

Supplemental Digital Content (SDC)

Title: Acute effects of electronic and tobacco cigarettes on vascular and respiratory function in healthy volunteers: A cross-over study

Short Title: Cardiovascular effects of e-cigarettes

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SCD 1 Nicotine and chemical compounds identified in e-liquid used in this study

Flavour brand name	Labelled nicotine concentration (mg/ml)	Determined nicotine concentration (mg/ml)	Identified chemicals	CAS Registry Number
American Red Tobacco	18	17.27	Pyridine, 3-(1-methyl-2-pyrrolidinyl)-, (S)-	54-11-5
			Propylene Glycol	57-55-6
			Glycerin	56-81-5
			Vanillin	121-33-5
			Vanillin propylene glycol acetal	68527-74-2
			Ethyl Vanillin	121-32-4
			Ethyl Vanillin propylene glycol acetal, cis-	68527-76-4
			2(3H)-Furanone, 5-butyldihydro-	104-50-7
2(3H)-Furanone, dihydro-5-pentyl-	104-61-0			

SCD 2: Two-Way Repeated Measures ANOVA for physiological and biomarker parameters following electronic cigarette and tobacco cigarette use

Parameter	Two-way RM ANOVA interaction of Intervention (EC or TC) with time point	Intervention	Pre-Intervention	Post-intervention	Change following intervention	P-value
HR (bpm)	<0.001	Electronic Cigarette	65 (2.1)	73 (1.9)	8 (1.2)	<0.001
		Tobacco Cigarette	64 (1.9)	86 (2.9)	23 (2.7)	<0.001
		EC and TC Difference	1.5 (1.7)	13.1 (2.5)		
		EC and TC Difference P-Value	0.381	<0.001		
SBP (mmHg)	0.048	Electronic Cigarette	124 (2.6)	123 (2.5)	1 (1.2)	0.431
		Tobacco Cigarette	121 (3.1)	125 (3.0)	4 (2.1)	0.058
		EC and TC Difference	3.2(1.4)	2(1.7)		
		EC and TC Difference P-Value	0.034	0.267		
DBP* (mmHg)	0.405	Electronic Cigarette	80 (2.4)	80 (2.3)*	0 (1.2)	0.805
		Tobacco Cigarette	75 (2.4)	77 (2.2)	2 (1.1)	0.166
		EC and TC Difference	-4 (2.0)	-3 (1.5)		
		EC and TC Difference P-Value	0.044	0.067		
RHI*	0.153	Electronic Cigarette	1.68 (0.07)*	1.96 (0.10)	0.28 (0.09)	0.004
		Tobacco Cigarette	1.86 (0.10)	1.97 (0.11)	0.10 (0.10)	0.302
		EC and TC Difference	0.18 (0.12)	0.01 (0.08)		
		EC and TC Difference P-Value	0.140	0.921		
PWA occluded arm* (AU)	0.501	Electronic Cigarette	860 (89)	465 (80)	-395 (69)	<0.001
		Tobacco Cigarette	895 (88)	437 (87)*	-458 (72)	<0.001

		EC and TC Difference	35 (84)	-28 (52)		
		EC and TC Difference P-Value	0.679	0.592		
PWA control arm * (AU)	0.379	Electronic Cigarette	906 (97)	507 (89)	-399 (79)	<0.001
		Tobacco Cigarette	966 (101)	475* (88)	-492 (76)	<0.001
		EC and TC Difference	61 (97)	-32 (60)		
		EC and TC Difference P-Value	0.540	0.598		
AI (%)	0.005	Electronic Cigarette	-10.5 (2.9)	-6.9 (3.0)	3.7 (1.3)	0.010
		Tobacco Cigarette	-9.0 (2.2)	-10.9 (3.0)	-1.9 (1.7)	0.265
		EC and TC Difference	1.6 (1.7)	-4.0 (1.7)		
		EC and TC Difference P-Value	0.368	0.026		
AI@75 (%)	0.165	Electronic Cigarette	-16.6 (3.2)	-14.3 (3.3)	2.3 (1.4)	0.131
		Tobacco Cigarette	-15.5 (2.3)	-16.2 (3.1)	-0.7 (0.7)	0.709
		EC and TC Difference	-1.1 (1.8)	-1.9 (0.4)		
		EC and TC Difference P-Value	0.558	0.358		
sICAM-1* (ng/ml)	0.280	Electronic Cigarette	61.6* (21.8)	44.4* (6.9)	-17.2 (16.2)	0.302
		Tobacco Cigarette	42.4* (5.8)	41.4 (4.6)	-0.9 (2.2)	0.673
		EC and TC Difference	-19.2 (17.5)	-2.9 (3.9)		
		EC and TC Difference P-Value	0.286	0.457		
sP-selectin* (ng/ml)	0.202	Electronic Cigarette	117.8* (23.8)	84.7 (6.1)	-33.11 (21.1)	0.135
		Tobacco Cigarette	89.1 (7.2)	82.4* (6.9)	-6.7 (4.4)	0.145
		EC and TC Difference	-28.7 (21.8)	-2.3 (6.8)		
		EC and TC Difference P-Value	0.204	0.737		
sVCAM-1* (ng/ml)	0.214	Electronic Cigarette	787.1* (96.0)	701.8 (27.9)	-85.3 (88.2)	0.347

