Electronic cigarettes: an evaluation of exposure to chemicals and fine particulate matter (PM)

Article *in* Annali di igiene: medicina preventiva e di comunità · November 2011

Source: PubMed

8 authors, including:

Roberto Maria Pellegrino
Università degli Studi di Perugia
43 PUBLICATIONS **508** CITATIONS
SEE PROFILE

Giacomo Mangiaracina
Sapienza University of Rome
27 PUBLICATIONS **67** CITATIONS
SEE PROFILE

Matteo Vitali
Sapienza University of Rome
93 PUBLICATIONS **774** CITATIONS
SEE PROFILE

Carmela Protano
Sapienza University of Rome
56 PUBLICATIONS **322** CITATIONS
SEE PROFILE

Ann Ig 2012; 24: 279-288

Electronic cigarettes: an evaluation of exposure to chemicals and fine particulate matter (PM)

R.M. Pellegrino*, B. Tinghino**, G. Mangiaracina***, A. Marani****, M. Vitali****, C. Protano****, J.F. Osborn****, M.S. Cattaruzza****

Key words: Electronic cigarette emissions, flavouring mixture, fine particulate matter, PM
Parole chiave: Emissioni sigaretta elettronica, miscela aromatizzante, particolato fine, PM

Riassunto

La sigaretta elettronica: una valutazione dei componenti chimici e del particolato sottile (PM)

L'uso della sigaretta elettronica sta generando un importante dibattito scientifico. La sua popolarità sta crescendo in tutto il mondo come metodo per ridurre o smettere di fumare e per fumare nei luoghi chiusi dove è vietato. L'OMS tuttavia raccomanda cautela fino a quando non sia stata chiarita la sua reale efficacia come aiuto ai fumatori e non sia stato valutato l'eventuale possibile danno associato al suo utilizzo.
L'obiettivo di questo studio è stato quello di analizzare, per una marca italiana di sigaretta elettronica, il contenuto liquido della miscela aromatica, il suo vapore e le emissioni di Particolato Sottile (PM) confrontandole con quelle di una sigaretta convenzionale.
Il propilene glicole (66%) e la glicerina (24%) sono risultati i principali componenti del liquido, mentre le sostanze aromatiche ammontavano a meno dello 0,1%. Le medesime sostanze, all'incirca nelle stesse proporzioni, sono state ritrovate nel vapore emesso.
Le emissioni fini ed ultrafini di PM sono risultate notevolmente più alte per la sigaretta convenzionale rispetto a quella elettronica (rispettivamente PM_{10}: 922 e 52 μg/m³; PM_1: 80 e 14 μg/m³).
La sigaretta elettronica sembra dare alcuni vantaggi quando è usata al posto della sigaretta convenzionale, anche se gli studi sono ancora scarsi: potrebbe aiutare i fumatori a gestire la ritualità e a ridurre o a smettere di fumare, evitando l'esposizione al fumo passivo. Tuttavia determina anche l'esposizione a sostanze chimiche diverse rispetto alla sigaretta convenzionale e quindi si rende necessaria un'accurata valutazione dei rischi potenzialmente connessi con il suo uso e con l'esposizione di fumatori e non fumatori al suo vapore.

Introduction and obiectives

Recently, an electric device called an "electronic cigarette", "e-cigarette" or "e-cig" has become more commonly used by smokers to replace conventional cigarettes.

The e-cigarette is an integrated electric device, shaped like a cigarette, consisting of a stainless steel shell, a lithium ion battery assembly, a smart chip with program controlled circuits, an atomization chamber and a removable cartridge. Flavouring is housed in the removable

* *Department of Chemistry, University of Perugia, Italy*
** *Center for Smoking Cessation, ASL Monza e Brianza, Italy*
*** *Faculty of Medicine and Psychology, Sapienza University of Rome, Italy*
**** *Department of Public Health and Infectious Diseases, Sapienza University of Rome, Italy*

cartridge, which contains propylene glycol and other products obtained from an extraction of tobacco flavours. Some e-cigarettes even contain nicotine in the removable cartridge together with flavour. Some companies add other flavours to the mixture such as: mint, strawberry, orange etc (18). These products may be very attractive to minors who may be drawn to the technology, flavouring and accessibility (41).

