Harmful and potentially harmful constituents in e-Cigarettes

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Global Forum on Nicotine | 27-28 June 2014 | Warsaw

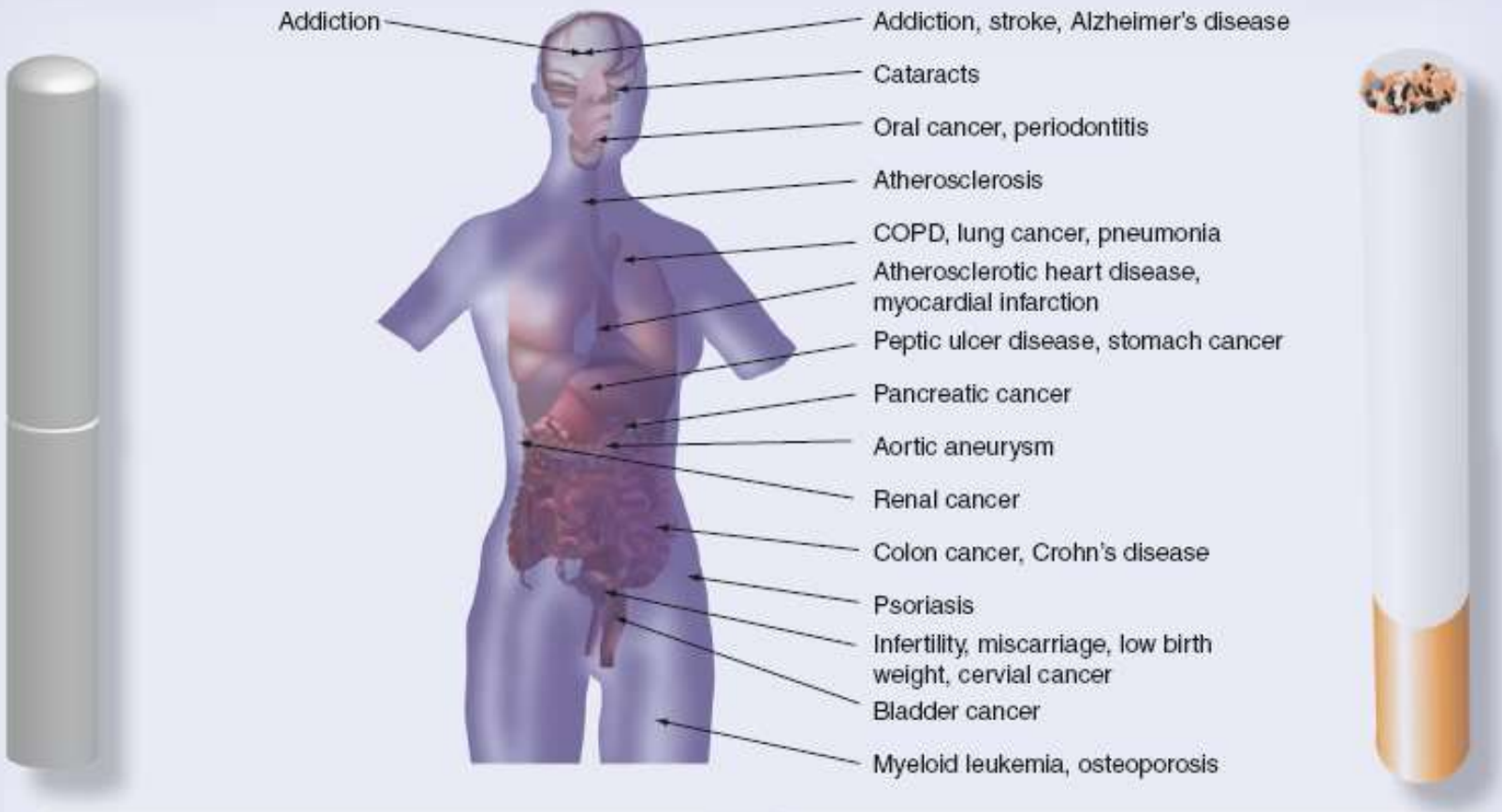
Conflict of interest – Riccardo Polosa

- I am full Professor of Internal Medicine and I am supported by the University of Catania, Italy.
- I undertake research and consultancy for pharma companies that develop and manufacture smoking cessation medications (i.e. Pfizer, GlaxoSmithKline and Novartis) as well as for E-cig and E-liquid companies.
- I served a consultancy role for the Global Health Alliance for treatment of tobacco dependence, and LIAF (the Italian Anti Smoking League).

e-Cigarette facts

No tobacco, no combustion

Tobacco, and combustion



Electronic cigarette contains:

Propylene glycol, glycerin, nicotine and food flavoring

Traditional cigarette contains:

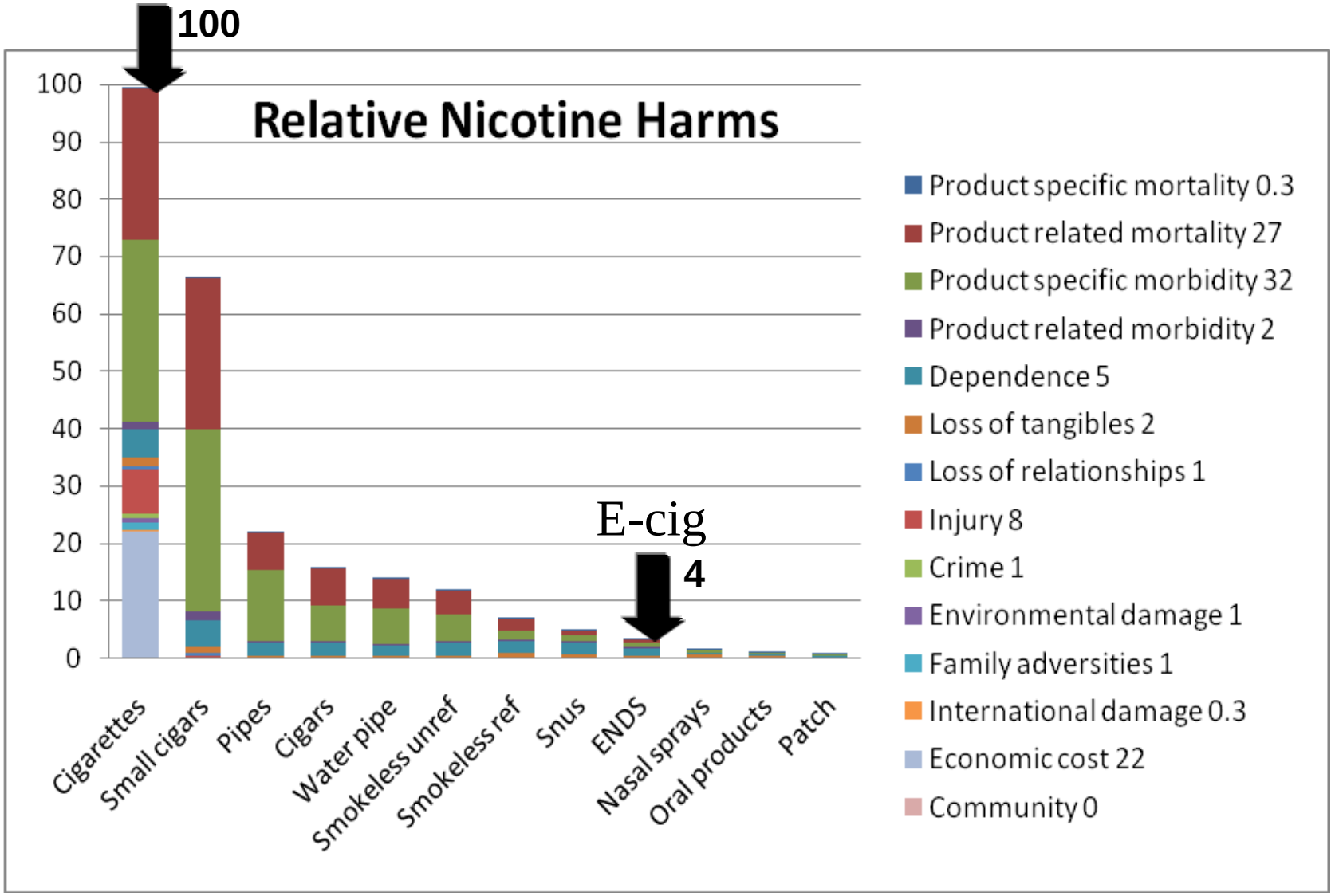
Nicotine, benzene, formaldehyde, lead, tar, methanol, hydrogen cyanide, butane, ammonia, chloroform, carbon monoxide, acetone, nitrosamines, aluminum, carbon dioxide, cadmium, arsenic, ethanol, vinyl chloride, radon, +3500 more chemicals and +50 known carcinogens

Vaporisation of nicotine-containing solvents

Nicotine facts

- Nicotine is a neurostimulant (NOT a poison)
- Nicotine IS NOT the reason for smoking-related disease
  - Officially IS NOT a carcinogen (IARC)
  - DOES NOT cause lung disease
  - Has minimal effect in CVD
- Even in e-cigarettes, it is NOT nicotine but other chemicals that may be problematic

Nicotine containing products – risk estimates



DJ Nutt, LD Phillips, D Balfour, HV Curran, M Dockrell, J Foulds, K Fagerstrom, K Letlape, A Milton, R Polosa, J Ramsey, D Sweanor. Estimating the harms of nicotine-containing products using the MCDA approach. Eur J Addiction 2014

Polosa *et al. Harm Reduction Journal* 2013, **10**:19
http://www.harmreductionjournal.com/content/10/1/19

HARM REDUCTION JOURNAL

REVIEW Open Access

A fresh look at tobacco harm reduction: the case for the electronic cigarette

Riccardo Polosa[1,2*], Brad Rodu[3], Pasquale Caponnetto[1], Marilena Maglia[1] and Cirino Raciti[1]

