Electronic Supplementary Material (ESI) for Analytical Methods.

Electronic Supplementary Material for:

Determination of Thermal Degradants in E-Cigarette Fluid via Direct Sample Introduction (DSI) Gas Chromatography-Tandem Mass Spectrometry

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Description: The supplementary material contains validation characteristics for the determination of nicotine in EC fluids via DSI-GC-MS, GC-MS, and GC-FID (Table S1). It contains reported and calculated concentrations of nicotine in three EC fluids as determined with GC-FID, GC-MS, and DSI GC-MS (Table S2). It also includes EI mass spectra for e-cigarette (EC) fluid solvents and possible thermal degradation products (Figure S1), and a comparison of thermal breakdown product formation during autosampler and DSI injections for propylene glycol (Figure S2).

Table S1. Method validation characteristics for nicotine in EC fluids as determined via three different methods.

Parameter	**DSI-GC-MS[a]**	**AS-GC-MS[a]**	**WN-GC-FID[a]**
LOD (mg/mL)[b]	0.23	0.39	0.14
LOQ (mg/mL)[c]	0.70	1.18	0.43
Accuracy (% of Target)[d]	115	135	100
Precision (%RSD)[d]	13.0	2.6	2.4
Linearity (R^2-value)	0.994	0.985	0.972
Range (mg/mL)	0-20	0-20	0-20

[a]DSI = direct sample introduction, AS = autosampler, WN = wet needle

[b]Limit of detection, computed according to USFDA guidelines[1,2] for method validation (LOD = 3.3σ/slope, where σ is the standard deviation of a 0.5 mg/mL standard)

[c]Limit of quantitation, computed according to USFDA guidelines[1,2] for method validation (LOQ = 10σ/slope, where σ is the standard deviation of a 0.5 mg/mL standard)

[d]Spiking concentration = 4 mg/mL (n = 3)

Table S2. Reported and calculated concentrations of nicotine in three EC fluids found with DSI-GC-MS, AS-GC-MS, and GC-FID (n=3)

EC Fluid	***Reported (mg/mL)***	***DSI-GC-MS***	***AS-GC-MS***	***WN-GC-FID***
Lost Art Cottontail Cream	6.0	5.6 ± 1.8	7.6 ± 0.58	5.5 ± 1.3
Vapor Chef Apple Bourbon	6.0	6.1 ± 1.3	7.0 ± 0.47	8.6 ± 1.6
Beard Vape Co. No. 51	6.0	7.6 ± 2.3	4.33 ± 0.20	6.31 ± 0.98
Deep Thought	6.0	7.28 ± 0.94	---	---
Iced Punch	3.0	3.78 ± 0.74	---	---
HYDRO	0.0	< LOQ	---	---