The popularity of the e-cigarette among smokers has increased worldwide, as a method to reduce or quit smoking, to smoke in an indoor environment when smoking restrictions are present, or to "feign a smoking experience" reducing health risks (10, 19). Besides, now-a-days the e-cigarette is an "online leader" in popularity among smoking alternatives, such as snus (a moisturized tobacco powder used as an alternative to chewing tobacco), nicotine replacement therapy, and other medications (4). Even in the South Korean market, the e-cigarette, described as the "healthy cigarette", was advertised as an incredible and effective and healthy smoking cessation device (25).

On the other hand, in September 2008 the World Health Organization (WHO) decided that e-cigarettes cannot be considered as a way to stop smoking, because there were not enough studies demostrating its effectiveness in reducing and replacing the consumption of nicotine. Besides, WHO recommended caution in its use, until its effectiveness in helping smokers is clarified and the possible harm of some substances is evaluated (34, 42). After the WHO recommendations, the topic "e-cigarette" has generated significant scientific debate about the promises and perils of the device (17 30, 39). Nevertheless, even now there is little research on e-cigarette safety, while some data on plasma nicotine, carbon monoxide concentration, heart rate and subjective effects have been evaluated (38). In the first reports, e-cigarettes seem to alleviate craving and to be well tolerated, at least in short-term clinical observations (6, 11, 27, 32), but evaluation of the toxicity of the different electronic devices, the long-term safety, and the smoking cessation efficacy is needed (14, 15). In particular, the first priority of studies in this field should be the characterization of the safety profile (14, 15).

The US Food and Drug Administration (FDA) analyzed results of a two widely commercialized electronic cigarette products, suggesting that these devices may include some of the same toxic or carcinogenic compounds as the conventional cigarette. Moreover, some e-cigarettes contain ethylene glycol, a toxic chemical (18, 23).

The aim of the present study was to contribute to the knowledge on toxicity of e-cigarettes during a smoking simulation of an Italian brand by:

- a quali-quantitative determination of the aromatic mixture and the vapour content;
- the evaluation of particulate matter emission according to their size (Total Suspended Particulate - TSP, and particles with size ≤ 10, 7, 2.5 and 1 μm - $PM_{10, 7, 2.5, 1}$ fractions, respectively).

Materials and methods

Analytical determinations were performed on two types of an Italian brand (e-cigarette Aria™ - Auripen, Italy) of e-cigarettes: one with nicotine (Nic) and one without nicotine (W Nic). The study was performed in three phases.

1. In the first phase, the aromatic liquid of the e-cigarette was analysed. The cartridge had a cylindrical shape (diameter 9 mm; length 40 mm) and contained

about 0.5 grams of liquid. Analyses were performed using Agilent 5975-6890 gas-chromatography/mass-spectrometry (GC/MS) by injecting undiluted liquid in split mode (500:1). Chromatographic column was a JW 5-MS (0.2 μm thickness, 0.25 mm ID, 30 m Length) used in programmed mode (45°C for 3 min, next increment of 10°C/min to 320°C for 2 min) with Helium as carrier gas at constant flow of 1.1 mL/min. Qualitative data were obtained by comparison of 70 eV electronic impact mass spectra of each compound with database library (Wiley and NIST). Quantitative data expressed by weight/weight (% w/w) were obtained by internal normalization method: the area of the total ion current (TIC) signal of each chromatographic peak was multiplied by the respective response factor, that was previously determined for each compound by analysing various synthetic mixtures gravimetrically prepared.