Abstract

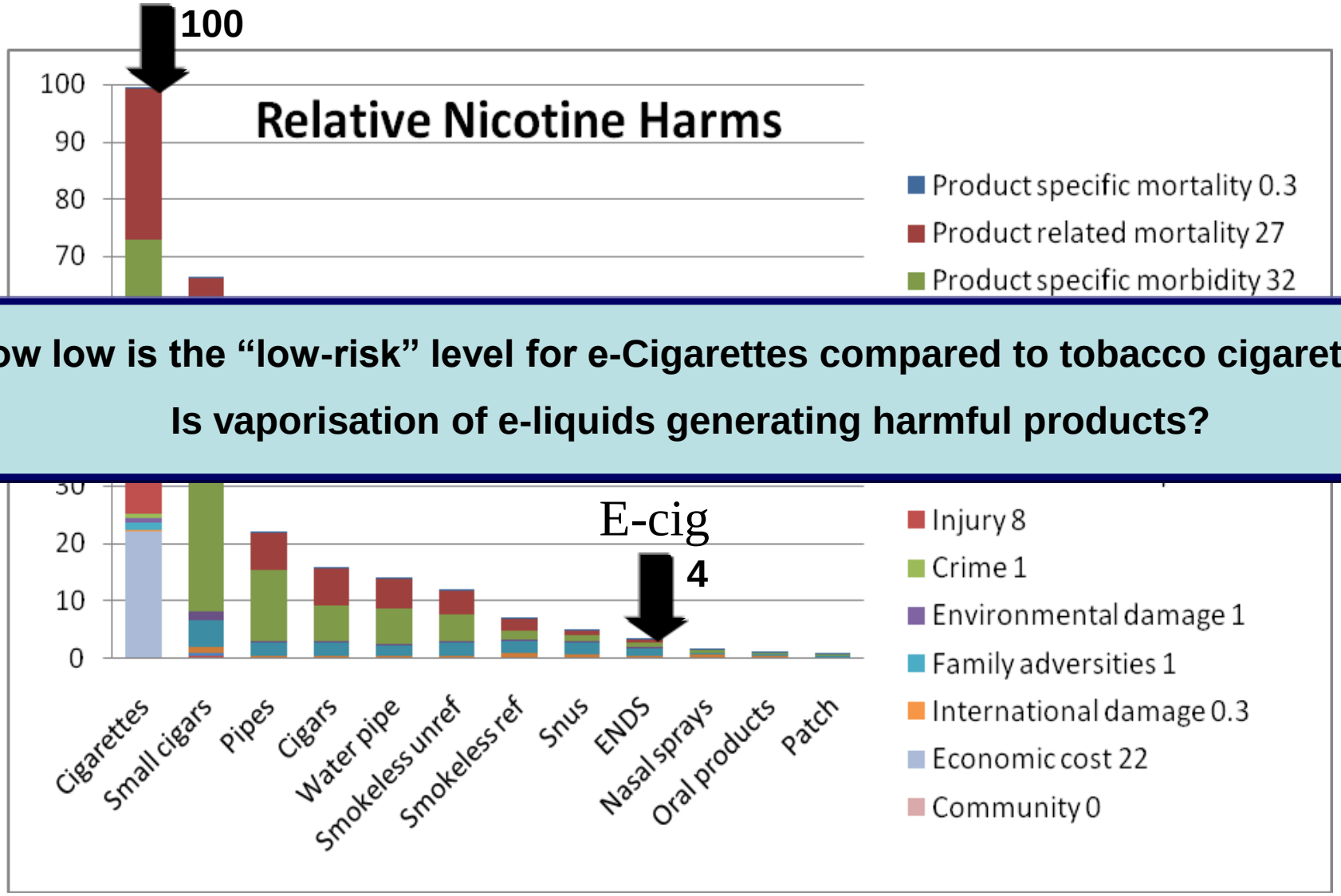
Smokers of any age can reap substantial health benefits by quitting. In fact, no other single public health effort is likely to achieve a benefit comparable to large-scale smoking cessation. Surveys document that most smokers would like to quit, and many have made repeated efforts to do so. However, conventional smoking cessation approaches require nicotine addicted smokers to abstain from tobacco and nicotine entirely. Many smokers are unable – or at least unwilling – to achieve this goal, and so they continue smoking in the face of impending

Tobacco harm reduction (THR), the substitution of low-risk nicotine containing products (e.g. e-Cigarettes) for cigarette smoking, may offer huge public health benefits.

Vaping is an alternative to smoking.

e-Cigarettes should be marketed for smokers only.

Harm reduction categories – risk estimates



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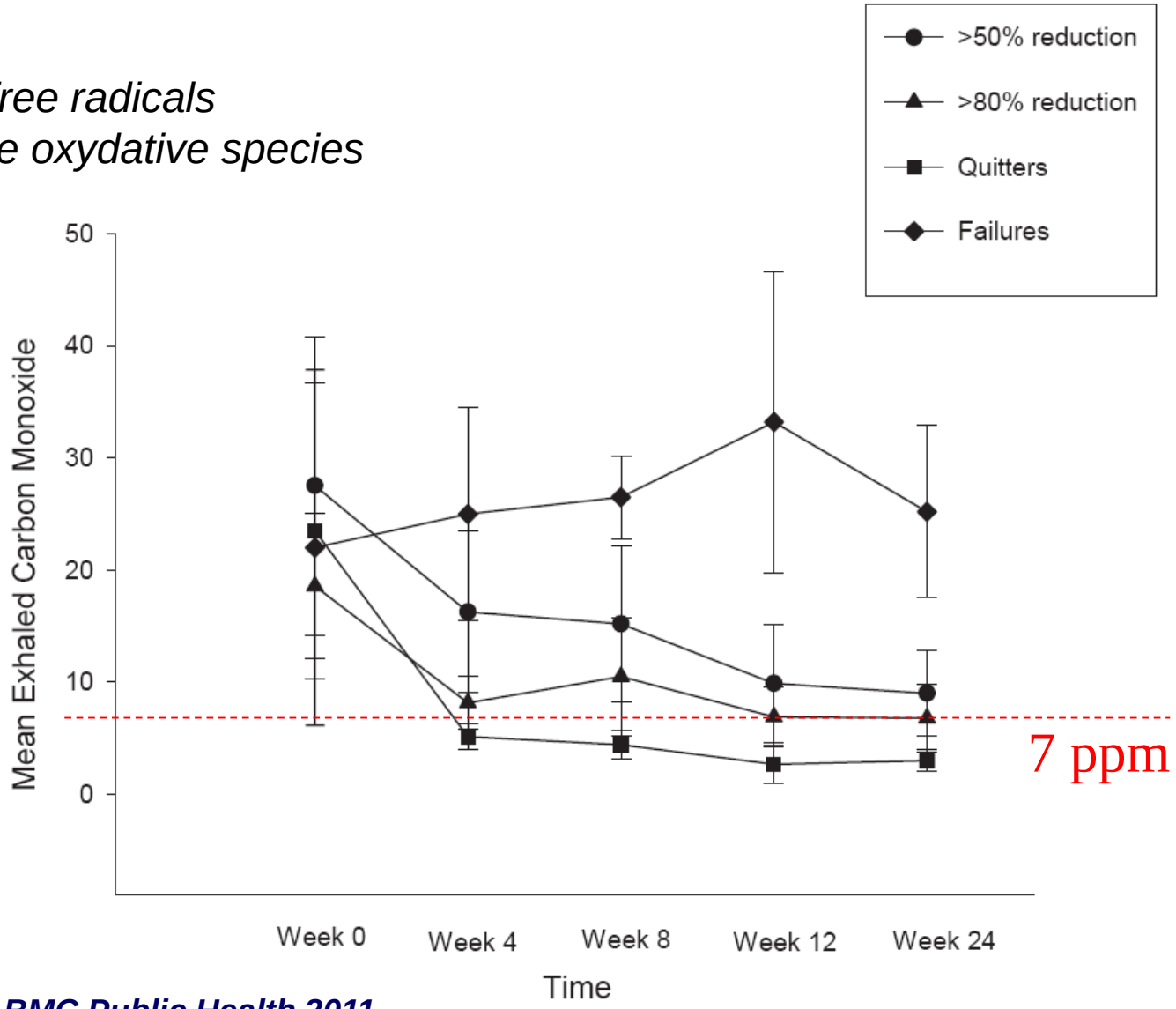
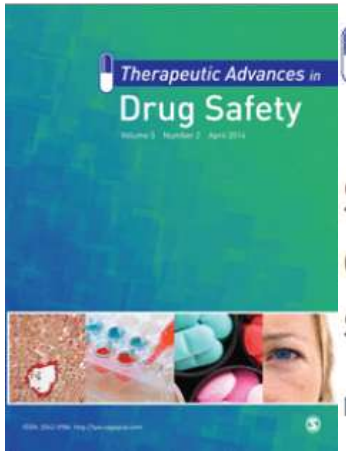
Exhaled CO in ECIG users

- *eCO*
- *Stable free radicals*
- *Reactive oxydative species*



R. Polosa et al. BMC Public Health 2011

Harmful and potentially harmful constituents



Therapeutic Advances in Drug Safety Review

Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review

Konstantinos E. Farsalinos and Riccardo Polosa

Ther Adv Drug Saf
1–20
DOI: 10.1177/2042098614524430

Nicotine

Main ingredients (PG/VG)

Flavorings

Impurities-other

Nicotine toxicity in e-cigs

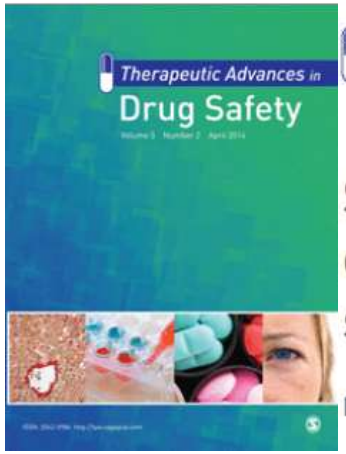
Table 4. Myocardial cell viability according to nicotine concentration of the electronic cigarette samples tested at 3.7 volts (6.2 watts).

Viability according to nicotine concentration (mg/mL)			
Extract concentrations	**6–11 (n = 9)**	**12–24 (n = 11)**	***p* ***
100%	89.5 ± 14.1%	74.8 ± 37.1%	0.247
50%	98.6 ± 6.7%	83.6 ± 30.6%	0.141
25%	97.4 ± 5.2%	97.3 ± 8.9%	0.981
12.5%	98.3 ± 3.7%	102.0 ± 7.3%	0.181
6.25%	98.1 ± 3.7%	100.5 ± 6.8%	0.357

Nicotine concentration is NOT associated with cytotoxicity

Farsalinos et al, Int J Environm Res Public Health 2013

Harmful and potentially harmful constituents



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Main ingredients (PG/VG)

- Animal studies showed that PG is safe for inhalation (Robertson et al, J Pharmacol Exp Ther 1947)
- Theatrical fog exposure in actors causes irritation but no long-term health implications (Varughese et al, Am J Ind Med 2005; American Chemistry Council, 2003)
- Theatrical fog is not USP-grade PG, added oils to increase fog thickness
- Glycerol inhalation caused mild changes in the upper respiratory tract in rats (Renne et al, Inhal Toxicol 1992)
- PG/VG added to tobacco does not elevate toxicity, but tobacco cigarette is already highly toxic

Main ingredients (PG/VG)

Table 2. Myocardial cell viability in cigarette smoke extract and in electronic cigarette vapour extracts produced at 3.7 volts.

