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Levels of selected carcinogens and toxicants in vapor from electronic cigarettes

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Abstract

Significance—Electronic cigarettes, also known as e-cigarettes, are devices designed to imitate regular cigarettes and deliver nicotine via inhalation without combusting tobacco. They are purported to deliver nicotine without other toxicants and to be safer alternative to regular cigarettes. However, little toxicity testing has been performed to evaluate the chemical nature of vapor generated from e-cigarettes. The aim of this study was to screen e-cigarette vapors for content of four groups of potentially toxic and carcinogenic compounds: carbonyls, volatile organic compounds, nitrosamines, and heavy metals.

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CONTRIBUTORS

MLG and NB designed the study and wrote the paper. JK, MG and LK tested the products using smoking machine. AS and JK developed the analytical method and measured carbonyl compounds and VOCs. AP, MJ, and CRD developed the analytical method and measured metals. CH and PJ developed the analytical method and measured TSNAs. MLG and JK analyzed the data. All contributors approved final version of the manuscript.

COMPETING INTEREST

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DATA SHARING STATEMENT

Data could be made available to qualified researchers by request to the corresponding author.

Materials and methods—Vapors were generated from 12 brands of e-cigarettes and the reference product, the medicinal nicotine inhaler, in controlled conditions using a modified smoking machine. The selected toxic compounds were extracted from vapors into a solid or liquid phase and analyzed with chromatographic and spectroscopy methods.

Results—We found that the e-cigarette vapors contained some toxic substances. The levels of the toxicants were 9 to 450 times lower than in cigarette smoke and were, in many cases, comparable to trace amounts found in the reference product.

Conclusions—Our findings are consistent with the idea that substituting tobacco cigarettes with electronic cigarettes may substantially reduce exposure to selected tobacco-specific toxicants. E-cigarettes as a harm reduction strategy among smokers unwilling to quit warrants further study.

Keywords

electronic cigarette; smoking; formaldehyde; acetaldehyde; acrolein; nitrosamines; volatile organic compounds

INTRODUCTION

An electronic cigarette, also known as e-cigarette, is a type of nicotine inhaler, imitating ordinary cigarettes. Although the majority of e-cigarettes look similar to other tobacco products, such as cigarettes or cigars, certain types resemble pens, screwdrivers, or even harmonicas. E-cigarettes contain nicotine solution in a disposable cartridge. The cartridge is replaced when the solution is finished or might be re-filled by the e-cigarette user. In contrast with ordinary cigarettes, which involve tobacco combustion, e-cigarettes use heat to transform nicotine solution into vapor. Processed and purified nicotine from tobacco leaves, suspended in a mixture of glycerin or propylene glycol with water, is vaporized. Nicotine present in such vapor enters the respiratory tract, from where it is absorbed to the bloodstream.[1-4]

Distributors of e-cigarettes promote the product as completely free of harmful substances. The basis for the claim of harmlessness of the e-cigarettes is that they do not deliver toxic doses of nicotine and the nicotine solution lacks harmful constituents. E-cigarettes are new products and, as such, require further testing to assess their toxic properties. Currently, the scientific evidence on the lack or presence of toxic chemicals in the vapor generated from e-cigarettes, and inhaled by their users is very limited. In August 2008, Ale Alwen, the Assistant Director-General for Non-communicable Diseases and Mental Health, stated that ‘the electronic cigarette is not a proven nicotine replacement therapy. WHO has no scientific evidence to confirm the product’s safety and efficacy. However, WHO does not discount the possibility that the electronic cigarette could be useful as a smoking cessation aid. The only way to know is to test.’.[5] Douglas Bettcher, Director of the WHO’s Tobacco Free Initiative stated that only clinical tests and toxicity analysis could permit considering e-cigarettes a viable method of nicotine replacement therapy.[6]