		Tobacco Cigarette	687.3 (31.0)	710.4 (31.4)	23.1 (27.5)	0.414
		EC and TC Difference	-99.8 (94.5)	8.6 (29.1)		
		EC and TC Difference P-Value	0.306	0.774		
sE-selectin(ng/ml)	0.395	Electronic Cigarette	72.2 (7.1)	73.1 (7.1)	0.9 (2.0)	0.660
		Tobacco Cigarette	76.1 (7.6)	74.3 (7.9)	-1.8 (1.9)	0.347
		EC and TC Difference	3.9 (2.9)	1.2 (2.7)		
		EC and TC Difference P-Value	0.195	0.660		
PECAM-1* (ng/ml)	0.234	Electronic Cigarette	0.97* (0.07)	0.96 (0.07)	-0.02 (0.04)	0.664
		Tobacco Cigarette	1.06 (0.07)	1.00 (0.07)	-0.07 (0.03)	0.018
		EC and TC Difference	0.09 (0.40)	0.04 (0.05)		
		EC and TC Difference P-Value	0.045	0.468		
log ₁₀ MPs/mL*	0.018	Electronic Cigarette	5.8 (0.1)	5.7 (0.1)	-0.0 (0.2)	0.862
		Tobacco Cigarette	5.8 (0.1)	6.4 (0.1)*	0.6 (0.2)	<0.001
		EC and TC Difference	0.0 (0.2)	0.7 (0.2)		
		EC and TC Difference P-Value	0.802	0.001		
log ₁₀ EMPs/mL	0.008	Electronic Cigarette	4.9 (0.2)	4.9 (0.2)	0.0 (0.2)	0.896
		Tobacco Cigarette	4.9 (0.2)	5.8 (0.2)	0.9 (0.2)	<0.001
		EC and TC Difference	0.0 (0.2)	0.9 (0.2)		
		EC and TC Difference P-Value	0.919	<0.001		
log ₁₀ PMPs/mL	0.856	Electronic Cigarette	5.0 (0.2)	6.2 (0.2)	1.2 (0.2)	<0.001
		Tobacco Cigarette	5.0 (0.2)	6.3 (0.2)	1.2 (0.2)	<0.001
		EC and TC Difference	0.1 (0.3)	0.1 (0.3)		

		EC and TC Difference P-Value	0.813	0.644		
FEV ₁ (L)	0.564	Electronic Cigarette	4.2 (0.1)	4.1 (0.2)	-0.1 (0.1)	0.132
		Tobacco Cigarette	4.3 (0.1)	4.2 (0.3)	0.0 (0.0)	0.373
		EC and TC Difference	0.1 (0.0)	0.1 (0.1)		
		EC and TC Difference P-Value	0.105	0.214		
FVC (L)	0.541	Electronic Cigarette	5.2 (0.2)	5.1 (0.2)	-0.1 (0.1)	0.187
		Tobacco Cigarette	5.3 (0.2)	5.2 (0.2)	0.0 (0.1)	0.609
		EC and TC Difference	0.1 (0.1)	0.1 (0.1)		
		EC and TC Difference P-Value	0.221	0.197		
FEV ₁ /FVC (%)	0.918	Electronic Cigarette	81.1 (1.5)	80.9 (1.6)	-0.2 (0.4)	0.654
		Tobacco Cigarette	81.3 (1.6)	81.0 (1.6)	-0.3 (1.2)	0.782
		EC and TC Difference	0.2 (0.8)	0.1 (0.8)		
		EC and TC Difference P-Value	0.796	0.875		
PEF (L/min)	0.594	Electronic Cigarette	562 (14)	531 (22)	-31 (12)	0.019
		Tobacco Cigarette	567 (16)	545 (18)	-22 (12)	0.074
		EC and TC Difference	5 (9)	13 (12)		
		EC and TC Difference P-Value	0.565	0.270		
CO (ppm)*	<0.001	Electronic Cigarette	9 (2)*	7 (2)*	-2 (1)	0.024
		Tobacco Cigarette	9 (2)*	20 (2)*	11 (0)	<0.001
		EC and TC Difference	0 (1)	13 (1)		
		EC and TC Difference P-Value	0.676	<0.001		