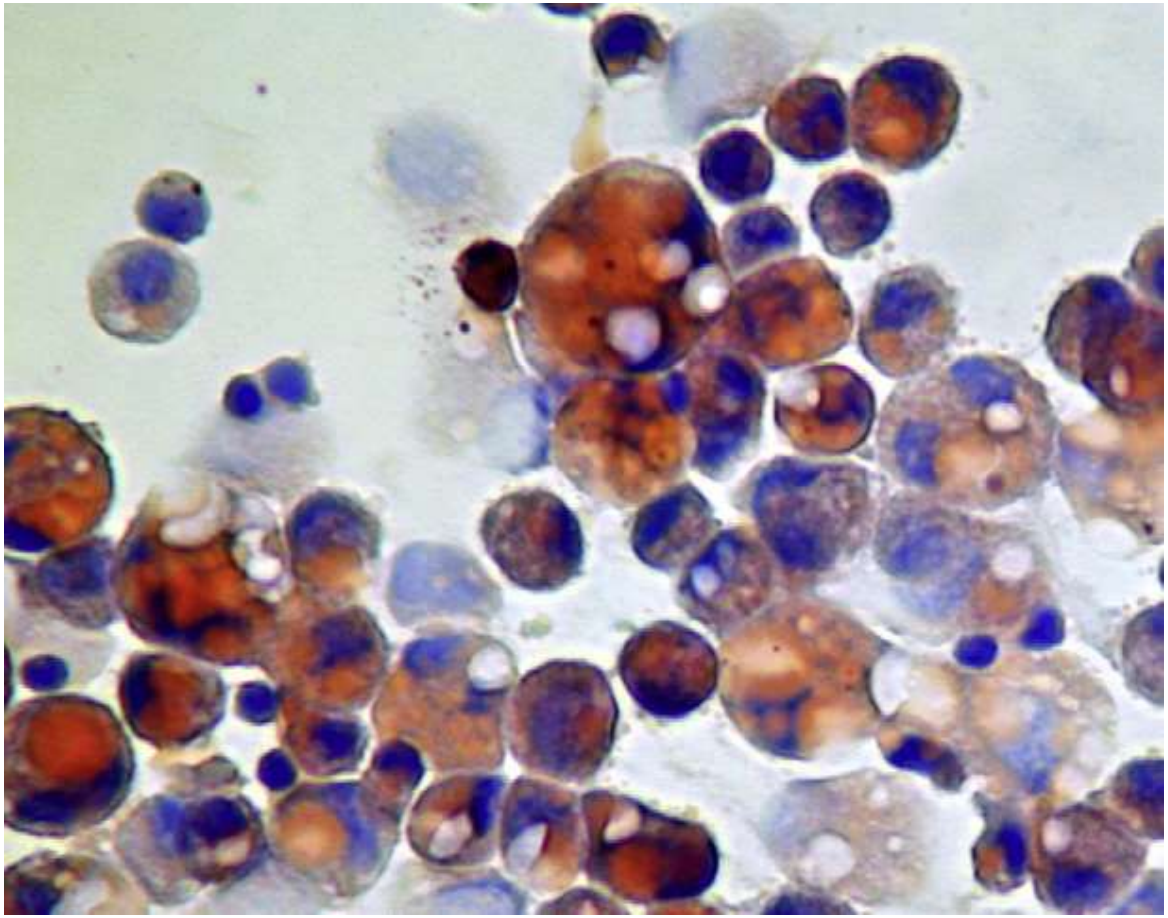
	Dilutions					
Samples-nicotine (mg/mL)	100% [a]	50% [b]	25% [c]	12.5% [d]	6.25% [e]	*p* *
Base-0	105.1 ± 1.2	103.5 ± 1.9	101.3 ± 4.2	100.7 ± 3.4	100.4 ± 2.3	0.251
Golden Margy-6	89.2 ± 0.2	93.0 ± 2.2	92.1 ± 1.3	95.3 ± 3.6	93.0 ± 6.3	0.361
RY69-6	98.9 ± 4.6	101.2 ± 5.4	96.0 ± 13.0	100.5 ± 2.7	100.2 ± 9.2	0.932
City-6						0.282
Cinnamon Cookies-6						<0.001
Golden Virginia-8					97.1 ± 1.4	<0.001
RY4-9	73.8 ± 3.7	106.6 ± 1.1	104.4 ± 1.9	103.6 ± 4.0	100.7 ± 0.8	<0.001
MaxBlend-9	104.4 ± 1.6	102.4 ± 2.0	102.4 ± 2.8	101.2 ± 7.6	102.7 ± 2.0	0.901
Americano-9	85.0 ± 2.0	98.3 ± 1.7	90.9 ± 4.4	94.7 ± 3.5	94.1 ± 5.9	0.017
American Tobacco-11	109.0 ± 1.6	106.8 ± 0.5	104.9 ± 1.0	101.3 ± 3.1	103.6 ± 2.5	0.007
Tribeca-12	110.8 ± 2.8	103.9 ± 5.5	106.6 ± 7.9	102.4 ± 5.1	101.7 ± 3.0	0.268
Gr						
El Toro						

Base liquid = 50% PG and 50% VG
NO CYTOTOXICITY

Farsalinos et al, *Int J Environm Res Public Health 2013*

Main ingredients (PG/VG)

e-liquid and lipoid pneumonia?



Oil red O staining of alveolar macrophages recovered by BAL showing their cytoplasm full of large rounded lipid vacuoles

CHEST Postgraduate Education Corner

PULMONARY AND CRITICAL CARE PEARLS

An Unexpected Consequence of Electronic Cigarette Use

Lindsay McCauley, DO; Catherine Markin, MD, FCCP; and Danielle Hosmer, MD

CHEST 2012; 141(4):1110–1113

A 42-year-old woman was admitted to the hospital with a 7-month history of dyspnea, productive cough, and subjective fevers. She had been seen multiple times in the ED with similar complaints and had received several courses of antibiotics.

The patient had recently started using electronic cigarettes (e-cigarettes), about 7 months prior, which coincided with the onset of her respiratory symptoms. Her past medical history also was significant for asthma, reported rheumatoid arthritis, fibromyalgia, schizoaf-

Laboratory Tests and Imaging Findings

Laboratory findings showed a WBC count of 18.0 ($\times 10^3$) with a normal differential and hemoglobin level of 11.2 g/dL. The chemistry panel and brain natriuretic peptide levels were normal. Chest radiographic imaging showed new multifocal bilateral opacities. CT images (Fig 1) revealed extensive bilateral upper- and lower-lobe patchy ground glass pulmonary opacities in a "crazy paving" pattern. Results of an HIV test were negative. Results of a nasal *Pertussis* polymerase chain reaction swab were negative. Results of urine *Legionella* antigen and serum *Mycoplasma*

CHEST Postgraduate Education Corner

PULMONARY AND CRITICAL CARE PEARLS

An Unexpected Consequence of Electronic Cigarette Use

Secondary school chemistry

Glycerin is an ALCOHOL, not a lipid!!!

A 42-year-o
with a 7-
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The patient had recently started using electronic cigarettes (e-cigarettes), about 7 months prior, which coincided with the onset of her respiratory symptoms. Her past medical history also was significant for asthma, reported rheumatoid arthritis, fibromyalgia, schizoaf-

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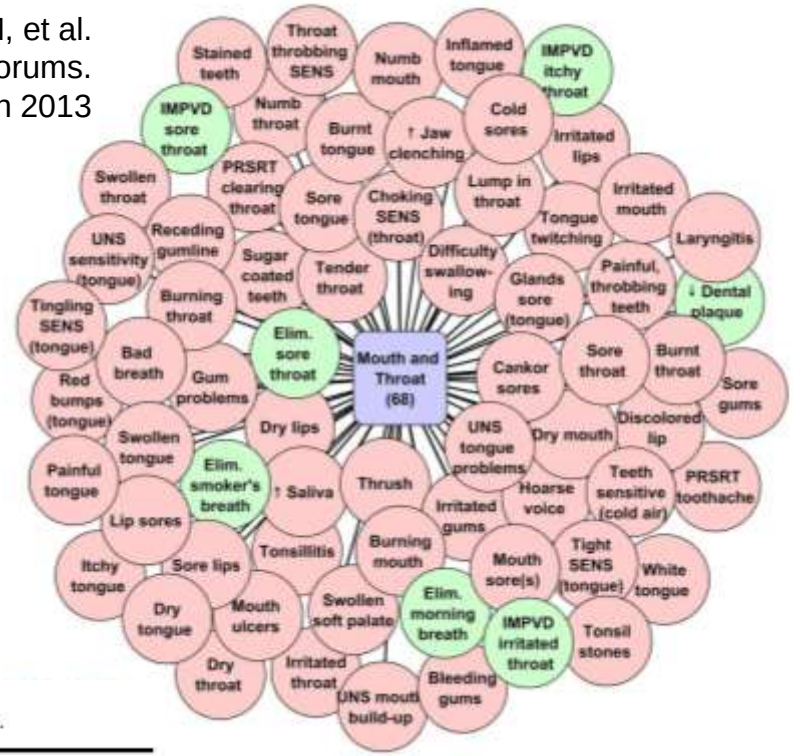
CT images (Fig 1) revealed extensive bilateral upper- and lower-lobe patchy ground glass pulmonary opacities in a "crazy paving" pattern. Results of an HIV test were negative. Results of a nasal *Pertussis* polymerase chain reaction swab were negative. Results of urine *Legionella* antigen and serum *Mycoplasma*

Hua M, et al.
Health-related effects reported by e-cigarette users in online forums.
Journal of medical Internet research 2013



Hypersensitivity response to components in the vapor (e.g. PG) may occur in predisposed individuals.

Farsalinos K, et al.
Characteristics, Perceived Side Effects and Benefits of E-Cigarette Use: A Worldwide Survey of More than 19,000 Consumers.
Int J Environ Res Public Health 2014

Table 4. Side effects and accidents associated with electronic cigarette use.

Side effects/accidents [1]	Total (n = 19,353)	Current smokers (n = 3682)	Former smokers (n = 15,671)	Statistic	*p* value
Sore or dry mouth and throat	7520 (38.9)	1441 (39.1)	6079 (38.8)	$\chi^2 = 0.1$	0.699
Headache	2140 (11.1)	433 (11.8)	1707 (10.9)	$\chi^2 = 2.3$	0.131
Gingivitis/gum bleeding	2534 (13.1)	273 (7.4)	2261 (14.4)	$\chi^2 = 128.8$	<0.001
Mouth or tongue sores/inflammation	973 (5.0)	151 (4.1)	822 (5.2)	$\chi^2 = 8.2$	0.004
Black tongue	145 (0.7)	31 (0.8)	114 (0.7)	$\chi^2 = 0.5$	0.469
Nose bleeding	601 (3.1)	84 (2.3)	517 (3.3)	$\chi^2 = 10.3$	0.001
Cough	2475 (12.8)	556 (15.1)	1919 (12.2)	$\chi^2 = 21.8$	<0.001
Dizziness	991 (5.1)	196 (5.3)	795 (5.1)	$\chi^2 = 0.4$	0.536
Sleepiness	661 (3.4)	139 (3.8)	522 (3.3)	$\chi^2 = 1.8$	0.182
Sleeplessness	1211 (6.3)	202 (5.5)	1009 (6.4)	$\chi^2 = 4.6$	0.032
Heart palpitations	959 (5.0)	216 (5.9)	743 (4.7)	$\chi^2 = 8.0$	0.005
Breathing difficulties	395 (2.0)	91 (2.5)	304 (1.9)	$\chi^2 = 4.2$	0.040
Allergies	343 (1.8)	57 (1.5)	286 (1.8)	$\chi^2 = 1.3$	0.252

RESPIRATORY AEs AFTER E-CIG USE

Side effects/accidents	Total (n = 19,353)	Current smokers (n = 3682)	Former smokers (n = 15,671)	Statistic	*p* value
		Dual users	Single users		
Asthma (N = 1173)					
Worse	14 (1.1)	5 (2.2)	9 (0.8)		
Stable	303 (23.2)	78 (34.4)	225 (20.8)	$\chi^2 = 27.3$	<0.001
Improved	856 (65.4)	116 (51.1)	742 (68.6)		
COPD (N = 1062)					
Worse	10 (0.8)	4 (1.7)	6 (0.6)		
Stable	151 (12.7)	39 (17.0)	112 (11.7)	$\chi^2 = 9.5$	0.009
Improved	901 (75.7)	158 (68.7)	743 (77.4)		

Farsalinos K, et al.
Characteristics, Perceived Side Effects and Benefits of E-Cigarette Use: A Worldwide Survey of More than 19,000 Consumers.
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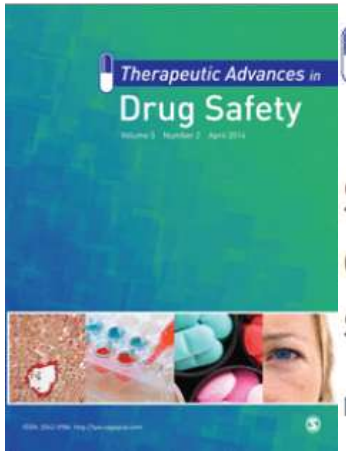
Harmful and potentially harmful constituents



