High-Performance Liquid Chromatography–Tandem Mass Spectrometry Analysis of Carbonyl Emissions from E-Cigarette, or Vaping, Products

Megan McGuigan,* Gala Chapman, Erica Lewis, Clifford H. Watson, Benjamin C. Blount, and Liza Valentin-Blasini*

ABSTRACT: A quantitative method was developed to measure four harmful carbonyls (acetaldehyde, acrolein, crotonaldehyde, and formaldehyde) in aerosol generated from e-cigarette, or vaping, products (EVPs). The method uses a commercially available sorbent bed treated with a derivatization solution to trap and stabilize reactive carbonyls in aerosol emissions from EVPs to reduce reactive analyte losses and improve quantification. Analytes were extracted from the sorbent material using acetonitrile and analyzed via high-performance liquid chromatography–tandem mass spectrometry (HPLC–MS/MS). The method was applied to aerosols generated from products obtained from case patients with EVP use-associated lung injury (EVALI). The method accuracy ranged from 93.6 to 105% in the solvent and 99.0 to 112% in the matrix. Limits of detection (LODs) were in the low nanogram range at 0.735–2.10 ng for all analytes, except formaldehyde at 14.7 ng. Intermediate precision, as determined from the replicate measurements of quality-control (QC) samples, showed a relative standard deviation (RSD) of less than 20% for all analytes. The EVALI case-related products delivered aerosol containing the following ranges of carbonyls: acetaldehyde (0.0856–5.59 μg), acrolein (0.00646–1.05 μg), crotonaldehyde (0.00168–0.108 μg), and formaldehyde (0.0533–12.6 μg). At least one carbonyl analyte was detected in every product. Carbonyl deliveries from EVALI-associated products of all types are consistent with the previously published results for e-cigarettes, and levels are lower than those observed in smoke from combustible cigarettes. This method is rugged, has high throughput, and is well suited for quantifying four harmful carbonyls in aerosol emissions produced by a broad spectrum of devices/solvents, ranging from e-cigarette containing polar solvents to vaping products containing nonpolar solvents.

INTRODUCTION

We developed a new analytical method for measuring four harmful carbonyls in aerosols generated by e-cigarette, or vaping, products (EVPs). Vaping devices convert a liquid chemical solution, often containing a psychoactive compound such as nicotine or various cannabinoids, to an inhalable aerosol. In addition to the active ingredients, EVP liquids can contain solvents, dilutants, flavors, and pH modifiers that are also aerosolized.¹⁻³ Evaluation of these products is important to quantify aerosolized chemicals and assess potential health harm related to chronic inhalation of these chemicals. Device designs and liquid chemistry matrices differ between nicotine products containing polar, hydrophilic liquids and cannabinoid products containing nonpolar hydrophobic liquids. A heating element vaporizes the liquid contents to form an aerosol. High temperatures in the heating element can cause thermal degradation and produce a much more chemically complex aerosol than initially present in the original EVP liquid. Carbonyls are a class of compounds that can be created during the aerosolization process. The amount of carbonyl formation is related to device power, which impacts the temperature of the heating element.⁴⁻⁵ Carbonyls have been studied in nicotine EVPs⁶⁻⁹ but less is known about carbonyl formation in cannabinoid EVPs.¹⁰⁻¹² Aerosol emission testing provides useful information to help assess any potential harmful chemical exposure associated with EVP use.