The majority of tests carried out on e-cigarettes until now consist of analyzing the chemicals in the cartridges or nicotine refill solutions.[7-18] The current tests show that the cartridges contain no or trace amounts of potentially harmful substances, including nitrosamines,

acetaldehyde, acetone and formaldehyde. However, using e-cigarettes requires heating the cartridges and under such conditions chemical reactions may result in formation of new compounds. Such a situation takes place in the case of ordinary cigarettes, where a number of toxic compounds are formed during combustion. The US Department of Health and Human Services of the FDA agency carried out tests which showed the presence of trace amounts of nitrosamines and diethylene glycol in e-cigarette vapor. These tests were conducted in a manner which simulated the actual use of the products.[19]

We developed analytical methods and measured concentrations of selected compounds in the vapor generated by different brands and types of e-cigarettes. We focused our study on the four most important groups of toxic compounds present in the tobacco smoke: carbonyl compounds, volatile organic compounds (VOCs), tobacco-specific nitrosamines (TSNAs), and metals (Table 1).

MATERIALS AND METHODS

Electronic cigarettes and reference product (Nicorette® inhalator)

Since the internet is currently the main distribution channel for the products, we searched price comparison websites, online marketplace (Allegro.pl auction service), and internet discussion forums for e-cigarette users to identify the most popular brands of e-cigarettes distributed from within Poland. The searching was limited to web pages from Poland, and only Polish language was allowed for in retrieval options. Some 30 brands were identified. The brands were entered into Google.pl, and ranked according to the number of hits they generated. The number of hits in the search engine for the selected 30 models allowed selection of the 11 most popular e-cigarettes brands. Additionally, one e-cigarette model purchased in Great Britain was used in the study. All e-cigarette models selected for the study were purchased online. Characteristics of the product tested in the study are shown in Table 2.

The suitable cartridges of the same brand name were used for the study. They were purchased from the same sources that e-cigarette and were matched to selected models. All cartridges were characterized by high nicotine content (16-18 mg). As a reference product the medicinal nicotine inhalator was used (Nicorette® 10 mg, Johnson&Johnson, Poland). The inhalator for the study was purchased in one of the local pharmaceutical warehouses.

Generation of vapor from e-cigarettes and reference product

Vapor from e-cigarettes was generated using smoking machine *Palaczbot*® (Technical University of Lodz, Poland) as described previously.[3] This is a one-port linear piston-like smoking machine with adjustable puffing regimes in a very wide range, controlled by computer interface.

Pilot samples demonstrated that it was impossible to generate vapor from e-cigarettes in standard laboratory conditions assumed for conventional cigarettes testing (ISO 3808).[24] Inhalation of a volume of 35 mL anticipated in conventional cigarette standard is insufficient for an activation of most of the e-cigarettes. Thus, we decided to generate vapor in conditions reflecting the actual manner of e-cigarettes using, determined based on the results

of inhalation topography measurement among 10 ‘e-smokers’, who declared that they regularly use e-cigarettes for a period longer that one month.[3] All testing procedures in this work were carried out using the same averaged puffing conditions: puff duration of 1.8 sec, intervals between puffs of 10 sec, puff volume 70 mL, and number of puffs taken in one puffing session was 15. A total of 150 puffs were taken from each e-cigarette in 10 series of 15 puffs with intervals between series of 5 minutes each. Each e-cigarette was tested three times on three following days after batteries were recharged during nights. A fresh cartridge was placed on the e-cigarettes each day they were tested. Vapor was visibly being produced during the full 150 puffs taken from each product tested.

Analytical chemistry

Note: The details of the sample preparation and analysis are given in the Supplementary Materials.

It was planned to absorb the analyzed vapor components in bulbs containing an organic solvent (extraction to liquid) or on suitable sorbents (extraction to solid phase). This required the modification of the system described above, in such a manner to enable quick connection of desirable sorption system. Carbonyl compounds and organic compounds due to their volatility were trapped in tubes packed with solid adsorbent. Metals and nitrosamines in turn, which are characterized by lower volatility, were to be absorbed in two gas washing bottles with methanol (50 mL in each bottle). Both washing bottles were immersed in acetone-dry ice bath in order to avoid any losses of volatile solvent. A picture of set for vapor generation from e-cigarette and metals or nitrosamines absorption is presented in Supplementary Figure 2.