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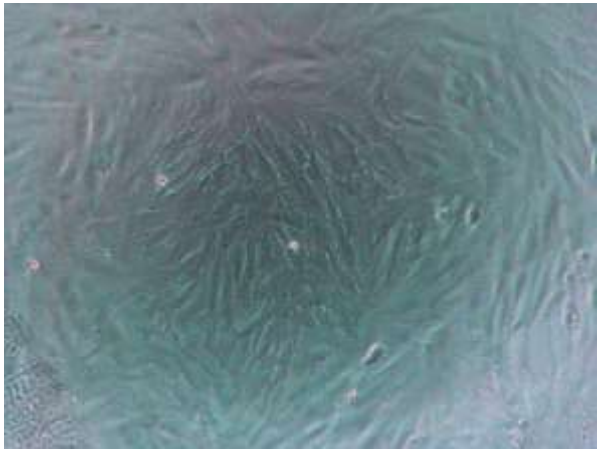
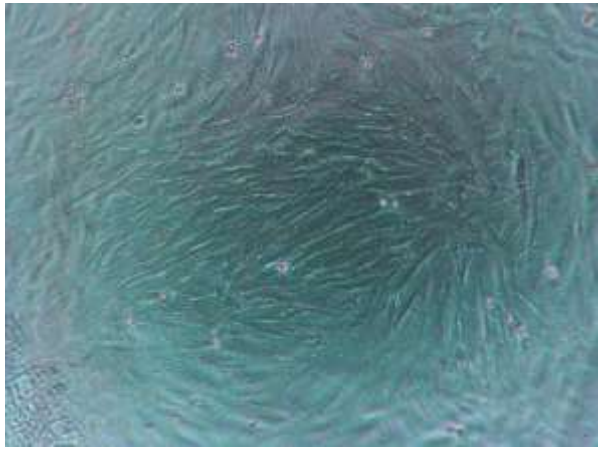
Impurities-other