Historically, carbonyls have been measured in the emissions of combustible tobacco products. The FDA includes numerous
carbonyls in their harmful and potentially harmful (HPHC) tobacco constituents list. Inhalation exposure to carbonyls is associated with respiratory effects ranging from irritation and congestion to cancer. Carbonyls can be analytically challenging to measure accurately because of their reactivity, thermal instability, and wide range of concentrations present. A variety of approaches for the collection of carbonyls in mainstream smoke have been presented in the past, including Tedlar bags, solvent-filled impingers, and Cambridge filter pads. Challenges with these approaches include loss upon collection because of the volatility and reactivity of the analytes and large volumes of solvents associated with impingers. More recently, sorbent packed cartridges have been used as an effective means for collecting and trapping carbonyls immediately after formation. This approach has also been used for analyzing e-cigarette emissions from products containing nicotine, glycerol, and propylene glycol. We present a validated method for the quantitative measurement of four carbonyls (formaldehyde, acetaldehyde, acrolein, and crotonaldehyde) in the aerosol emissions from a variety of EVP types with varying liquid compositions including cannabis-related active ingredients diluted in vitamin E acetate, medium chain triglycerides, squalene, and other nonpolar solvents. Method parameters are presented along with ISO 17025 validation and performance data. In addition, we measured carbonyl levels in aerosols generated by 77 products collected from EVP use-associated lung injury (EVALI) patients. We demonstrated that our approach is applicable to both nicotine e-cigarettes as well as cannabis vape products and report carbonyl contents in the emissions from a diverse set of products collected from EVALI patients.

### RESULTS

**Method Performance.** Vigorous validation criteria were established and maintained to ensure optimal and reproducible method performance. Method blank samples collected and analyzed on a daily basis showed no residual carbonyl content in the solvents, cartridges, or the vaping machine. Each analyte’s calibration range was established to span over the expected analyte delivery levels. The calibration curve regression coefficients (R) were greater than 0.995 for each analyte. Initial analyte recoveries were tested by spiking into 2,4-dinitrophenylhydrazine (DNPH) solutions, and comparable recoveries were seen with spiking on the cartridge. Method accuracy was assessed by spiking known amounts of calibration standard solution from a separate ampoule onto Rezorian cartridges at the low and high ends of the linear range and measured using the extraction procedure described in the Experimental Section. An additional set of spikes was prepared and extracted using a solvent that contained a sample matrix to check for any matrix effect. Accuracies in the clean solvent were close to 100% in all cases (range 93.6–105%), demonstrating the accuracy of the method at the low and high ends of the linear range. For matrix-based accuracy, the accuracy was slightly higher (99–114%) and within the acceptable limits.

The limit of detection (LoD) was determined using the method described by Taylor, where repeat analyses of low-level standards approaching zero concentration were done. The LoDs were all mathematically determined to be in the low nanogram range. Repeated analyses of the QC samples (both solvent- and matrix-based) were done to assess method variability. The analysis of this data showed %RSDs of less than 15% for most analytes, in solvent and in matrix, except for formaldehyde and acetaldehyde in the matrix with %RSDs less than 20%. A summary of the method validation results is presented in Table 1.

In addition to the experiments described above, other experiments were performed to test the suitability of the method. A vaping experiment was performed with two DNPH–Rezorian cartridges connected in series to test for breakthrough from the front cartridge. The analysis of the rear cartridge showed negligible carbonyl content (less than 1% of the front cartridge). Extensive ruggedness experiments were performed to optimize various experimental steps with a focus specifically on the sample extraction steps. The optimization of on-cartridge time, extraction volume, extraction (orbital shaker) settings, and cartridge materials (extraction of just the DNPH-silica vs the entire cartridge contents and body) was done. Final method parameters were chosen to reflect conditions determined to result in optimal recoveries with minimal variation.

**EVALI Case-Related Products.** We detected carbonyls in aerosol emissions from both polar nicotine products and nonpolar Δ9-tetrahydrocannabinol (THC) products. Table 2 summarizes acetaldehyde, acrolein, crotonaldehyde, and formaldehyde levels in aerosols generated from 45 EVALI case-related EVPs. These data include results for all measurements made within the reportable range of the method. Results are presented as the total μg per 15 puffs (at 55 mL/puff). Acetaldehyde was detected in 89% of the products with a range of 0.0856 to 5.59 μg. Acrolein was detected in 71% of the products with a range of 0.00719 to 1.05 μg. Crotonaldehyde was detected in 87% of the products with a range of 0.00175 to 1.5 μg.
0.108 μg. Finally, formaldehyde was detected in 42% of products with a range of 0.0235 to 12.6 μg. In the case where a result was outside of the calibration range, a result of "NR" (not reported) was used.