The samples, after preparation and condensation procedure, were analyzed using analytical methods with high specificity and sensitivity allowing detection of even trace amounts of analyzed compounds. Figure 1 shows the sample preparation procedure; and all analytical methods are described in details in the Supplementary Materials. The following carbonyl compounds were analyzed in this work using high-performance liquid chromatography with spectrophotometric detector (HPLC-DAD): formaldehyde, acetaldehyde, acrolein, acetone, propionic aldehyde, crotonaldehyde, butanol, benzaldehyde, isovaleric aldehyde, valeric aldehyde, m-methylbenzaldehyde, o-methylbenzaldehyde, p-methylbenzaldehyde, hexanal, 2,5-dimethylbenzaldehyde. Volatile organic compounds (VOCs) included benzene, toluene, chlorobenzene, ethylbenzene, m,p-xylene, o-xylene, styrene, 1,3-dichlorobenzene, 1,4-dichlorobenzene, 1,2-dichlorobenzene, naphthalene and were analyzed with gas chromatography-mass spectrometry (GC-MS). Among tobacco-specific nitrosamines (TSNAs) two compounds were measured: N’-nitrosonornicotine (NNN) and 4-(methylonitrosoamino)-1-(3-pirydyl)-l-butanone (NNK) with ultra-performance liquid chromatography-mass spectrometry (UPLC-MS). An inductively coupled plasma mass spectrometry technique (ICP-MS) was used to quantify following metals: cobalt (Co), nickel (Ni), copper (Cu), zinc (Zn), cadmium (Cd), lead (Pb), arsenic (As), chromium (Cr), selenium (Se), manganese (Mn), barium (Ba), rubidium (Rb), strontium (Sr), silver (Ag), thallium (Tl), and vanadium (V). All analytical methods used in this work were validated as per the International Conference on Harmonization guideline Q2(R1).[25]

Statistical analysis

Results were presented as mean±SEM levels of selected compounds in vapor generated from e-cigarettes (per 150 puffs). The study aimed to compare the results obtained for aerosol from Nicorette® inhalator with the results obtained for all examined e-cigarettes models. Due to small size of the groups, the difference between mean from two groups was assessed based on *t* Student's test. All statistical analyses were conducted using the software for statistical data analysis Statistica 9.0 (StaftSoft, Tulsa, USA). The significance level was established as $p<0.05$.

RESULTS

Carbonyl compounds

Among 15 carbonyls analyzed, only 4 were found in vapor generated from e-cigarettes (Table 3); and these compounds were identified in almost all examined e-cigarettes. The exception was one e-cigarette marked with code EC09, where acrolein was not detected. Three of the carbonyls have known toxic and irritating properties: formaldehyde, acetaldehyde, and acrolein. The content of formaldehyde ranged from 2.0 to 56.1 μg, acetaldehyde from 1.1 to 13.6 μg, and acrolein from 0.7 to 41.9 μg per one e-cigarette (150 puffs). Trace amounts of formaldehyde, acetaldehyde and o-methylbenzaldehyde were also detected from the Nicorette® inhalator. None of these compounds were detected in blank samples.

Volatile Organic Compounds (VOCs)

Among 11 volatile organic compounds analyzed, only 2 were found in samples of vapor generated from e-cigarettes (Table 3), and these compounds were identified in almost all examined e-cigarettes. The only one exception was e-cigarette marked with code EC02, where toluene and m,p-xylene were not detected. The content of toluene ranged from 0.2 to 6.3 μg per one e-cigarette (150 puffs). Although the m,p-xylene levels found in analyzed samples of e-cigarette vapors ranged from 0.1 to 0.2 μg, it was also found on the same level in blank samples. In Nicorette® inhalator in turn, none of compounds analyzed in that group was noted.