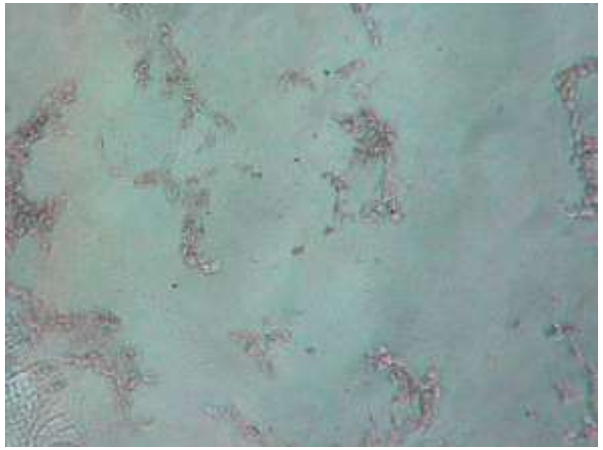
Toxicological studies



Untreated cells

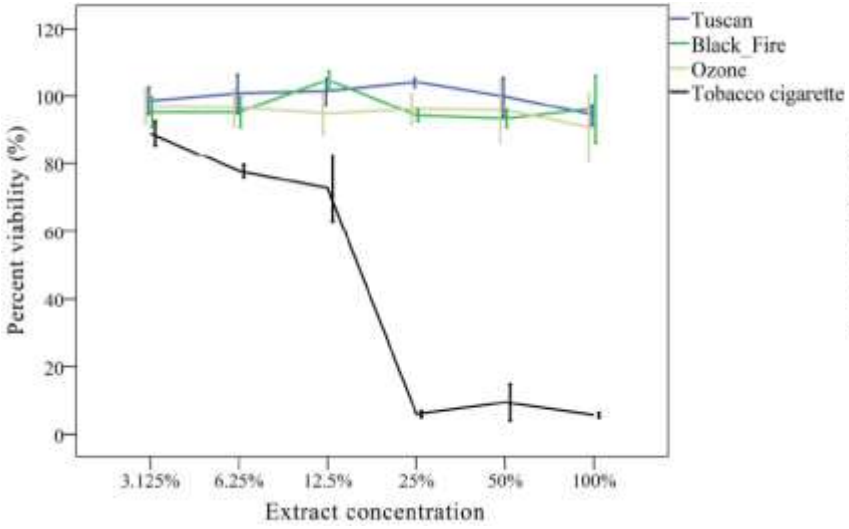


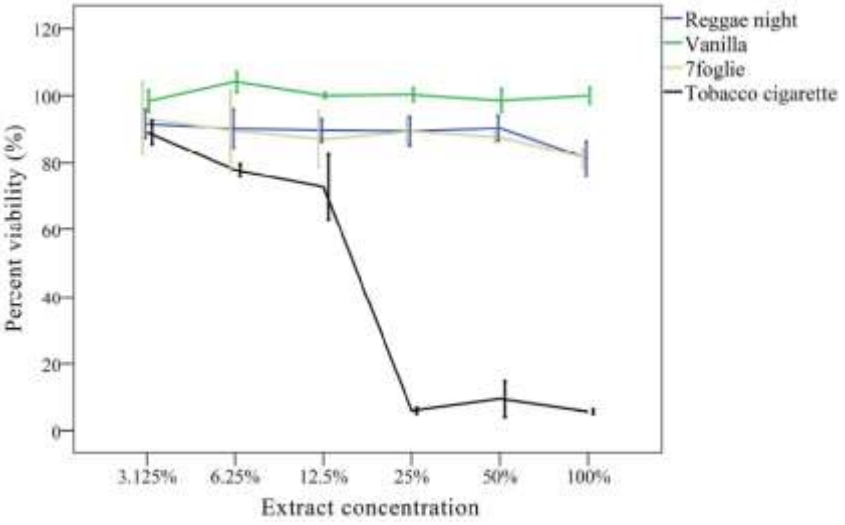
E-cigarette vapor treated cells

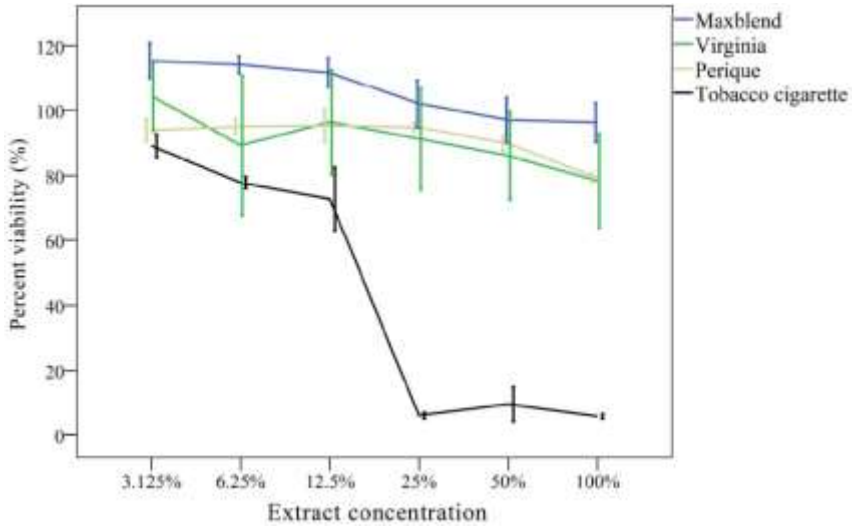


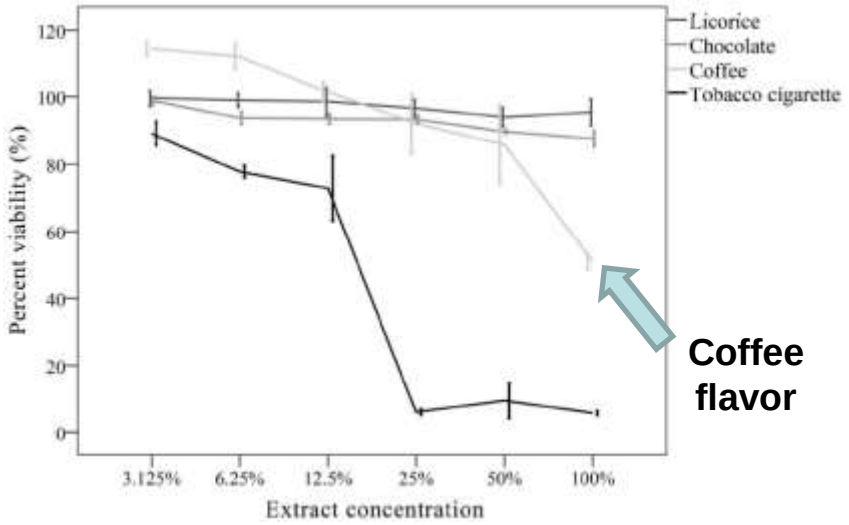
Cigarette smoke treated cells

Flavourings: coffee cytotoxicity



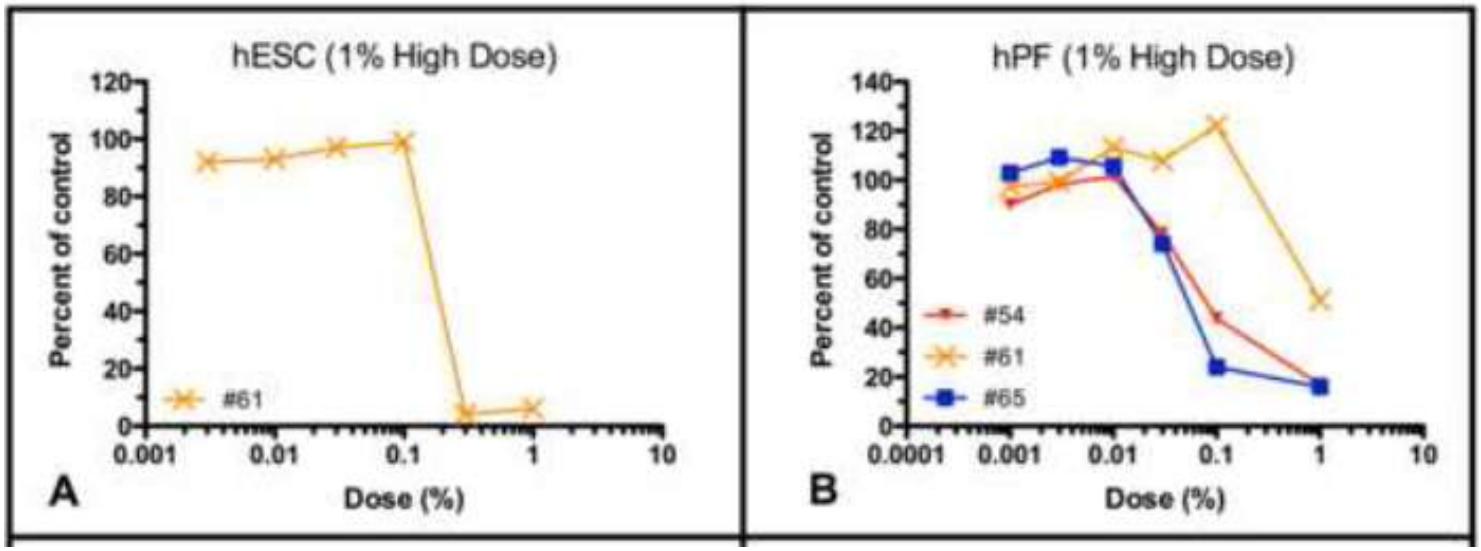


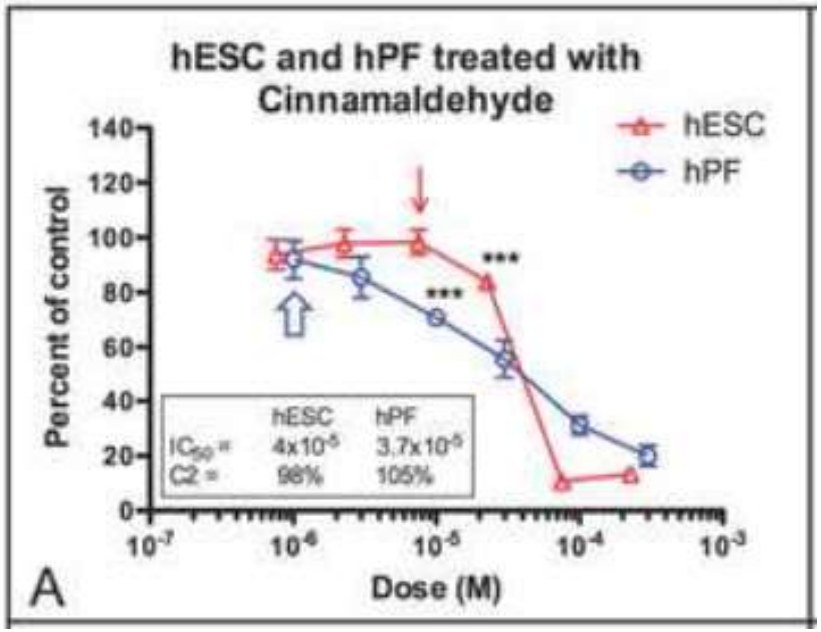




Romagna, Farsalinos et al, Inhal Toxicol 2013

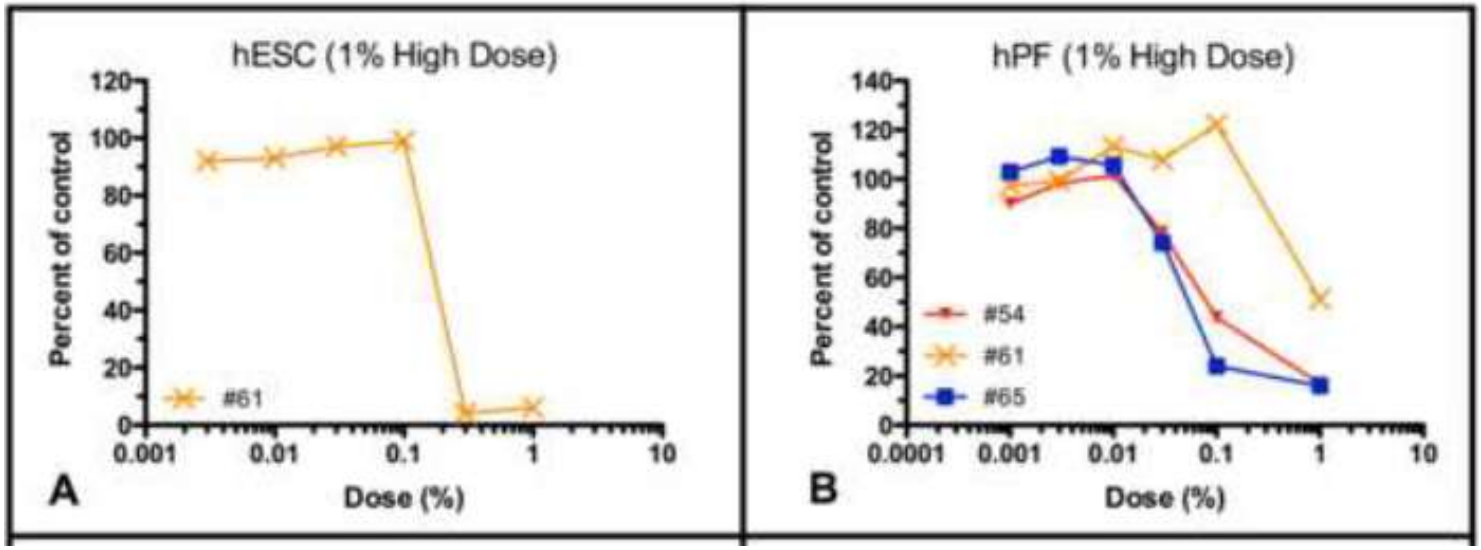
Flavourings: cinnamon cytotoxicity

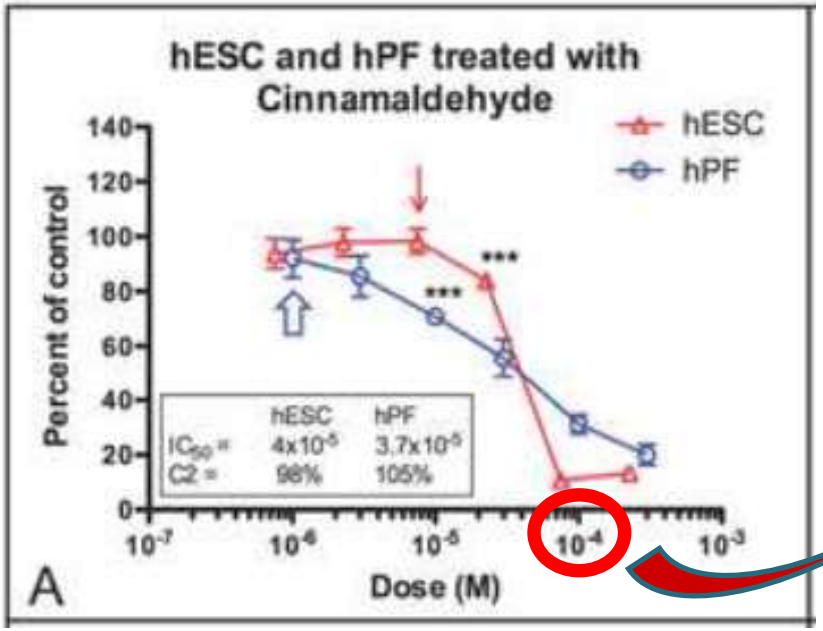




Behar et al, *Toxicol in Vitro* 2013

Flavourings: cinnamon cytotoxicity



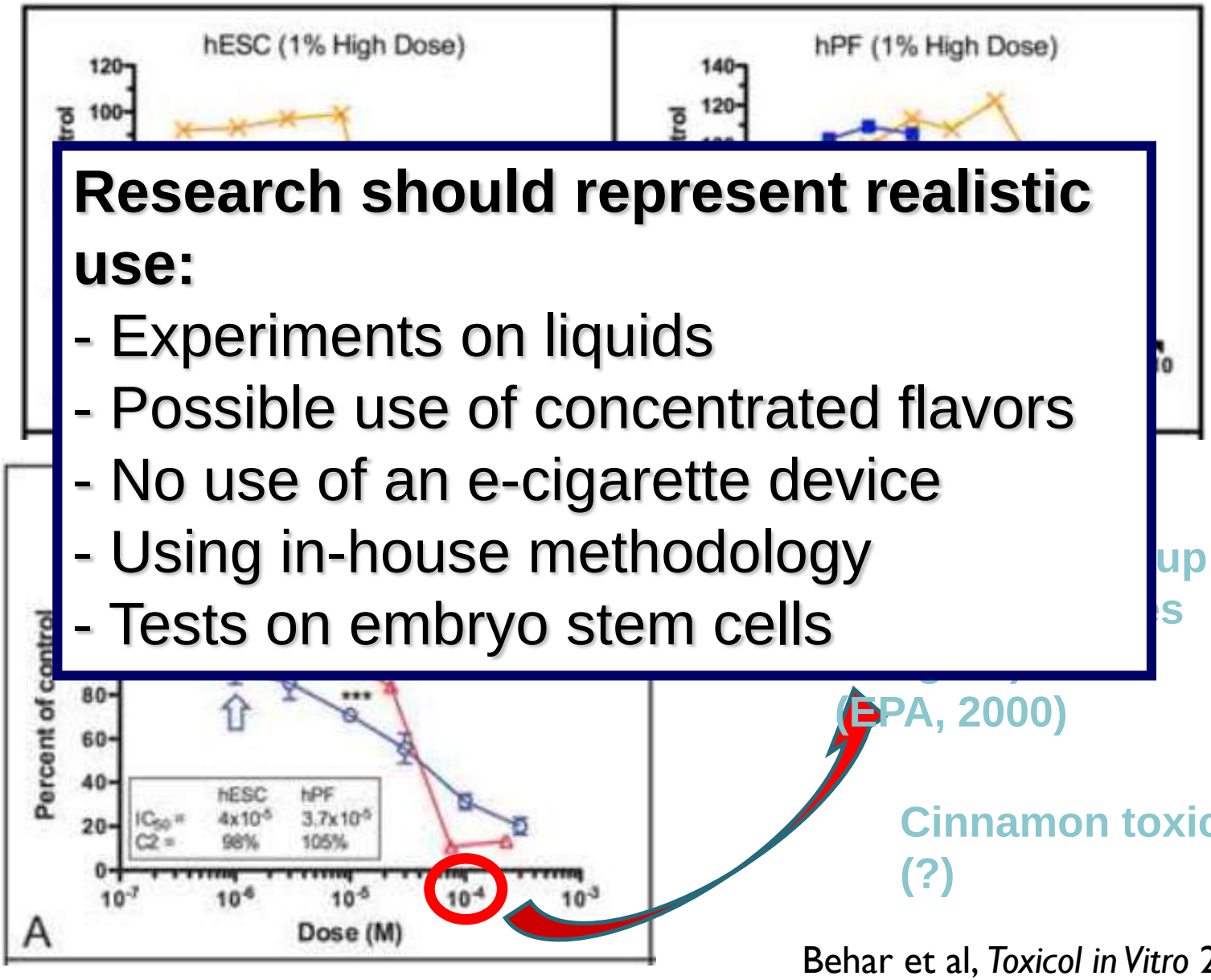


Approved cinnamaldehyde dose up to 4 x 10^{-2} M (400 times higher) (EPA, 2000)

Cinnamon toxicity (?)

Behar et al, *Toxicol in Vitro* 2013

Flavourings: cinnamon cytotoxicity



Research should represent realistic use:

- Experiments on liquids
- Possible use of concentrated flavors
- No use of an e-cigarette device
- Using in-house methodology
- Tests on embryo stem cells

up
s

(EPA, 2000)

Cinnamon toxicity (?)

Behar et al, *Toxicol in Vitro* 2013

Flavourings: diacetyl and acetyl propionyl

E-cigarette liquids are available in a variety of flavorings

In most cases, they are safe for ingestion (but safety not assessed for inhalation)

Diacetyl (DA) and acetyl propionyl (AP) are used for their buttery taste in a variety of food preparations; they are safe (and approved) for food use

They can be harmful when inhaled (they cause development of obliterative bronchiolitis)

Farsalinos KE, et al. Evaluation of electronic cigarette liquids and vapour for the presence of selected inhalation toxins. Poster presentation at GFN Warsaw.

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Is there any DA and/or AP in sweet-flavored EC liquids?

