MLG received the Global Research Award for Nicotine Dependence funded by Pfizer, a manufacturer of stop smoking medications.

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PRESS RELEASE

THORAX

Cherry flavoured e-cigs may deliver higher levels of benzaldehyde than other flavours

Doses of this respiratory irritant often higher than those derived from conventional cigarettes

[Research letter: Cherry flavoured electronic cigarettes expose users to the inhalation irritant, benzaldehyde. doi 10.1136/thoraxjnl-2015-207895]

Cherry flavoured e-cigarettes may expose vapers to significantly higher levels of the respiratory irritant benzaldehyde than other flavours, suggests a laboratory study published online in ***Thorax***.

The doses inhaled with 30 puffs were often higher than those breathed in from a conventional cigarette, the findings show.

Many e-cigarettes contain flavourings, most of which are recognised as safe when used in food products, but concerns have been raised about their potential harm when inhaled, particularly over the long term.

Benzaldehyde is routinely used in foodstuffs and cosmetics, and is a key ingredient in 'natural' fruit flavourings. But it has been shown to irritate the airways in animal and workplace exposure studies.

The researchers therefore wanted to quantify the levels of benzaldehyde that a vaper might breathe in from fruit flavoured e-cigarettes, purchased online.

The 145 e-cigarettes were grouped according to their labelling: berry/tropical fruit (40); tobacco (37); alcohol (15); chocolate/sweet (11); coffee/tea (11); mint/menthol (10); cherry (10); and 'other' (11).

Aerosol vapour was generated using an automatic smoking simulator, with 30 puffs taken from each e-cigarette in two series of 15 puffs with a 5 minute interval in between, and the quantities of benzaldehyde measured.

The researchers calculated a daily inhaled dose of benzaldehyde for each product, assuming that an experienced vaper puffs on an e-cigarette 163 times a day

The inhaled dose from 30 puffs was compared with that from a conventional cigarette and with a hypothetical maximum permissible dose that healthy workers might be exposed to over the course of an 8 hour shift.

Benzaldehyde was detected in 108 out of 145 e-cigarettes (74%), with the highest levels detected in the cherry flavoured products. Yields of the chemical were around 43 times higher than in these products.

The doses of benzaldehyde inhaled from 30 puffs from flavoured e-cigarettes were often higher than those inhaled from a conventional cigarette.

The estimated daily inhaled dose from cherry flavoured e-cigarettes was 70.3 ug, which is more than 1000 times lower than the maximum permissible workplace exposure level.

The researchers emphasise that their study used a simulator, so may not reflect actual inhalation during vaping, but suggest that it still points to a potential risk associated with cherry flavoured e-cigarettes.

“Users of cherry flavoured products may inhale significantly higher doses of benzaldehyde compared with users of other flavoured products,” they write.

“Although e-cigarettes may be a promising harm reduction tool for smokers, the findings indicate that using these products could result in repeated inhalation of benzaldehyde, with long term users risking regular exposure to the substance,” they add.

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