Tobacco-Specific Nitrosamines (TSNAs)

Both nitrosamines analyzed in the study were identified in all but three vapors generated from e-cigarettes (Table 3). NNN was not found in e-cigarettes marked with code EC01, EC04 and EC05 and NNK was not identified in products EC04, EC05, and EC12. The content of NNN ranged from 0.8 to 4.3 ng, and NNK from 1.1 to 28.3 ng per one e-cigarette (150 puffs). In Nicorette® inhalator nor in blank samples in turn, none of these compounds was noted.

Metals

Among 12 metals analyzed in the study, cadmium, nickel and lead were identified, and were present in all vapors generated from e-cigarettes (except cadmium, which was not detected in a product of code EC12; Table 3). The content of cadmium ranged from 0.01 to 0.22 μg,

nickel from 0.11 to 0.29 μg, and lead from 0.03 to 0.57 μg per one e-cigarette (150 puffs). The same metals in trace amounts were detected in Nicorette® inhalator and in blank samples.

DISCUSSION

We examined vapors generated from 12 models of e-cigarettes for the presence of four groups of toxic compounds found in tobacco smoke. The Nicorette inhalator was used as a reference product. Such a choice was dictated by the premise that a therapeutic product like Nicorette® inhalator should fulfill specified safety standards and should not contain significant levels of any of the analyzed toxic compounds.

Our results confirm findings from the previous studies, in which small amounts of formaldehyde and acetaldehyde were detected in cartridges.[9, 18] However, the presence of acrolein in a cartridge or nicotine solution has not been reported so far. Formaldehyde and acetaldehyde were also found in vapor exhaled to test chamber by volunteers who used e-cigarette filled with three various nicotine solutions.[26] Recently, Uchiyama et al. demonstrated that vapor generated from single brand of e-cigarette contained low levels of formaldehyde, acetaldehyde, and acrolein.[27] There is a possibility that acrolein is present in vapor only, since this compound may be formed as a result of heating glycerin which is a component of the solution. Pyrolysis of glycerin has been studied in steam with acrolein, formaldehyde, and acetaldehyde observed as the major products.[28, 29] These products appear to result from dehydration and fragmentation of glycerin. Although energy calculations of the dehydration of glycerin by the neutral mechanisms indicate that these processes can only occur at relatively high temperatures such as occur in pyrolysis or combustion, the addition of acids allows substantially lower dehydration temperatures.[30]

All three carbonyls compounds found in the study and discussed above have been shown to be toxic in numerous studies: formaldehyde is classified as carcinogenic to humans (group 1 by IARC);[31] acetaldehyde as possibly carcinogenic to humans (group 2B),[31] and acrolein causes irritation to the nasal cavity, and damage to the lining of the lungs and is thought to contribute to cardiovascular disease in cigarette smokers.[32] Exposure to carbonyl compounds found in vapor might cause mouth and throat irritation which are the most frequently reported adverse events among e-cigarette users.[1, 33] A study by Cassee et al. showed that sensory irritation in rats exposed to mixtures of formaldehyde, acetaldehyde and acrolein is more pronounced than that caused by each of the compounds separately.[34] Future studies should evaluated possible adverse health outcomes of short and long term exposure to these compounds among users of e-cigarettes and people involuntary exposed to exhaled vapors.

We found that vapor of some e-cigarettes contains traces of the carcinogenic nitrosamines NNN and NNK, whereas neither was detected in aerosol from the Nicorette® inhalator. The studies conducted previously reported the presence of NNN and NNK in e-cigarette cartridges in amount of 3.9-8.2 ng per cartridge,[18, 19] which corresponds to the results in vapor obtained in the present paper. However some other studies have reported that some cartridges are free of nitrosamines.[12] This inconsistency of findings of various studies

might be due to different analytical methodologies of variable sensitivity applied in the studies discussed above.