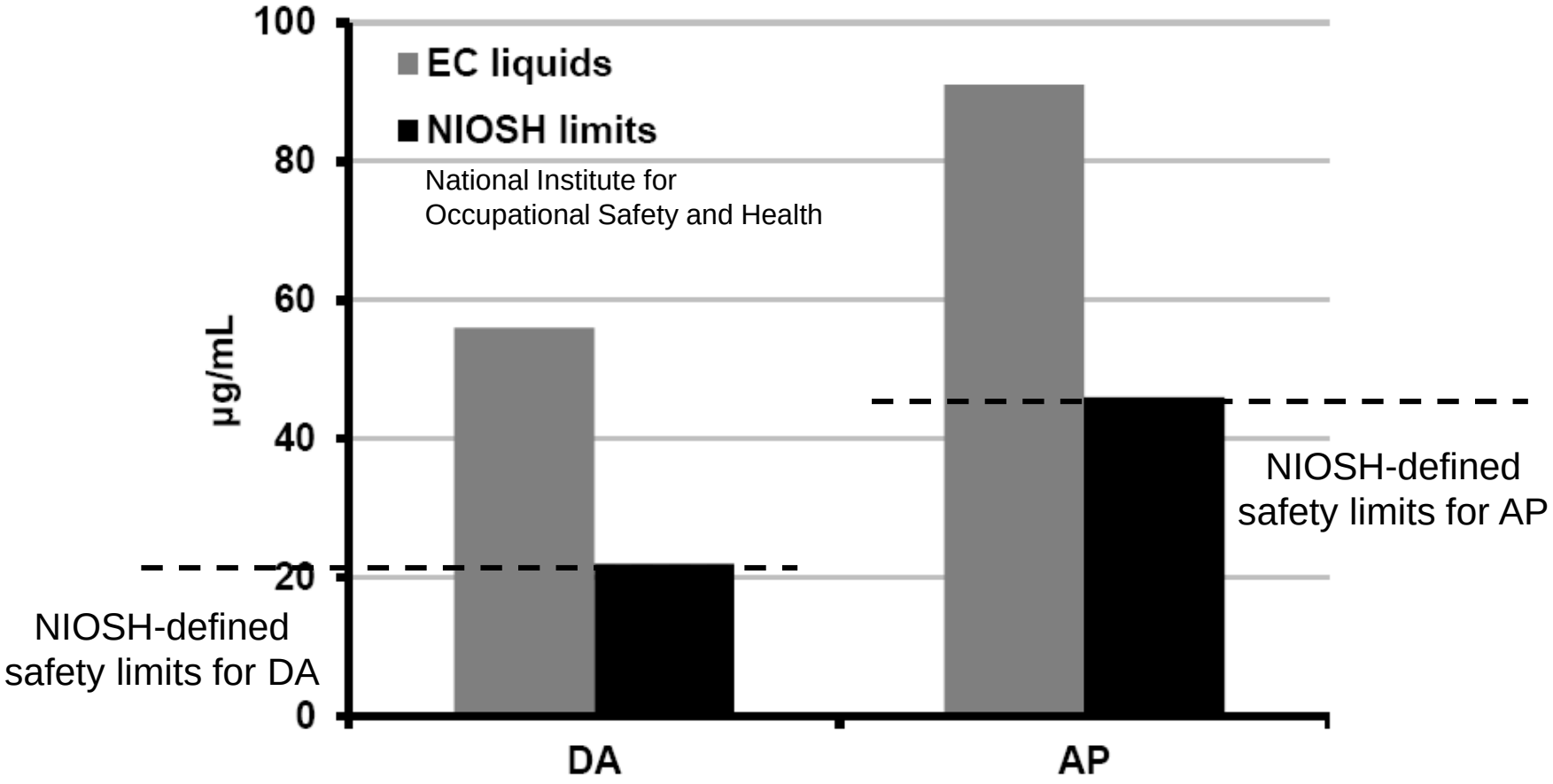
159 e-liquids purchased from 36 manufacturers/retailers; tested for the presence of DA and AP by HPLC.

DA and AP were found in 74.2% of the samples (more samples containing DA)

Farsalinos KE, et al. Evaluation of electronic cigarette liquids and vapour for the presence of selected inhalation toxins. Poster presentation at GFN Warsaw.

Estimated daily exposure to diacetyl (DA) and acetyl propionyl (AP)

(assuming an average daily EC liquid consumption of 3ml)



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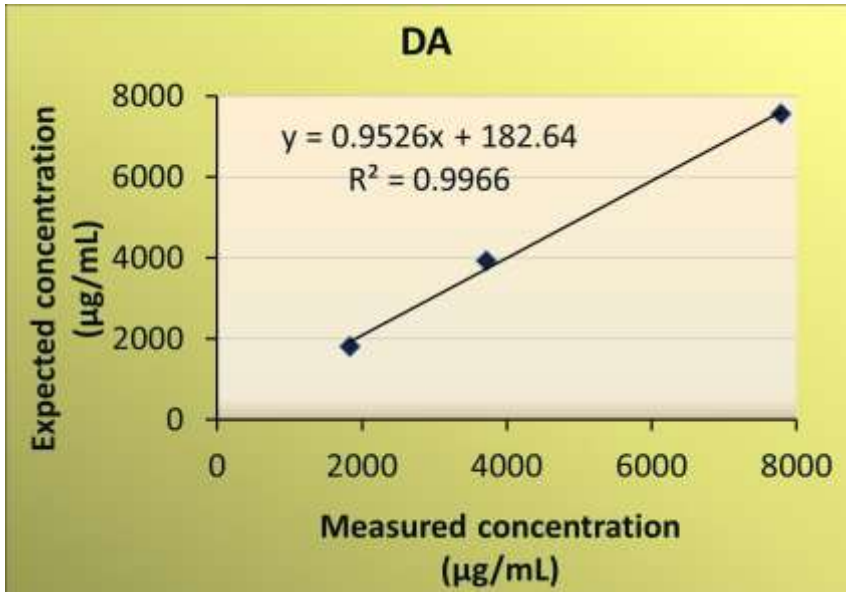
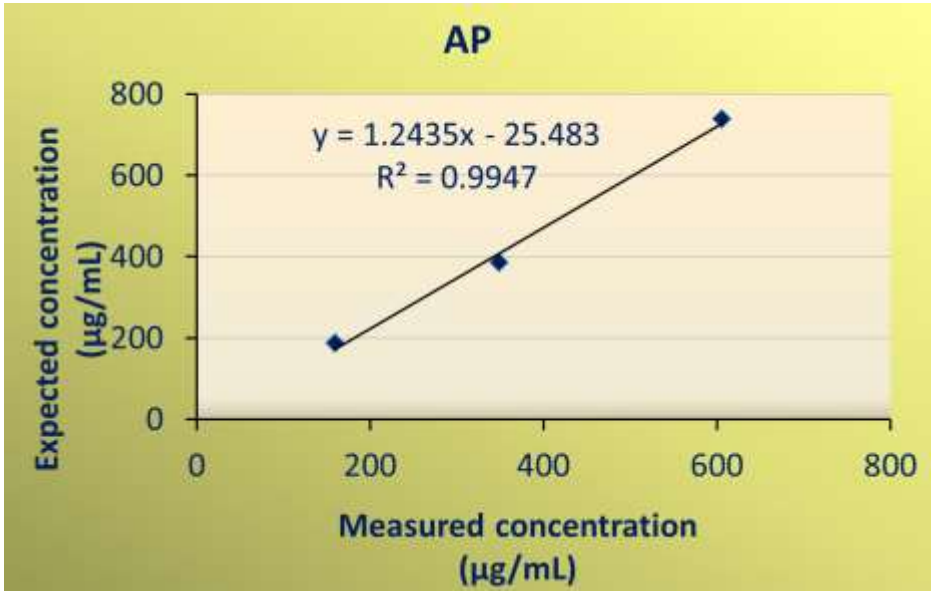
Correlation between expected and measured concentrations of diacetyl (DA) and acetyl propionyl (AP) in vapour





Farsalinos KE, et al. Evaluation of electronic cigarette liquids and vapour for the presence of selected inhalation toxins. Poster presentation at GFN Warsaw.

TABLE I. Amounts of carbonyl compounds determined in the main stream of cigarette smoke from various brands of cigarettes

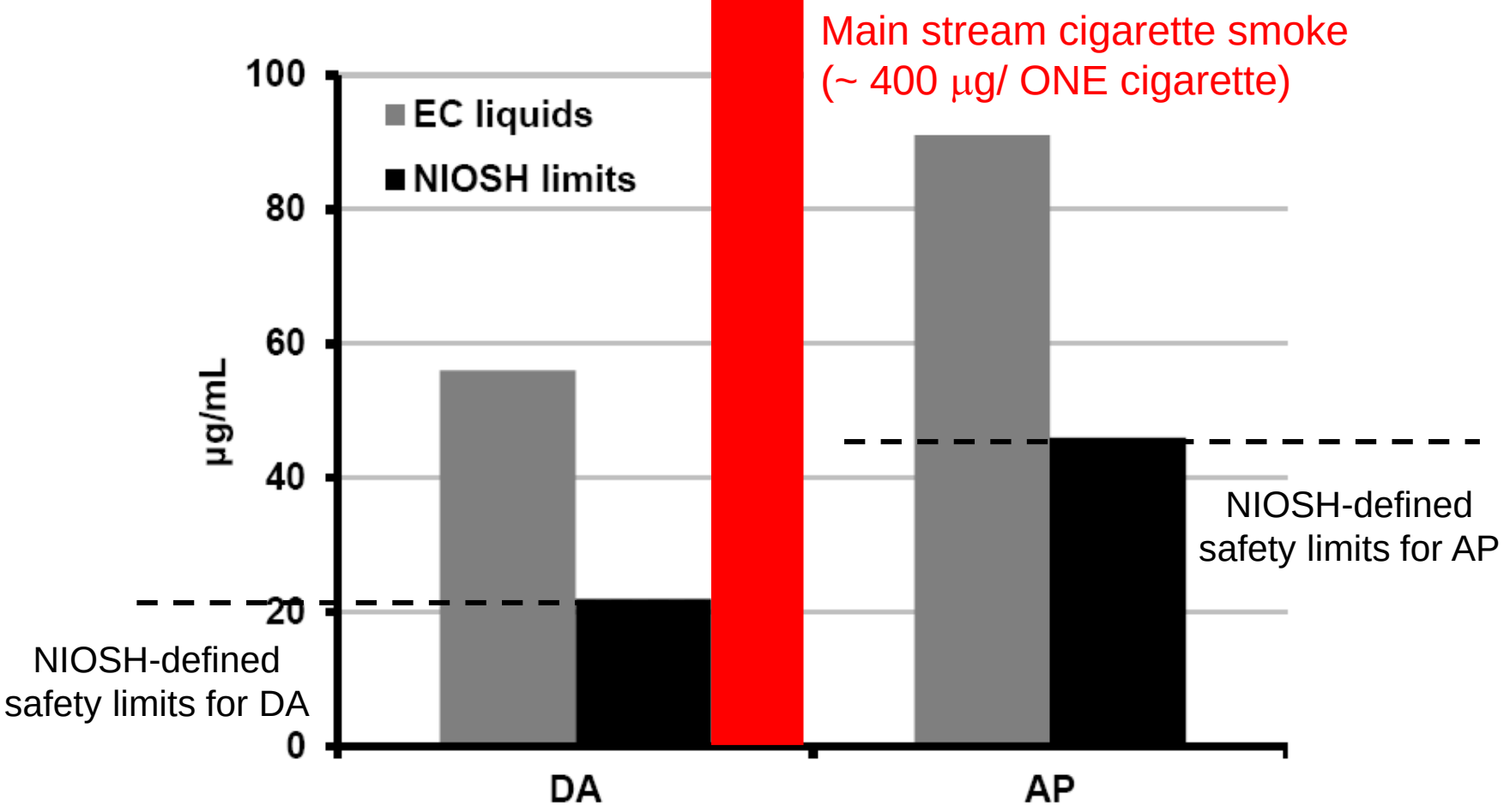
	Amounts (μg/cigarette^{-1})							
Brand	Malonaldehyde	Acrolein	Glyoxal	Methylglyoxal	Diacetyl	Formaldehyde	Acetaldehyde	Propanal
A[a,b]	28.8 ± 0.60	431 ± 13.0	1.93 ± 0.01	13.4 ± 0.10	433 ± 11.0	116 ± 5.00	2040 ± 16.0	167 ± 1.00
B[b,e]	18.9 ± 2.20	220 ± 9.00	2.09 ± 0.1	45.3 ± 0.90	308 ± 19.0	127 ± 7.00	1110 ± 21.0	87.0 ± 3.00
C[b]	28.9 ± 0.90	423 ± 1.00	2.99 ± 0.18	29.1 ± 1.70	335 ± 29.0	194 ± 17.0	1978 ± 16.0	164 ± 1.00
D[b]	26.7 ± 2.00	315 ± 19.0	3.19 ± 0.17	24.1 ± 1.70	349 ± 13.0	114 ± 5.00	1784 ± 49.0	149 ± 5.00
E[b]	29.0 ± 1.10	391 ± 4.00	3.39 ± 0.10	53.5 ± 2.20	359 ± 23.0	165 ± 5.00	1788 ± 25.0	150 ± 2.00
F[b]	28.3 ± 1.40	238 ± 6.00	4.78 ± 0.14	34.2 ± 0.70	355 ± 17.0	121 ± 9.00	1518 ± 63.0	132 ± 6.00
G[b]	29.0 ± 1.00	411 ± 11.0	2.95 ± 0.11	35.0 ± 0.90	303 ± 9.00	135 ± 5.00	1877 ± 39.0	155 ± 2.00
H[b,d]	26.2 ± 0.10	405 ± 5.00	2.76 ± 0.23	23.6 ± 1.70	320 ± 14.0	149 ± 5.00	1788 ± 20.0	148 ± 1.00
I[b,d]	24.4 ± 0.80	419 ± 27.0	2.94 ± 0.11	27.0 ± 2.60	311 ± 16.0	153 ± 1.00	1709 ± 22.0	141 ± 1.00
J[b]	24.2 ± 0.80	288 ± 4.00	2.61 ± 0.11	20.4 ± 0.70	307 ± 8.00	87.0 ± 3.00	1511 ± 31.0	123 ± 4.00
K[b,d]	21.0 ± 0.80	321 ± 10.0	3.05 ± 0.07	30.6 ± 0.60	345 ± 12.0	149 ± 5.00	1573 ± 24.0	129 ± 2.00
L[b,d]	28.7 ± 0.60	418 ± 32.0	2.21 ± 0.10	27.8 ± 0.50	357 ± 8.00	135 ± 10.0	2013 ± 81.0	161 ± 6.00
M[b,e]	19.3 ± 0.90	285 ± 22.0	2.47 ± 0.19	25.4 ± 0.40	331 ± 12.0	120 ± 3.00	1727 ± 23.0	105 ± 3.00
N[c]	27.9 ± 3.20	439 ± 28.0	3.06 ± 0.02	40.4 ± 0.20	325 ± 15.0	174 ± 3.00	1832 ± 33.0	148 ± 3.00
O[c,e]	36.0 ± 0.50	468 ± 17.0	6.98 ± 0.38	59.6 ± 2.30	301 ± 24.0	243 ± 11.0	2101 ± 28.0	176 ± 4.00

