





Non-targeted screening using GC×GC-TOFMS for in-depth chemical characterization of aerosol from a heat-not-burn tobacco product

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Compound identification distribution (numeric and mass) 5416.03 µg/item (98.74%) TOTAL: 384 TOTAL: 5485.14 µg/item compounds 12.51 µg/item (3.1%) (0.23%) Medium 2.07 µa/item

Compound class distribution (numeric and mass [µg/item])



<u>3. Non-targeted differential screening (NTDS)^[5] of /QOS aerosol versus 3R4F smoke</u>

compound names and

Top 10 significantly elevated compounds in *IQOS* aerosol versus 3R4F smoke Hit numbers, proposed

CASI score, probability of

structures fo respective	the structure proposals and final confidence level				allocated to corresponding compound classes or 2D(rel)RTs			Compound present in Blank \rightarrow Exclusion Constituent Origin \rightarrow Aerosol, Material, Plant, Flavor						
						,	SEMI-QUAN	TIFICATION	`	+ Identification details CASI	+ Structure identifier	+ Ranking / testing	+ BLANK	+ Origin / probable source
# Proposed compound name	Structure	Method	CASI Score	Probability	Confidence		IQOS Sum conc. [µg/test item]	3R4F Sum conc. [µg/test item]	X-fold change	Retention Index measured	CAS	Rank	Presence / absence	Aerosol (from database)
1 Propylene glycol	ностон	Polar	928	HIGH	IDENTIFIED	Confirmed by REF STD	174.92	23.73	7.4	996.70	57-55-6	43786.26	-	x
2 1-Hydroxy-2-propanone	OH OH	Nonpolar	858	HIGH	IDENTIFIED	Confirmed by REF STD	161.80	96.80	1.7	589.87	116-09-6	4656.56	-	x
3 2-Furanmethanol	Sin and a set of the set of t	Nonpolar	861	HIGH	IDENTIFIED	Confirmed by REF STD	39.18	7.00	5.6	814.86	98-00-0	1602.12	-	х
		Polar	862	HIGH	IDENTIFIED	Confirmed by REF STD				1053.41	98-00-0	703.97	-	х
4 2-Furancarboxaldehyde, 5-methyl-	Ļ	Nonpolar	923	HIGH	IDENTIFIED	Confirmed by REF STD	11.10	2.94	3.8	963.74	620-02-0	1393.53	-	х
		Polar	886	HIGH	IDENTIFIED	Confirmed by REF STD				984.98	620-02-0	3.07	-	х
5 cis-4-Hydroxymethyl-2- methyl-1,3-dioxolane	[₩] °,, ,	Nonpolar	846	HIGH	IDENTIFIED	Confirmed by REF STD	2.09	0.04	47.4	881.28	3773-93-1	83.00	-	х
		Polar	835	HIGH	IDENTIFIED	Confirmed by REF STD				1006.05	3773-93-1	961.67	-	х
6 Butyrolactone	₩	Nonpolar	917	HIGH	IDENTIFIED	Confirmed by REF STD	4.08	0.73	5.6	898.62	96-48-0	764.63	-	х
		Polar	942	HIGH	IDENTIFIED	Confirmed by REF STD				1066.73	96-48-0	53.08	-	х
7 Furfural	Í,	Nonpolar	884	HIGH	IDENTIFIED	Confirmed by REF STD	31.08	25.91	1.2	787.36	98-01-1	767.93	-	x
8 4-Cyclopentene-1,3- dione	, Core	Nonpolar	723	MEDIUM	IDENTIFIED	Confirmed by REF STD	3.80	0.76	5.0	856.11	930-60-9	670.29	-	x
9 2-Propanone, 1- (acetyloxy)-	°	Nonpolar	891	HIGH	IDENTIFIED	Confirmed by REF STD	16.92	8.01	2.1	833.48	592-20-1	569.52	-	
10 1-Hydroxy-2-butanone	~ <u>_</u> ~~	Nonpolar	852	HIGH	IDENTIFIED	Confirmed by REF STD	0.95	0.47	2.0	704.76	5077-67-8	473.50	-	x
Table 4 Tap 4					mificar		voted in 1000 v						 Domla	 .[6]

Table 1. Top 10 compounds that are significantly elevated in IQOS aerosol versus 3R4F smoke; sorted according to Rank¹⁰

		С
GC×GC-TOFMS nical composition	non-targeted of the IQOS	screening aerosol.

workflow has been applied successfully to characterize the The In total, 384 compounds (corresponding to a mass of 5.485 chen mg/item) were found to be present at a concentration of 100 ng/stick or greater, 220 (57.3%) in NFDPM, 125 (32.6%) in GVP, and 39 (10.2%) were found to be partitioned between both NFDPM and GVP. A total of 332 (86.5%) could be confirmed by reference standards so far (corresponding to a mass of 5.416 mg/item, 98.7%).

[1] Roemer, E., et al., Contributions to Tobacco Research, 2012, 25, 316 [2] Knorr, A., et al., Anal. Chem., 2013, 85(23), 11216

[3] Martin, E., et al., J. Cheminform., 2012, 4, 11 [4] Official Method T-115, Determination of "Tar", Nicotine and Carbon Monoxide in **2013**, Jul 4





Nonpolar - confirm Polar - confirmed olatile - confirm

In a parallel investigation, the chemical composition of the IQOS aerosol was compared with 3R4F smoke using a NTDS approach. These data were reported to the FDA on December 8, 2017, as part of the Modified Risk Tobacco Product Application. A total of only 42 compounds (three unique) were significantly higher (p-value < 0.05) in the IQOS aerosol versus 3R4F smoke, whereas approximately 1,070 compounds were found to be elevated in 3R4F smoke compared with the IQOS aerosol.

> Semi-quantitative (N=3) values based on predefined rules, where ISTDs are

Additional columns for more details on CASI \rightarrow RI/2DreIRT/BP deviation (pred vs exp/calc) Structure \rightarrow CAS/PMICODE/MW/Formula/Smiles

onclusion

References

Mainstream Tobacco Smoke, *Department of Health*, Canada, **1999** [5] Almstetter, M., et al., Researchgate, 2016, DOI10.13140/RG.2.2.32692.55680 [6] Knorr, A., International Patent, WO 2013098169 A1, PCT/EP2012/076244,

Competing Financial Interest

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