2. In the second phase, the chemical composition of the vapour was analysed. The e-cigarette was applied to a device that simulated 16 aspirations, each lasting for 3 seconds with a flow rate of 0.166 L/sec and with intervals between one aspiration and the other of 8 seconds. Exhaled steam produced by the e-cigarette was collected into an Supelco ORBO™ 100 HBR on Carbotrap™ B. The analytes were eluted from the adsorbent with 5 mL of carbon disulphide and collected in a 10 mL glass tube. The solution was dried to 100 μL with a gentle stream of nitrogen gas, placing the bottom of the tube in a water/ice bath. Finally, 1 μL of the obtained solution was injected into GC/MS apparatus under the same conditions described in phase 1.

3. In the third phase, the indoor emission of particulate matter by the e-cigarette (Nic) was measured and compared with that of a traditional cigarette brand (nicotine = 0.8 mg/cigarette; tar = 10 mg/cigarette), using a device that produced 4 aspirations per minute, for 3 minutes overall. Measurements were performed with a portable laser operated aerosol mass analyser (Aerocet 531, Metone Instruments Inc, USA) in an air volume of 11 m^3.

The measurements were taken before lighting the cigarette (T0), 1.5 minutes after lighting (T1 = half smoking simulation time) and after 3 minutes (T2 = end of smoking simulation).

There was a wash-out period of 30 minutes with air exchange between the measurements for the e-cigarette and the conventional cigarette. This allowed the air to return to basal indoor values, as measured by the mass analyser. The ambient temperature and humidity were 19.5°C and 60% respectively.

Results

The results of GC/MS analyses of the aromatic mixtures (Nic and W Nic) are shown in Table 1. The content of the aromatic mixtures of Nic and W Nic e-cigarettes are very similar: propylene glycol was the main component found in liquid of both e-cigarettes (66.001 and 66.115 %w/w for Nic e-cigarettes and for W Nic e-cigarettes, respectively). Propylene glycol together with glycerine represented more of 90% of the total ingredients, while the other substances were less than 0.1% of the total. L-nicotine was present only in the device with nicotine (0.250 %w/w).

The substances in the e-cigarettes' steam found by GC/MS analysis are reported in Table 2. A total of 11 and 10 chemicals were found at detectable levels, respectively in the analyzed steam of Nic and W Nic e-cigarettes (L-nicotine was

Table 1 - Composition of the e-cigarette's aromatic mixture and their percentages expressed as %weight/weight (%w/w)

Substance	CAS[a]	Nic (% w/w)[b]	W Nic (%w/w)[c]
1,2-propanediol (propylene glycol)	57-55-6	66.001	66.115
1,2,3-propanetriol (glycerin)	56-81-5	24.056	24.200
L-nicotine	54-11-5	0.250	< 0.001
Flavouring agents:			
methyl pyrazine	109-08-0	0.028	0.024
2,3-dimethyl pyrazine	5910-89-4	0.012	0.012
5-methyl-2-furaldehyde	620-02-0	0.011	0.010
1-hydroxy-2-propanone	116-09-6	0.011	0.008
β-damascon	23726-91-2	0.010	0.010
2,5-dimethyl pyrazine	123-32-0	0.010	0.010
3-hydroxy-2-methyl-4-pyranone (maltol)	118-71-8	0.004	0.002
2,3,5,6-tetramethyl pyrazine	1124-11-4	0.001	0.002
TOTAL	-	90.394[d]	90.393[d]

[a] CAS: Chemical Abstracts Service (Registry number of each product)
[b] Nic: e-cigarette with nicotine
[c] W Nic: e-cigarette without nicotine
[d] Remaining % w/w of aromatic mixtures (9.606% and 9.607%) is presumably due to the water content.

Table 2 - Composition of the steam from e-cigarettes expressed as mg/m^3

Name	CAS[a]	Nic[b] mg/m^3	W Nic[c] mg/m^3
1,2-propanediol (propylene glicol)	57-55-6	1660	1650
1, 2, 3-propanetriol (glycerin)	56-81-5	610	580
L-nicotine	54-11-5	6.21	< 0.01
methyl pyrazine	109-08-0	0.54	0.54
2,3-dimethyl pyrazine	5910-89-4	0.29	0.30
5-methyl-2-furaldehyde	620-02-0	0.27	0.27
1-hydroxy-2-propanone	116-09-6	0.26	0.26
β-damascon	23726-91-2	0.25	0.25
2,5-dimethyl pyrazine	123-32-0	0.24	0.24
3-hydroxy-2-methyl-4-pyranone (maltol)	118-71-8	0.06	0.06
2,3,5,6-tetramethyl pyrazine	1124-11-4	0.03	0.02