[a] Reference cigarette 2R1F.

Range
301-433
μg/cig

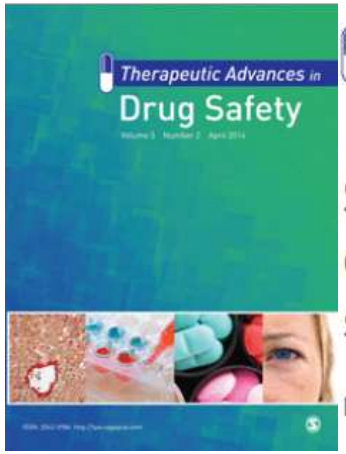
Fujioka K et al. Environ Toxicol 2006

Estimated daily exposure to di yl (DA) and acetyl propionyl (AP)
(assuming an average da C liquid consumption of 3ml)



Farsalinos KE, et al. Evaluation of electronic cigarette liquids and vapour for the presence of selected inhalation toxins. Poster presentation at GFN Warsaw.

Harmful and potentially harmful constituents



Therapeutic Advances in Drug Safety *Review*

Safety evaluation and risk assessment of electronic cigarettes as tobacco cigarette substitutes: a systematic review

Konstantinos E. Farsalinos and Riccardo Polosa

Ther Adv Drug Saf
1–20
DOI: 10.1177/2042098614524430

Nicotine

Main ingredients (PG/VG)

Flavorings

Impurities-other

Heavy Metals

Goniewicz ML, et al. Levels of selected carcinogens and toxicants in vapour from e-cigarettes. Tob Control 2013

Compound	blank	e-cigs (150 puffs)	inhalator (1 cartridge)
Metals (μg)			
Cd	0.02	0.09 (ND-0.17)	0.03
Ni	0.17	0.19 (0.11-0.29)	0.19
Pb	0.02	0.09 (0.03-0.57)	0.04

Heavy Metals

Goniewicz ML, et al. Levels of selected carcinogens and toxicants in vapour from e-cigarettes. Tob Control 2013

Compound	blank	e-cigs (150 puffs)	inhalator (1 cartridge vs 16 cartridges)
Metals (μg)			
Cd	0.02	0.09 (ND-0.17)	0.03 vs 0.48
Ni	0.17	0.19 (0.11-0.29)	0.19 vs 3.00
Pb	0.02	0.09 (0.03-0.57)	0.04 vs 0.64

Heavy Metals

OPEN ACCESS Freely available online

PLOS | ONE

Metal and Silicate Particles Including Nanoparticles Are Present in Electronic Cigarette Cartomizer Fluid and Aerosol

Monique Williams[1], Amanda Villarreal[1], Krassimir Bozhilov[2], Sabrina Lin[1], Prue Talbot[1]*

Table 1. Elemental abundance in EC aerosol and cigarettes and associated health effects.

Element	Aerosol μg/10 puffs	Smoke μg/cig (~10 puffs)	Health Effects
Sodium	4.18	1.3 [40]	Inhalation may cause lung irritation, shortness of breath, bronchitis [41].
Boron	3.83		Inhalation exposure: acute respiratory and ocular irritation [42].
Silicon	2.24		Upper respiratory irritation, coughing, shortness of breath, bronchitis [43,44].
Calcium	1.03		Nose/throat irritation, coughing/wheezing [45].
Iron	0.52	0.042 [40]	Respiratory irritation, fume metal fever, siderosis, fibrosis [46].
Aluminum	0.394	0.22 [40]	Impaired lung function, asthma, and pulmonary fibrosis [47].
Potassium	0.292	70 [40]	May originate from silicate beads along with sodium, calcium, and magnesium.
Sulfur	0.221		Nose/throat/lung irritation, coughing, shortness of breath, and bronchitis [48].
Copper	0.203	0.19 [40]	Respiratory irritation, coughing, sneezing, thoracic pain, runny nose and vineyard sprayer's lung [49].
Magnesium	0.066	0.070 [40]	Metal fume fever, respiratory irritation, tightness in chest, difficulty breathing [50].
Zinc	0.058	0.12–1.21 [40] 11.9 [51]	Metal fume fever, impaired pulmonary function, chest pain, coughing, dyspnea, shortness of breath [52].
Tin	0.037		Inorganic tin: pneumoconiosis (stannosis) and inflammation [53].
Lead	0.017	0.017–0.98 [40] 0.072 [54] 0.14 [51]	Can damage nervous system and kidneys [55]. Is a CA, RT, and RDT [56].

Heavy Metals

Table 1. Elemental Impurities for Drug Products

Element	Oral Daily Dose PDE[a] (µg/day)	Parenteral Daily Dose PDE (µg/day)	Inhalational Daily Dose PDE (µg/day)
Cadmium	25	2.5	1.5
Lead	5	5	5
Inorganic arsenic[b]	1.5	1.5	1.5
Inorganic mercury[b]	15	1.5	1.5
Iridium	100	10	1.5
Osmium	100	10	1.5
Palladium	100	10	1.5
Platinum	100	10	1.5
Rhodium	100	10	1.5
Ruthenium	100	10	1.5
Chromium	—[c]	—[c]	25
Molybdenum	100	10	10 (ERR 1-Oct-2012)
Nickel	500	50	1.5
Vanadium	100	10	30
Copper	1000	100	100 (ERR 1-Feb-2013)

[a] PDE = Permissible daily exposure based on a 50-kg person.
[b] See *Speciation* section.
[c] Not a safety concern.

US Pharmacopoeia, 2013

Levels of tobacco-specific nitrosamines in electronic and conventional cigarettes

Based on information from Laugesen [2009], Cahn and Siegel [2011] and Kim and Shin [2013].

Product	Total nitrosamines levels (ng)	Daily exposure (ng)	Ratio[4]
Electronic cigarette (per ml)	13	52[1]	1
Nicotine gum (per piece)	2	48[2]	0.92
Winston (per cigarette)	3365	50 475[3]	971
Newport (per cigarette)	3885	50 775[3]	976
Marlboro (per cigarette)	6260	93 900[3]	1806
Camel (per cigarette)	5191	77 865[3]	1497

[1]Based on average daily use of 4ml liquid
[2]Based on maximum recommended consumption of 24 pieces per day
[3]Based on consumption of 15 cigarettes per day
[4] Difference (number-fold) between electronic cigarette and all other products in daily exposure to nitrosamines

TSNAs are major carcinogens in tobacco cigarettes!

Farsalinos K, Polosa R. Safety evaluation and risk assessment of ecigs as tobacco cigarette substitutes: a systematic review. Ther Adv Drug Saf 2014

Thermal degradation: aldehydes production

Goniewicz ML, et al.
Levels of selected carcinogens and toxicants in vapour from e-cigarettes.
Tob Control 2013

Table 4 Comparison of toxins 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
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

Counts ME, et al.
Regul Toxicol Pharmacol 2005

Thermal degradation: aldehydes production

TABLE I. Amounts of carbonyl compounds determined in the main stream of cigarette smoke from various brands of cigarettes

	Amounts (μg/cigarette^{-1})							
Brand	Malonaldehyde	Acrolein	Glyoxal	Methylglyoxal	Diacetyl	Formaldehyde	Acetaldehyde	Propanal
A[a,b]	28.8 ± 0.60	431 ± 13.0	1.93 ± 0.01	13.4 ± 0.10	433 ± 11.0	116 ± 5.00	2040 ± 16.0	167 ± 1.00
B[b,e]	18.9 ± 2.20	220 ± 9.00	2.09 ± 0.1	45.3 ± 0.90	308 ± 19.0	127 ± 7.00	1110 ± 21.0	87.0 ± 3.00
C[b]	28.9 ± 0.90	423 ± 1.00	2.99 ± 0.18	29.1 ± 1.70	335 ± 29.0	194 ± 17.0	1978 ± 16.0	164 ± 1.00
D[b]	26.7 ± 2.00	315 ± 19.0	3.19 ± 0.17	24.1 ± 1.70	349 ± 13.0	114 ± 5.00	1784 ± 49.0	149 ± 5.00
E[b]	29.0 ± 1.10	391 ± 4.00	3.39 ± 0.10	53.5 ± 2.20	359 ± 23.0	165 ± 5.00	1788 ± 25.0	150 ± 2.00
F[b]	28.3 ± 1.40	238 ± 6.00	4.78 ± 0.14	34.2 ± 0.70	355 ± 17.0	121 ± 9.00	1518 ± 63.0	132 ± 6.00
G[b]	29.0 ± 1.00	411 ± 11.0	2.95 ± 0.11	35.0 ± 0.90	303 ± 9.00	135 ± 5.00	1877 ± 39.0	155 ± 2.00
H[b,d]	26.2 ± 0.10	405 ± 5.00	2.76 ± 0.23	23.6 ± 1.70	320 ± 14.0	149 ± 5.00	1788 ± 20.0	148 ± 1.00
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L[b,d]	28.7 ± 0.60	418 ± 32.0	2.21 ± 0.10	27.8 ± 0.50	357 ± 8.00	135 ± 10.0	2013 ± 81.0	161 ± 6.00
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O[c,e]	36.0 ± 0.50	468 ± 17.0	6.98 ± 0.38	59.6 ± 2.30	301 ± 24.0	243 ± 11.0	2101 ± 28.0	176 ± 4.00

[a] Reference cigarette 2R1F.