Two of analyzed volatile organic compounds were detected: toluene and m,p-xylene. None of the studies conducted until now reported the presence of these compounds in a cartridge, nicotine solution, or e-cigarette vapor. None of these compounds were found in a study by Schripp et al. on passive exposure to e-cigarette vapors.[26] Three toxic metals, cadmium, nickel and lead, were detected in vapor of analyzed e-cigarettes. Since the same elements were also detected in trace amounts in Nicorette® inhalator and in blank samples it is possible that there were other sources of these metals. This limitation of the study does not allow us to conclude with whether e-cigarette alone may be significant source of exposure to these chemicals.

Recently, we published a study on tests for nicotine delivery of Polish and UK e-cigarettes brands.[3] Many of the same brands in that paper have been also included in this study and tested for toxicants delivery. It should be mentioned that the leading brands with the highest nicotine delivery did not have the highest yields for toxicant delivery. This is important as selecting the brands for nicotine the worst brands for toxicants generally can be avoided.

The results allowed us to compare the content of harmful substances between various e-cigarettes models and conventional cigarettes (based on literature data).[35] To compare levels of selected toxins in e-cigarette vapor and mainstream smoke of conventional cigarette we assumed that users of e-cigarettes smoker take on overage 15 puffs during one session of product use, and it would correspond to smoking one conventional cigarette. In our study the vapors from e-cigarettes were generated from 150 puffs (10 series of 15 puffs each). For comparison purposes, we assumed that 150 puffs of e-cigarette correspond to smoking 10 cigarettes. The comparison of toxic substances levels between conventional cigarette and e-cigarette is presented in Table 4.

As shown in Table 4 levels of selected toxic compounds found in the smoke from a conventional cigarette were from 9 to 450-fold higher than levels in in the vapor of an e-cigarette. Smoking (also referred to as ‘vaping’) an e-cigarette can result in comparable exposure to carcinogenic formaldehyde as that received from cigarettes smoking. Formaldehyde was also found in the vapor of medicinal inhalator, at levels that overlapped with those found in e-cigarette vapor. Exposure to acrolein, an oxidant and respiratory irritant thought to be a major contributor to cardiovascular disease from smoking, is 15 times lower on average in e-cigarette vapor compared to cigarette smoke. The amounts of toxic metals and aldehydes in e-cigarettes are trace and comparable to amounts contained in examined therapeutic product.

The results of the study support the proposition that the vapor from e-cigarette is less injurious than the smoke from cigarettes. Thus one would expect that if a person switched from conventional cigarettes to e-cigarettes that exposure to toxic chemicals and related adverse health effects would be reduced. The confirmation of that hypothesis requires however further studies involving people using e-cigarette devices.

The primary limitation of our research is that the puffing profile we used may not reflect actual user puff topography. Hua et al. reported that e-cigarette users take longer puffs, and that puff duration varied significantly among e-cigarette brands and users.[36] This suggests that actual doses of toxicants inhaled by e-cigarette users might be higher than measured in our study. Similarly to results of tobacco cigarette testing with smoking machines (ISO, FTC) the values obtained in our study should be interpreted with caution. The other limitation of our research is that we have tested only 12 brands of e-cigarettes. There are numerous different brands on the market, and there is little information on their quality control.

CONCLUSIONS

The vapor generated from e-cigarettes contains potentially toxic compounds. However, the levels of potentially toxic compounds in e-cigarette vapor is from 9 to 450-fold lower than those in the smoke from conventional cigarette, and in many cases comparable to the trace amounts present in pharmaceutical preparation. Our findings are support the idea that substituting tobacco cigarettes with electronic cigarettes may substantially reduce exposure to tobacco-specific toxicants. The use of e-cigarettes as a harm reduction strategy among cigarettes smokers who are unable to quit warrants further study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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WHAT THIS PAPER ADDS

- Distributors of e-cigarettes promote the product as completely free of harmful substances. Currently, there is no comprehensive research on the presence of toxic chemicals in the vapor generated from e-cigarettes and inhaled by their users.
- This study of chemical composition of vapor generated from 12 brands of e-cigarettes revealed that the vapor contained some toxic substances.
- The levels of potentially toxic compounds in e-cigarette vapor were found to be from 9 to almost 450-fold lower compared to smoke from conventional cigarette, and in many cases comparable to trace amounts present in pharmaceutical preparation.