[a] CAS: Chemical Abstracts Service (Registry number of each product)
[b] Nic: e-cigarette with nicotine
[c] W Nic: e-cigarette without nicotine

Table 3 - Particulate matter emissions (PM) according to their size (Total Suspended Particulate matter - TSP, and particle with size lower than 10, 7, 2.5 and 1 μm - $PM_{10, 7, 2.5, 1}$) at basal time (T0), after 1.5 min (T1) and after 3 min (T2) of use of the e-cigarette and conventional cigarette

	e-cigarette			Conventional cigarette			Density ratio conventional/e-cigarettes
	T0	T1	T2	T0	T1	T2	T2
PM_1 μg/m^3	1	0	14	0	42	80	6
$PM_{2.5}$ μg/m^3	2	3	43	3	281	901	21
PM_7 μg/m^3	4	8	50	5	291	919	18
PM_{10} μg/m^3	6	10	52	7	293	922	18
TSP μg/m^3	13	17	63	16	305	933	15

found only in Nic e-cigarettes). Even in this case, the major component of the steam of both e-cigarettes is propylene glycol (1660 mg/m^3 for Nic and 1650 mg/m^3 for W Nic e-cigarettes, respectively), followed by glycerine (610 and 580 mg/m^3 for Nic and W Nic e-cigarettes, respectively). The other analytes recovered in the steam, detected in trace levels, were the same as compared to those found in the aromatic mixture.

The maximum temperature of the steam vapour exiting the device was 43°C.

Fine and ultrafine PM emissions measured for the electronic and conventional cigarettes are reported in Table 3.

PM emissions measured after smoking simulation with the electronic and the conventional cigarettes were higher than those detected before the experiment in both cases. However, comparison of PM levels produced by the electronic and conventional cigarettes shows a much greater increase (up to hundreds of times) of each PM fraction for conventional cigarette.

At the end of the experiments (after 3 minutes from the lighting of the conventional cigarette and e-cigarettes), PM emissions produced by conventional cigarette in the indoor air were several times higher than PM emissions produced by e-cigarette. Overall, total suspended particulate matter emissions derived from a conventional cigarette were 15 times higher than those derived from an e-cigarette. For each of the different fractions of PM, ($PM_{1, 2.5, 7, 10}$), there was an higher density (ranging from 6 to 21 times) for conventional compared to e-cigarette.

Discussion

Much research is being done on strategies that may help smokers to quit, either using drugs or control strategies to manage craving and behaviour (3, 5, 7, 20, 40). The use of e-cigarettes should be seen in this way, that is, as a tool to reduce the damage caused by real tobacco smoke. However, well-conducted clinical trials showing the effectiveness of these devices for treating tobacco addiction are lacking.

"*The first priority is to characterize the safety profile of these products, including in long-term users. If these products are demonstrated to be safe, their efficacy as smoking cessation aids should then be tested in appropriately designed trials. Until these studies are conducted, continued marketing constitutes an uncontrolled experiment and the primary outcome measure, poorly assessed, is user health*." (14).

Some data are available about the ingredients of different e-cigarettes (8), but it must be considered that there are different types of commercially available formulations of e-cigarettes; thus, toxicological aspects related to these devices may differ widely.

The e-cigarettes analysed in this study are produced by a single Italian manufacturer.

The major constituent of both the aromatic mixture (liquid) and vapour was propylene glycol, as shown in previous studies on different e-cigarettes (2, 9, 12, 13, 35, 37). Propylene glycol is a clear, colourless, odourless and tasteless liquid at room temperature; it may exist in air in vapour form, and it is widely used as an antifreeze and de-icing solution for cars, airplanes and boats, as a solvent in the paint and plastics industries, as a chemical to generate artificial smoke for theatrical productions, as an additive for several drugs, cosmetics or food products, as a solvent for food colours and flavours (1).