Range 220-468 μg/cig

Range 87-243 μg/cig

Range 1110-2101 μg/cig

Fujioka K et al. Environ Toxicol 2006

Thermal degradation: aldehydes production

Goniewicz ML, et al.
Levels of selected carcinogens and toxicants in vapour from e-cigarettes.
Tob Control 2013

Table 4 Comparison of toxins levels between conventional and electronic cigarettes

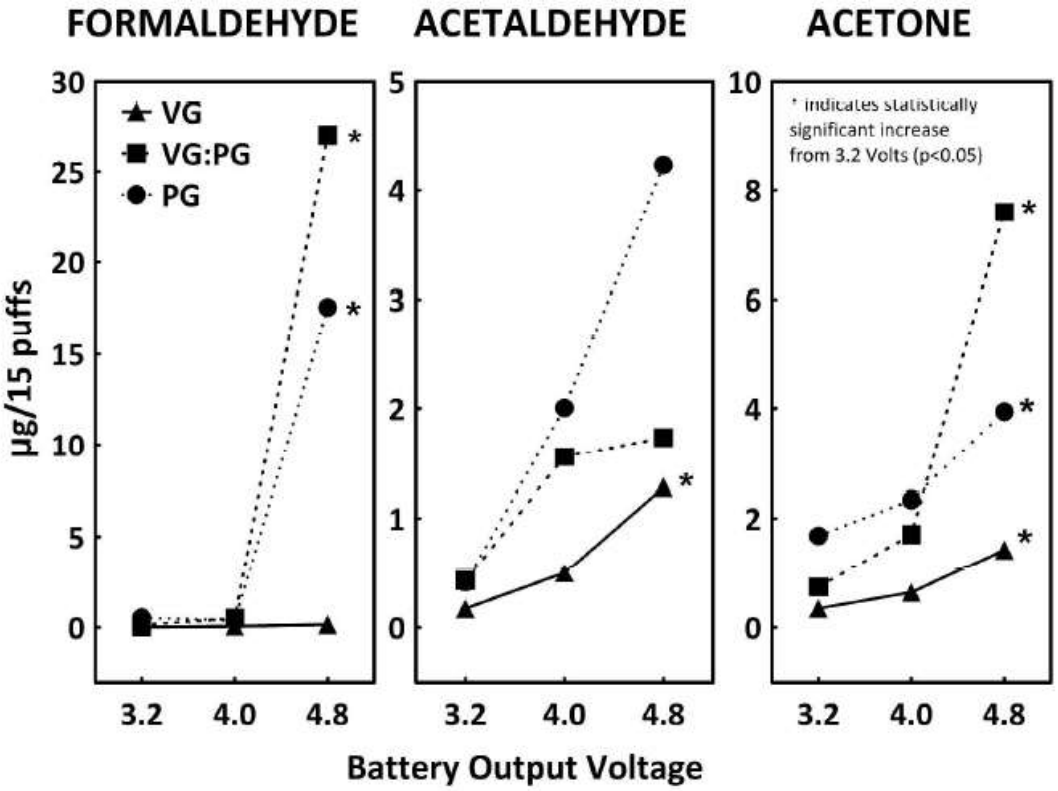
Toxic compound	Conventional cigarette (µg in mainstream smoke) [35]		Electronic cigarette (µg per 15 puffs)	Average ratio (conventional vs electronic	
Formaldehyde	1.6–52	87-243	0.20–5.61	9	57
Acetaldehyde	52–140	1110-2101	0.11–1.36	450	2184
Acrolein	2.4–62	220-468	0.07–4.19	15	161
Toluene	8.3–70		0.02–0.63	120	
NNN	0.005–0.19		0.00008–0.00043	380	
NNK	0.012–0.11		0.00011–0.00283	40	

Counts ME, et al.
Regul Toxicol Pharmacol 2005

Fujioka K et al.
Environ Toxicol 2006

Toxic substances do exist,
but levels far lower compared to tobacco cigarettes!

Thermal degradation: aldehydes production



Solvent and power levels interaction

Different puffing regime depending on equipment

Kosmider L, et al. Carbonyl compounds in e-cigarette vapors: effects of nicotine solvent and battery output voltage. Nicotine Tob Res 2014

NJOY Electronic Cigarettes: Chemicals Below Limit of Detection or Limit of Quantification

Tobacco-specific nitrosamines
NNN
NNK

Carbonyls
Acrolein
Crotonaldehyde

Metals
Cadmium

Volatile Organic Compounds
Benzene
Acrylonitrile
1,3-butadiene

Poly-aromatic amines
4-aminobiphenyl

Poly-aromatic hydrocarbons
2-aminonaphthalene

Formaldehyde: Detected at 2.5% of level in cigarettes

Acetaldehyde: Detected at <0.1% of level in cigarettes

Rabinowitz JD, Leischow SJ. Electronic cigarettes that product nicotine aerosols substantially devoid of known toxic impurities. Presented at the annual meeting of the Society for Research on Nicotine and Tobacco, February 5-8, 2014.

VUSE Electronic Cigarettes: Chemicals Below Limit of Detection or Limit of Quantification

Tobacco-specific nitrosamines
NNN
NNK
NAT
NAB

Carbonyls
Formaldehyde
Acetaldehyde
Acrolein
Acetone

Metals
Arsenic
Cadmium
Chromium
Lead
Nickel

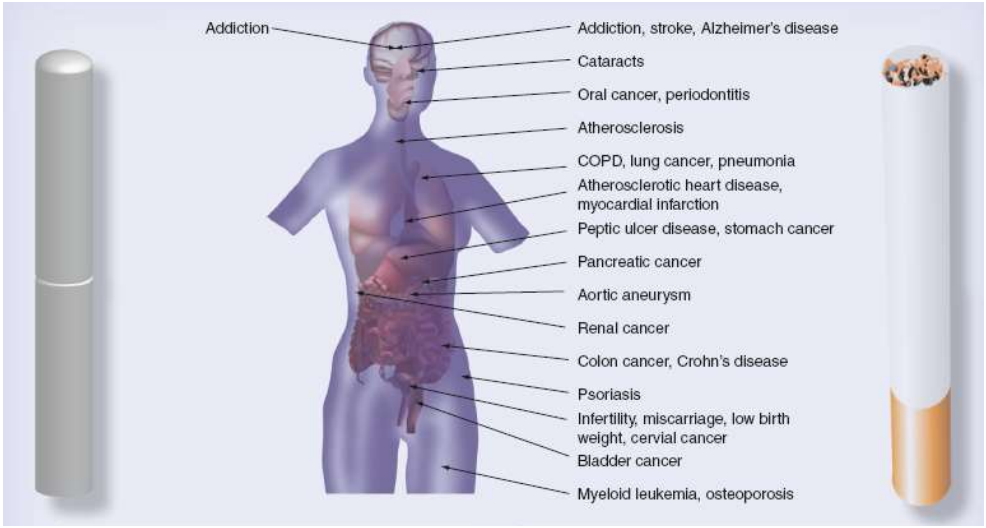
Volatile Organic Compounds
Benzene
Acrylonitrile
Propylene oxide
Toluene
Vinyl chloride

Poly-aromatic amines
4-aminobiphenyl

Poly-aromatic hydrocarbons
Benzo(a)pyrene
Benzo(a)anthracene
Naphthalene
Flourene

Theophilus EH, et al. VUSE electronic cigarette aerosol characterization (poster). R.J. Reynolds Tobacco Company. Presented at the Annual Meeting of the Society of Toxicology, March 24-27, 2014.

Relative Risk Scale



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100

Risk

Relative Risk Scale

CO

NO_x

CO_2

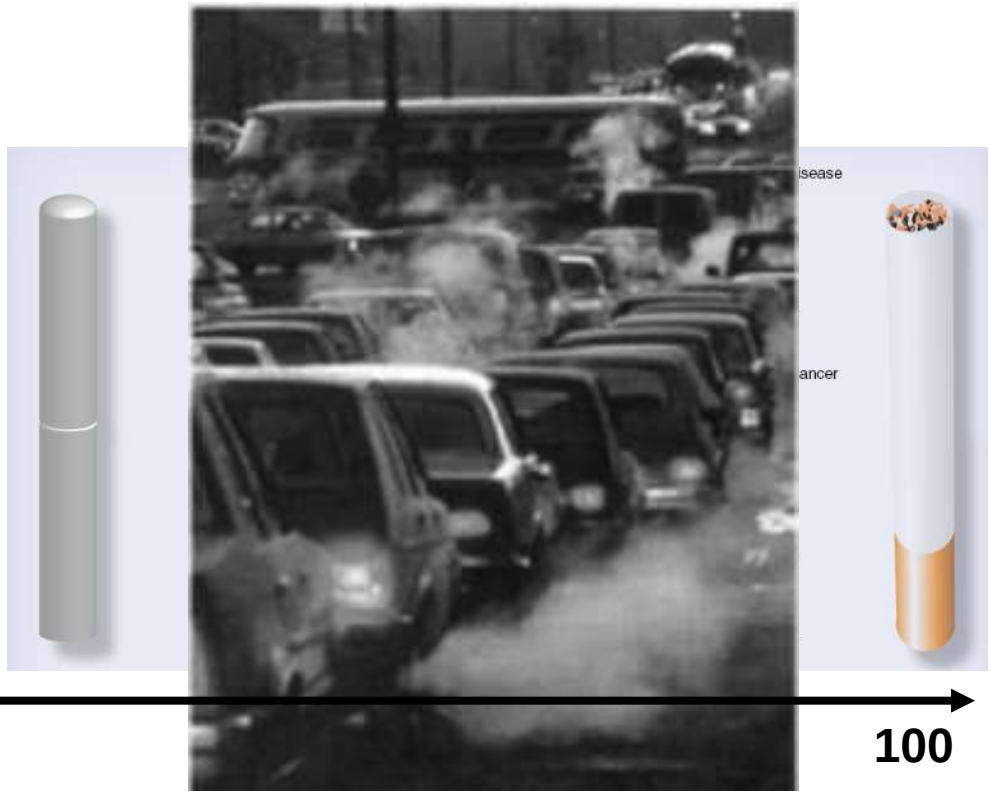
PAHs

PM_{10}

$PM_{2.5}$

NO_2

Benzene



0

100

Risk

No uncertainty!

Even in their current state, e-cigarettes are significantly less harmful compared to tobacco cigarettes

Harmful and potentially harmful constituents ‘handprint’

Synthetic chemical flavourings

Temperature regulation

Safer atomizer materials (wick, coil, plastics)

Pharma grade (nicotine, solvents)

Customer Safety

GMP standards