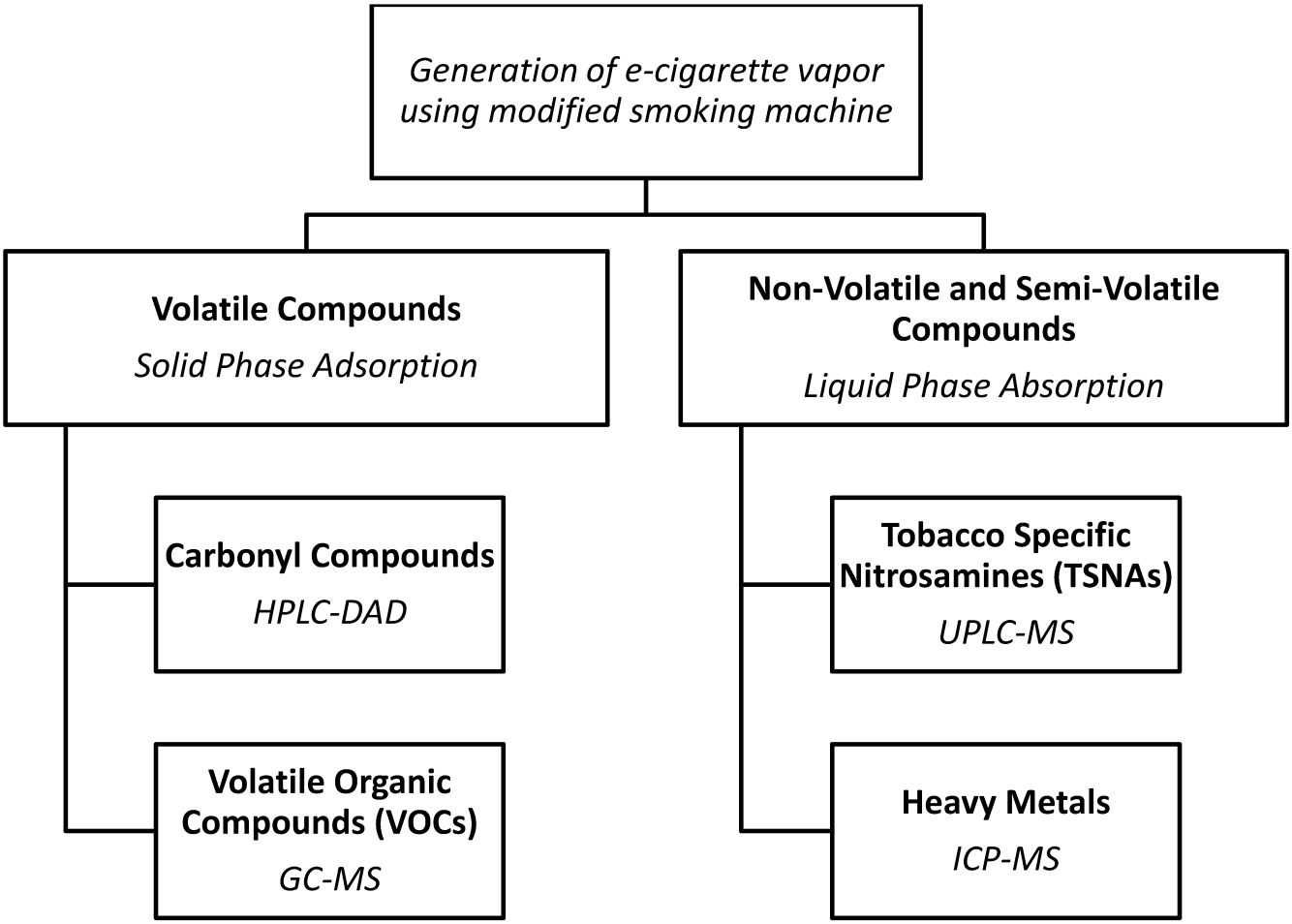

Figure 1.
Analytical procedures applied in the study to test carcinogens and selected toxicants in vapor from e-cigarettes

Table 1

Selected toxic compounds identified in tobacco smoke.[20-23]

Chemical compounds	Toxic effects
Carbonyl compounds	
formaldehyde*, acetaldehyde*, acrolein*	cytotoxic, carcinogenic, irritant, pulmonary emphysema, dermatitis
Volatile organic compounds (VOCs)	
benzene*, toluene*, aniline	carcinogenic, hematotoxic, neurotoxic, irritant
Nitrosamines	
N'–nitrosonornicotine (NNN)*, 4-(methylonitrosoamino)-1-(3-pirydyl)-l-butanone (NNK) *, N'-nitrosoethylomethyloamine	carcinogenic
Polycyclic aromatic compounds (PAHs)	
benzo(a)pyrene, benzo(a)anthracene, dibenzo(a)anthracene	carcinogenic
Free radicals	
methyl radical, hydroxyl radical, nitrogen monoxide	carcinogenic, neurotoxic
Toxic gases	
carbon monoxide, hydrogen sulfide, ammonia, sulphur dioxide, hydrogen cyanide	cardiovascular toxicants, carcinogenic, irritant
Heavy metals	
cadmium (Cd)*, lead (Pb)*, mercury (Hg)*	carcinogenic, nephrotoxic, neurotoxic, hematotoxic