In the e-cigarette, it is used to simulate the appearance of standard cigarette smoke (23).

The FDA classified propylene glycol as "generally recognized as safe", that is acceptable for use in flavorings, drugs, food, and cosmetics.

The toxicological profile of propylene glycol, traced by the Agency for Toxic Substances & Disease Registry (1), states that inhalation of its vapours presents no significant hazard in ordinary applications, but limited human experience indicate that its mists may be irritating for some individuals.

Propylene glycol is not classified as hazardous under the EC Regulation 1272/2008 (16) (which replaces Directive 67/548/EEC for substances and Directive 1999/45/EC for preparations) on the Classification, Labelling and Packaging of substances and mixtures (CLP).

In the liquid some "dangerous" substances (according to EC Regulation 1272/2008) were also present: methyl pyrazine, 2,3-dimethylpyrazine, β-damascon, 1-hydroxy-2-propanone, 2,5-dimethyl pyrazine, 2,3,5,6-tetramethyl pyrazine, 3-hydroxy-2-methyl-4-pyranone, 5-methyl-2-furaldehyde, but their concentrations were less than 0.1%, the maximum limit allowed by law. This statement, however, does not guarantee the safety of e-cigarettes for smokers, but it is related to just the production process, the manipulation and holding of the aromatic mixture.

The same substances recovered in liquid were also present in the steam. Their safety for users' health strictly depends on dosage (number of smoked cartridges) and duration of active and/or passive exposure, as well as on several other variables related to the user (age, gender, etc). Thus, it is difficult to trace a universal risk profile since the danger is related to personal habits. Moreover, the difficulty in outlining the personal risk profile is not only in evaluating the quantities of airborne chemicals to which one is exposed, but also the actual amount that enters into the body. For this purpose, it will be useful to study, in depth, users' behaviour and to perform quantitative risk assessment.

In the present study, both electronic and conventional cigarettes caused an increase of PM levels in indoor air. To our knowledge, this is the first empirical research on PM emissions of e-cigarettes; thus it is not possible to compare our data with other results. At the end of the experiment with a conventional cigarette PM emission was hundreds of times higher than before smoking, in the same order of magnitude as the results from previous studies (21, 26, 31).

In both cases, the levels of PM_{10} and $PM_{2.5}$ exceeded the WHO air quality

guideline values (50 and 25 μg/m^3 for PM_{10} and $PM_{2.5}$ respectively) (43). Nevertheless, the guideline values refer to a daily mean exposure, while PM concentrations of electronic and conventional cigarettes were measured only during and immediately after the experiment. Notice that the increase of PM slightly exceeds the WHO values in the case of e-cigarettes, but is particularly conspicuous in the case of a conventional cigarette. Thus, data presented in this study should not be considered a model of exposure to PM emission for electronic or conventional cigarettes, but they could be the rational starting point for studies to evaluate actual scenarios to compare daily PM emission derived from the smoking of electronic and conventional cigarettes. Besides, since PM is a mixture of substances, it would be interesting to assess not only the quantity of particles but also their chemical composition (e.g. metals or organic compounds).

However, it is important to highlight that e-cigarettes may be less harmful than tobacco given the lack of tar, carbon monoxide, combustion products and all the other chemicals (more than 4000 substances, some of them proven toxic and carcinogenic) released from a "tobacco" cigarette (23), and the lower production of PM.

An important "human health" question related to cigarette smoking is passive smoking, better defined as environmental tobacco smoke (ETS), that is the mixture of the chemicals released from the smouldering tobacco product. It is well known that ETS is a threat to the health of the non-smokers (36). In particular, ETS exposure in the first years of life may result in irreversible damages in adult age: together with the expected effects, such as leukaemia, other kinds of cancer and chronic respiratory diseases (28), recent research evidenced long-term cardiovascular effects in children exposed to ETS (22, 33).