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; RHI, reactive hyperaemia index; PWA, pulse wave amplitude, AU, arbitrary units, AI, augmentation index; AI@75, AI at heart rate of 75bpm; sICAM-1, soluble intercellular adhesion molecule 1; sP-selectin, soluble platelet selectin; sVCAM-1, soluble vascular adhesion molecule 1; sE-selectin, endothelial leukocyte adhesion molecule-1; PECAM-1, platelet endothelial cell adhesion molecule; MPs, microparticles; EMPs, endothelial microparticles, PMPs, platelet microparticles; CO, exhaled carbon monoxide; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity; FEV₁/FVC, forced expiratory volume in one second/ forced vital capacity ratio PEF, peak expiratory flow. Normality assessed by Shapiro-Wilks test of normality. Outliers assessed as studentized residuals with a value greater than 3 or less than -3. Data is presented as mean with standard error. *data contains outliers and/or is not normally distributed, which may affect validity of the ANOVA result.

SDC 3 Brands of tobacco cigarettes smoked during tobacco smoking intervention

Tobacco Brand	Number of Participants (n=20)
Amber Leaf	2
American Spirit	1
Café Crème	2
Golden Virginia	4
Marlboro Gold	10
Mayfair	1

SDC 4 Difference (Δ) in parameters follow study interventions

Parameters	Difference following Electronic Cigarette Use (Post-Pre)	Difference following Tobacco Cigarette Use (Post-Pre)	Difference between Δ EC and Δ TC (Δ EC - Δ TC)	P-value
Δ HR (bpm)	8 \pm 5	23 \pm 12	-15 \pm 12	<0.001
Δ SBP (mmHg)	-1 \pm 6	4 \pm 9	-5 \pm 11	0.046
Δ DBP (mmHg)	0 \pm 5	2 \pm 5	-1 \pm 7	0.333
Δ RHI	0.28 \pm 0.38	0.10 \pm 0.44	0.18 \pm 0.52	0.178
Δ AI (%)	3.7 \pm 5.7	-1.9 \pm 7.4	5.6 \pm 8.0	0.006
Δ AI@75	2.3 \pm 6.5	-0.7 \pm 7.8	-2.9 \pm 9.1	0.191
sICAM-1 (ng/ml)	-4.0 (-9.0;5.3)	-1.5 (-4.3;4.5)	-6.0 (-11.3; 6.8)	0.286
sP-selectin (ng/ml)	-19.5 (-33.0;5.5)	-12.5 (-19.0;9.0)	-20 (-31.3;16.5)	0.177
sVCAM-1 (ng/ml)	-25.0 (-85.3;73.3)	-3.0 (-50.3;78.3)	-45.0 (-156.8;87.5)	0.267
sE-selectin(ng/ml)	-0.9 (-3.2;5.8)	-0.8 (-6.6;2.6)	0.3 (-4.1;6.7)	0.433
PECAM-1 (ng/ml)	-0.04 (-0.07;0.05)	-0.06 (-0.12;0.00)	0.04 (-0.08;0.17)	0.201
Δ log ₁₀ MPs/ml	-0.2 (-0.5;0.7)	0.4 (0.2;1.1)	-0.7 (-1.6;0.2)	0.024
Δ log ₁₀ EMPs/ml	0.0 (-0.5;0.7)	0.6 (0.3;1.6)	-0.7 (-1.9;0.2)	0.016
Δ log ₁₀ PMPs/ml	1.4 (0.6;1.8)	1.0 (0.3;2.1)	-0.1 (-1.1;1.0)	0.799
Δ FEV ₁ (L)	-0.1 \pm 0.2	0.0 \pm 0.2	0.0 \pm 0.3	0.754
Δ FVC (L)	-0.1 \pm 0.3	0.0 \pm 0.3	-0.1 \pm 0.5	0.721
Δ FEV/FVC (%)	-0.2 \pm 2.0	-0.3 \pm 4.8	0.1 \pm 4.3	1.000
Δ PEF (L/min)	-31 \pm 54	-22 \pm 53	-9 \pm 71	0.709
Δ CO (ppm)	-2 \pm 3	11 \pm 2	-13 \pm 4	<0.001

Abbreviations as reported in previous tables. Data is presented as mean \pm SD or median (25th-75th

percentile). P-values derived from Related Samples Wilcoxon signed ranked test.