Other toxicants	
carbon disulphide	neurotoxic

* *Note:* indicates compounds analyzed in this study

Table 2

Characteristics of products tested in the study.

Product code	Brand name	Model	Cartridge type	Flavor	Labeled nicotine content (mg or mg/mL)	Measured nicotine content (mg) [3]	Retailer	Country
EC01	Joye	510	Cartridge	Marlboro	4	4	Inspired s.c.	Poland
EC02	Janty	eGo	Cartridge	Marlboro	16	5	Janty	Poland
EC03	Janty	Dura	Cartridge	Marlboro	16	5	Janty	Poland
EC04	DSE	901	Cartridge	Regular	16	9	Fausee	Poland
EC05	Trendy	808	Cartridge	Trendy	18	2	Damhess	Poland
EC06	Nicore	M401	Cartridge	Marlboro	18	5	Atina Poland	Poland
EC07	Mild	201	Cartridge	Marlboro	18	19	Mild	Poland
EC08	Colinss	Age	Cartomizer	Camel	18	11	Colinss	Poland
EC09	Premium	PR111	Cartomizer	Tobacco	16	12	Premium	Poland
EC10	Ecis	510	Cartridge	Menthol	11	5	Arcotech	Poland
EC11	Dekang	Pen	Cartridge	Regular	18	18	Ecigars Polska	Poland
EC12	Intellicig	Evolution	Cartridge	Regular	8	8	Intellicig	UK

Table 3

Levels of selected compounds in vapor generated from e-cigarettes (per 150 puffs). Values are mean±SEM.