ETS results in a combination of second- and third-hand smoke, where secondhand smoke is the mixture of chemicals derived from the smoke exhaled by a smoker together with the smoke from a burning cigarette, while thirdhand smoke is the combination of tobacco smoke pollutants that adhere to the clothing and hair of smokers and to surfaces, furnishings, and dust in indoor environments, persisting long after the clearing of secondhand smoke. Thus, secondhand smoke exposure consists of an unintentional inhalation of smoke that occurs close to people smoking during the period of active smoking. Thirdhand smoke exposure consists of unintentional intake of smoke that occurs in the absence of concurrent smoking - even long after smoking has ceased - through close contact with smokers and in indoor environments in which tobacco is regularly smoked (29).

In our opinion, this question should be evaluated for e-cigarette too.

Conclusions

Overall, the e-cigarette seems to give some advantages when used instead of the conventional cigarette:

the users' exposure to chemicals is limited to few compounds included in the aromatic mixture, while the combustion of tobacco and paper of a conventional cigarette produces more than 4000 substances;

PM emissions are significantly lower for the e-cigarette for all the investigated dimensional fractions;

given the above, the e-cigarette should be less dangerous for second- and thirdhand smoke.

Due to the lack of specific research, the e-cigarette should only be considered

a promising option to tobacco cigarettes. First, toxicological studies should be conducted on the whole chemical mixture, in order to asses possible risks and, consequently, to substitute the dangerous components. Furthermore, there is a strong need for studies on both users' risks and effectiveness in smoking cessation.

Abstract

The "electronic (e-)cigarette" generates intense scientific debate about its use. Its popularity is increasing worldwide as a method to reduce/quit smoking, and to smoke indoors when restrictions on smoking tobacco are present. WHO recommends caution, until its effectiveness in helping smokers is clarified, and the possible harm evaluated. The aim of this study was to assess the content of the aromatic liquid mixture and its vapour and the Particulate Matter (PM) emissions of an Italian brand of e-cigarette and to compare its PM emissions with a conventional cigarette.

Propylene glycol (66%) and glycerine (24%) were main components in the liquid, while the flavouring substances were less than 0.1%. The same substances were detected in the vapour in similar proportions.

Fine and ultrafine PM emissions were higher for the conventional versus the e-cigarette (e.g.: PM_{10}=922 vs 52 μg/m^3; PM_1=80 vs 14 μg/m^3).

The e-cigarette seems to give some advantages when used instead of the conventional cigarette, but studies are still scanty: it could help smokers to cope with some of the rituals associated with smoking gestures and to reduce or eliminate tobacco consumption avoiding passive smoking. However, the e-cigarette causes exposure to different chemicals compared with conventional cigarettes and thus there is a need for risk evaluation for both e-cigarettes and passive steam exposure in smokers and non smokers.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). Toxicological Profile for Propylene Glycol. Atlanta, GA: U.S. Department of Health and Human Services, Public Health Service, 1997. Available online: www.atsdr.cdc.gov/toxfaqs/tfacts189.pdf (last accessed on 2012 Jan 12).
2. Alliance Technologies LLC. Characterization of Liquid "Smoke Juice" for Electronic Cigarettes. Monmouth Junction, NJ: Alliance Technologies LLC, 2009. Available online: truthaboutecigs.com/science/4.pdf (last accessed 2012 Jan 20).
3. Aubin HJ, Karila L, Reynaud M. Pharmacotherapy for smoking cessation: present and future. Curr Pharm Des 2011; **17**: 1343-50.
4. Ayers JW, Ribisl KM, Brownstein JS. Tracking the rise in popularity of electronic nicotine delivery systems (electronic cigarettes) using search query surveillance. Am J Prev Med 2011; **40**: 448-53.
5. Barnes J, Dong CY, McRobbie H, Walker N, Mehta M, Stead LF. Hypnotherapy for smoking cessation. Cochrane Database Syst Rev 2010; **6**: CD001008.
6. Bullen C, McRobbie H, Thornley S, Glover M, Lin R, Laugesen M. Effect of an electronic nicotine delivery device (e cigarette) on desire to smoke and withdrawal, user preferences and nicotine delibery: randomized cross-over trial. Tob Control 2010; **19**: 98-103.
7. Cahill K, Lancaster T, Green N. Stage-based interventions for smoking cessation. Cochrane Database Syst Rev 2010; **10**: CD004492.
8. Cahn Z, Siegel M. Electronic cigarettes as a harm reduction strategy for tobacco control: A step forward or a repeat of past mistakes? J Public Health Policy 2011; **32**: 16-31.
9. Cai X, Kendall MW. Gas Chromatography Mass Spectrometry (GC-MS) Analysis Report. Sunnyvale, CA: Evans Analytical Group, 2009. Available online: truthaboutecigs.com/science/14.pdf (last accessed 2012 Jan 05).
10. Caponnetto P, Campagna D, Papale G, Russo C, Polosa R. The emerging phenomenon of electronic cigarettes. Expert Rev Respir Med 2012; **6**: 63-74.
11. Caponnetto P, Polosa R, Russo C, Leotta C, Campagna D. Successful smoking cessation with electronic cigarettes in smokers with a documented history of recurring relapses: a case series documented history of recurring relapses: a case series. J Med Case Rep 2011; **5**: 585.
12. Coulson H. Analysis of Components from Gamucci Electronic Cigarette Cartridges, Tobacco Flavour Regular Smoking Liquid. Lancashire, UK: Blackburn MicroTech Solutions, 2009. Available online: truthaboutecigs.com/science/7.pdf (last accessed 2012 Jan 05).