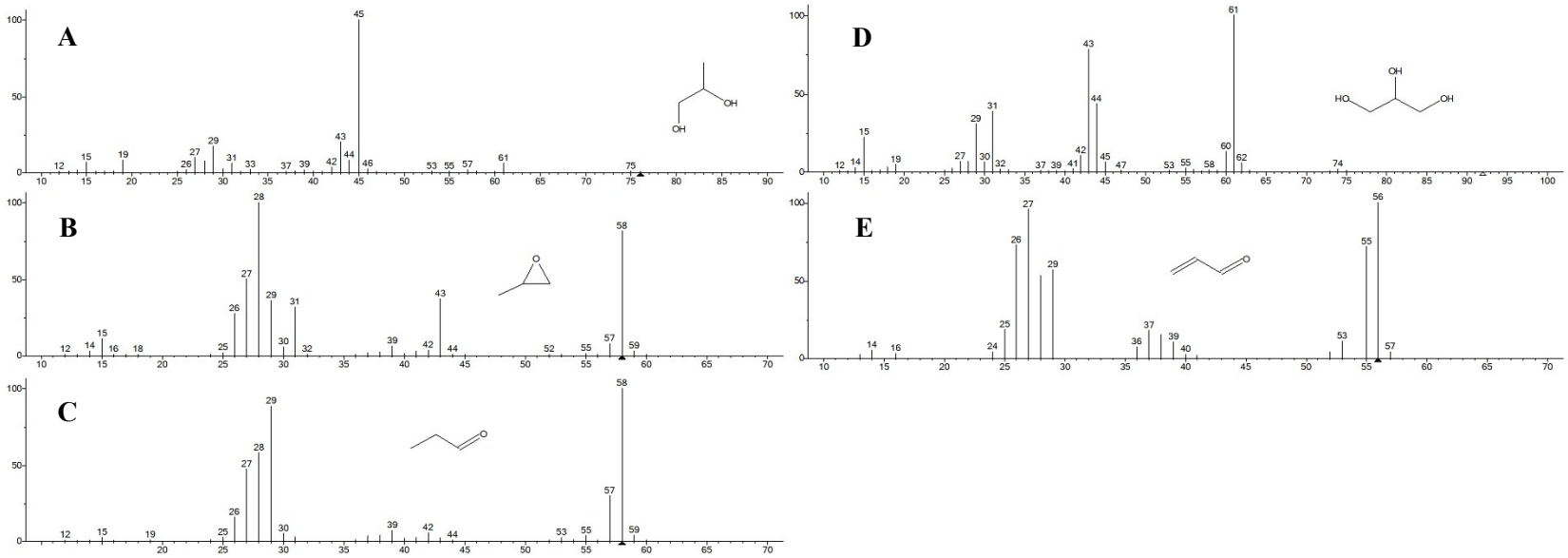

Figure S1. EI mass spectra[3] of EC carrier solvents and their proposed thermal breakdown products. (A.) Propylene Glycol (B.) Propylene Oxide (C.) Propanal (D.) Glycerol (E.) Acrolein

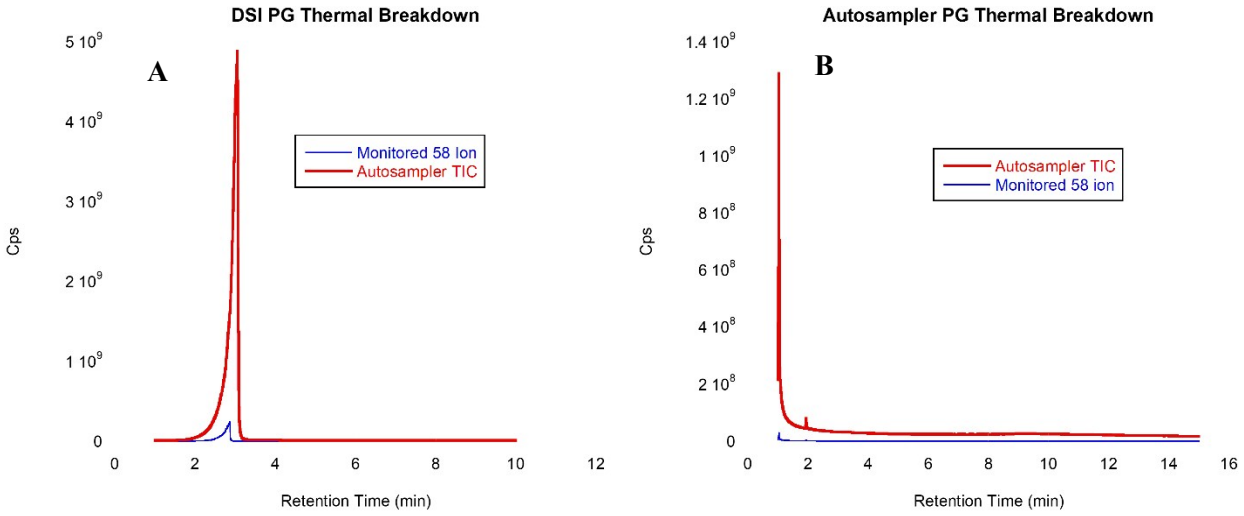

Figure S2. (A.) Comparison of PG elution against thermal breakdown product elution represented by a fragment at m/z 58 via DSI (B.) Comparison of PG elution against thermal breakdown product elution represented by a fragment at m/z 58 via Autosampler.

References

1. Food and Drug Administration, *Analytical Procedures and Methods Validation for Drugs and Biologics. Guidance for Industry,* U.S. Department of Health and Human Services, 2015. https://www.fda.gov/downloads/drugs/guidances/ucm386366.pdf, (accessed October 2018).
2. *ICH Q2 (R1) Validation of Analytical Procedures: Text and Methodology*, International Conference on Harmonization of Technical Requirements for Pharmaceuticals for Human Use, 1994. https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q2_R1/Step4/Q2_R1__Guideline.pdf, (accessed October 2018).
3. NIST Chemistry WebBook. NIST Standard Reference Database Number 69, https://webbook.nist.gov/chemistry/. (accessed July 2018).