Compound	BS	Levels in vapor from electronic cigarettes[1]											Reference product
		Product code											
		EC01	EC02	EC03	EC04	EC05	EC06	EC07	EC08	EC09	EC10	EC11	EC12	Inhalator
Carbonyl compounds [µg]														
Formaldehyde	ND	44.2±4.1*	23.6±8.7*	30.2±2.3*	47.9±0.2*	56.1±1.4*	35.3±2.7*	19.0±2.7*	6.0±2.0	3.2±0.8	3.9±1.5	23.9±11.1	46.3±2.1*	2.0±1.1
Acetaldehyde	ND	4.6±0.2*	6.8±3.2	8.2±2.5*	11.5±2.0*	3.0±0.2*	13.6±2.1*	11.1±3.3*	8.8±1.6*	3.5±0.3*	2.0±0.1	3.7±1.5	12.0±2.4*	1.1±0.6
Acrolein	ND	41.9±3.4*	4.4±2.5	16.6±2.5*	30.1±6.4*	22.0±1.6*	2.1±0.4*	8.5±3.6	0.7±0.4	ND	2.7±1.6	1.1±0.6	7.4±3.2*	ND
o-methylbenzaldehyde	ND	1.9±0.5	4.4±1.2*	3.2±1.0*	4.9±1.2*	1.7±0.1*	7.1±0.4*	1.3±0.8	5.5±0.0*	6.0±0.7*	3.2±0.5*	5.1±0.1*	2.2±0.6*	0.7±0.4
Volatile Organic Compounds (VOCs) [µg]														
Toluene	ND	0.5±0.1*	ND	0.2±0.0*	0.6±0.1*	0.2±0.0*	ND	0.3±0.2	0.2±0.1	6.3±1.5*	0.2±0.1*	0.5±0.1*	0.5±0.0*	ND
p,m-xylene	0.1	0.1±0.0*	ND	0.1±0.0*	0.2±0.1*	0.1±0.0	ND	0.1±0.1	0.1±0.0	0.1±0.0*	0.1±0.0*	0.1±0.1*	0.1±0.0	ND
Tobacco-Specific Nitrosamines (TSNAs) [ng]														
NNN	ND	ND	2.7±2.2	0.8±0.8	ND	ND	0.9±0.4	4.3±2.4	1.9±0.3*	1.2±0.6	2.0±1.1	3.2±0.6*	1.3±0.1	ND
NNK	ND	2.0±2.0	3.6±1.8	3.5±1.8	ND	ND	1.1±1.1	21.1±6.3*	4.6±0.4*	28.3±13.2	2.1±2.1	13.0±1.4*	ND	ND
Metals [µg]														
Cd	0.02	0.17±0.08	0.15±0.03*	0.15±0.05	0.02±0.01	0.04±0.01	0.22±0.16	0.02±0.01	0.08±0.03	0.01±0.01	0.17±0.10	0.03±0.03	ND	0.03±0.01
Ni	0.17	0.28±0.22	0.29±0.08	0.21±0.03	0.17±0.07	0.14±0.06	0.11±0.06	0.23±0.09	0.26±0.10	0.19±0.09	0.12±0.04	0.11±0.08	0.11±0.05	0.19±0.04
Pb	0.02	0.06±0.01	0.06±0.03	0.07±0.01	0.03±0.01	0.05±0.01	0.03±0.01	0.04±0.01	0.57±0.28	0.09±0.04	0.06±0.02	0.04±0.03	0.03±0.03	0.04±0.01

Note: SE, standard error; DL, detection limit; BS, blank sample; ND, not detected;

* significant difference with Nicorette inhalator ($p<0.05$)

[1] units are µg, except for nitrosamines units are ng

Table 4

Comparison of toxicants levels between conventional and electronic cigarettes.

Toxic compound	Conventional cigarette (μg in mainstream smoke) [35]	Electronic cigarette (μg per 15 puffs)	Average ratio (conventional vs. electronic cigarette)
Formaldehyde	1.6-52	0.20-5.61	9
Acetaldehyde	52-140	0.11-1.36	450
Acrolein	2.4-62	0.07-4.19	15
Toluene	8.3-70	0.02-0.63	120
NNN	0.005-0.19	0.00008-0.00043	380
NNK	0.012-0.11	0.00011-0.00283	40