13. Ellicott M. Analysis of Components from "e-Juice XX HIGH 36 mg/ml Rated Nicotine Solution" ref S 55434. Lancashire, UK: Blackburn MicroTech Solutions, 2009. Available online: truthaboutecigs.com/science/11.pdf (last accessed 2012 Jan 05).
14. Etter JF, Bullen C, Flouris AD, Laugesen M, Eissenberg T. Electronic nicotine delivery systems: a research agenda. Tob Control 2011; **20**: 243-8.
15. Etter JF, Bullen C. Electronic cigarette: users profile, utilization, satisfaction and perceived efficacy. Addiction 2011; **106**: 2017-28.
16. European Commission. Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. Official Journal of the European Union, 2008; L 353.
17. Flouris AD, Oikonomou DN. Electronic cigarettes: miracle or menace? BMJ 2010; **340**: c311.
18. Food and Drug Administration (FDA). Department of Health and Human Services. Evaluation of e-cigarettes. May, 4, 2009. Available online: fda.gov/downloads/Drugs/ScienceResearch/UCM173250.pdf (last accessed 2012 Jan 05).
19. Foulds J, Veldheer S, Berg A. Electronic cigarettes (e-cig): views of aficionados and clinical/public health perspectives. Int J Clin Pract 2011; **65**: 1037-42.
20. Gorini G. Individual, community, regulatory, and systemic approaches to tobacco control interventions. Epidemiol Prev 2011; **35** (3-4 Suppl 1): 33-49.
21. Invernizzi G, Ruprecht A, Mazza R, et al. Particulate matter from tobacco versus diesel car exhaust: an educational perspective. Tob Control 2004; **13**: 219-21.
22. Juonala M, Magnussen CG, Venn A, et al. Parental smoking in childhood and brachial artery flow-mediated dilatation in young adults: the Cardiovascular Risk in Young Finns study and the Childhood Determinants of Adult Health study. Arterioscler Thromb Vasc Biol 2012; **32**: 1024-31.
23. Kuehn BM. FDA: Electronic Cigarettes May Be Risky. JAMA 2009; **302**: 937.
24. Kuschner WG, Reddy S, Mehrotra N, Paintal HS. Electronic cigarettes and thirdhand tobacco smoke: two emerging health care challenges for the primary care provider. Int J Gen Med 2011; **4**: 115-20.
25. Lee S, Kimm H, Yun JE, Jee SH. Public health challenges of electronic cigarettes in South Korea. J Prev Med Public Health 2011; **44**: 235-41.
26. Maziak W, Rastam S, Ibrahim I, Ward KD, Eissenberg T. Waterpipe-associated particulate matter emissions. Nicotine Tob Res 2008; **10**: 519-23.
27. Polosa R, Caponnetto P, Morjaria JB, Papale G, Campagna D, Russo C. Effect of an electronic nicotine delivery device (e-Cigarette) on smoking reduction and cessation: a prospective 6-month pilot study. BMC Public Health 2011; **11**: 786.
28. Protano C, Andreoli R, Manini P, Guidotti M, Vitali M. A tobacco-related carcinogen: assessing the impact of smoking behaviours of cohabitants on benzene exposure in children. Tob Control 2012; **21**: 325-9.
29. Protano C, Vitali M. The new danger of thirdhand smoke: why passive smoking does not stop at secondhand smoke. Environ Health Perspect 2011; **119**: A422.
30. Riker CA, Lee K, Darville A, Hahn EJ. E-cigarettes: promise or peril? Nurs Clin North Am 2012; **47**: 159-71.
31. Saade G, Seidenberg AB, Rees VW, Otrock Z, Connolly GN. Indoor secondhand tobacco smoke emission levels in six Lebanese cities. Tob Control 2010; **19**: 138-42.
32. Siegel MB, Tanwar KL, Wood KS. Electronic cigarettes as a smoking-cessation: tool results from an online survey. Am J Prev Med 2011; **40**: 472-5.
33. Suzuki T, Tomiyama H, Higashi Y. Vascular dysfunction even after 20 years in children exposed to passive smoking: alarming results and need for awareness. Arterioscler Thromb Vasc Biol 2012; **32**: 841-2
34. Tinghino B, Enea D. E-cigarette: primi dati e possibili prospettive. Tabaccologia 2009; **2-3**: 36-9.
35. Tytgat J. "Super Smoker" Expert Report. Leuven, Belgium: Catholic University of Leuven 2007. Available online: truthaboutecigs.com/science/15.pdf (last accessed 2012 Jan 05).
36. United States Department of Health and Human Services. The health consequences of involuntary smoking: a report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control

and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2006.
37. Valance C, Ellicott M. Analysis of Chemical Components from High, Med & Low Nicotine Cartridges. Lancashire, UK: Blackburn Micro Tech Solutions 2008. Available online: truthaboutecigs.com/science/12.pdf (last accessed 2012 Jan 05).
38. Vansickel AR, Cobb CO, Weaver MF, Eissenberg TE. A clinical laboratory model for evaluating the acute effects of electronic "cigarettes": nicotine delivery profile and cardiovascular and subjective effects. Cancer Epidemiol Biomarkers Prev 2010; **19**: 1945-53.
39. Wagener TL, Siegel M, Borrelli B. Electronic cigarettes: achieving a balanced perspective. Addiction 2012 Apr 4. Doi: 10.1111/j.1360-0443.2012.03826.x.
40. White AR, Rampes H, Liu JP, Stead LF, Campbell J. Acupuncture and related interventions for smoking cessation. Cochrane Database Syst Rev 2011; 19: CD000009.
41. Wollscheid KA, Kremzner ME. Electronic cigarettes: Safety concerns and regulatory issues. Am J Health-Syst Pharm 2009; **66**: 1740-2.
42. World Health Organization (WHO). Marketers of electronic cigarettes should halt unproved therapy claims. 19 September 2008. Available online: www.who.int/mediacentre/news/releases/2008/pr34/en/ (last accessed 2012 Jan 05).
43. World Health Organization (WHO). WHO Air quality guidelines for particulate matter, ozone, nitrogen dioxide and sulfur dioxide. Global update 2005. Summary of risk assessment. Geneva, Switzerland: WHO Press, 2006.

Corresponding author: Prof. Maria Sofia Cattaruzza, Department of Public Health and Infectious Diseases, Sapienza University of Rome, P.le Aldo Moro 5, 00185 Rome, Italy
e-mail: mariasofia.cattaruzza@uniroma1.it