**DISCUSSION**

Comparable measurements noted in the literature for nicotine EVPs cover a wide range of deliveries for the carbonyl analytes included in this study. However, there is little data available on crotonaldehyde. Additionally, as the e-cigarette market continues to evolve with new liquid contents, coil designs, and wattages, it is challenging to make comparisons between data published with older generation devices. Our findings are broadly similar to the previously published results (Table 3), although most of the previously reported carbonyl results focus on aerosols from nicotine products. Also, in most of the prior publications, the results were generated from a limited number of dissimilar products. In many cases, the aerosols were generated under different conditions so that direct comparisons can be complicated. For example, puff counts varied across these studies with some counts as high as 150 puffs per product.

The results from our study shown in Table 3 have been converted to μg/puff in order to account for the puff total and make them more easily comparable to other literature results. The results from our study are presented including all products, with the results for only the nicotine products shown in parentheses below. The acetaldehyde measurements from the overall EVALI case-related products and the nicotine products specifically are within the ranges observed by others. It is notable that the acetaldehyde results reported by Geiss also used a DNPH cartridge trap and are similar to our EVALI EVP results. Similarly, acrolein aerosol levels from the EVALI products and the nicotine EVALI product subset are somewhat lower, but they appear within the range of other studies. Previously reported formaldehyde yields from EVPs span a wide range with studies noting results as high as ~80 μg/puff and down to the low nanogram/puff level. We observed a wide range of measurements most likely due to the broad range of product varieties examined in terms of the device type and output and the liquid composition. These results represent the range of carbonyl exposure experienced by EVALI patients. While little information has been published on crotonaldehyde in EVP aerosols, the numbers in this study are lower than that observed by Flora for a single product. It is important in assessing the possible risks associated with carbonyl exposure that, for all these results and methods, the levels for each of the carbonyls fall considerably lower than those observed in mainstream smoke produced by combustible cigarettes such as the University of Kentucky 1R6F reference product.

A summary of the carbonyl results broken down by the product type is presented in Table 4 and Figure 1. Results are presented as the total μg per 15 puffs. Acetaldehyde was detected in most of the products regardless of type; its delivery was the highest in the nicotine products. When compared to THC products (0.59 ± 0.537 μg), acetaldehyde delivery was 2.7 times higher in nicotine products (1.59 ± 1.48 μg). Acrolein was detected in the majority of the products (74% of THC products and 70% of nicotine products). The acrolein content was similarly 2.7 times higher in the nicotine products (0.360 ± 0.330 μg) compared with THC products (0.135 ± 0.263 μg), though the overall range of acrolein measurements was broader in THC products than in nicotine products. Crotonaldehyde was detected in all but one of the THC products (97% detection) and 60% of the nicotine products. Crotonaldehyde levels in the THC products had a mean delivery of 0.0256 ± 0.0267 μg, which was 9.4 times higher than levels observed in nicotine products (0.00272 ± 0.00145 μg). In the case of formaldehyde, mean deliveries were similar in both nicotine (1.93 ± 1.165 μg) and THC products (1.85 ± 4.35 μg). While the THC product results may appear to be more variable, note that the higher standard deviation was due to one product result near the high end (12.6 μg) of the calibration range, while the rest of the results were much lower. Formaldehyde was detected in 100% of the nicotine products but in only 24% of the THC products.

Table 3. Summary of our Current Results Compared with Those from Prior Comparable Studies

| study          | samples                        | carbonyl yield (μg/puff) | mean ± stdev (μg) | range (μg) | mean ± stdev (μg) | range (μg) | mean ± stdev (μg) | range (μg) | mean ± stdev (μg) | range (μg) | mean ± stdev (μg) | range (μg) |
|----------------|--------------------------------|--------------------------|-------------------|------------|-------------------|------------|-------------------|------------|-------------------|------------|-------------------|------------|
| CDC EVALI 2021 | 45 EVPs collected from EVALI cases (10 nicotine products) | ND-0.373 (ND-0.373) | 0.108 ± 0.054 | 0.373-ND | ND-0.070 (ND-0.054) | 0.0025 | ND-0.840 (ND-0.333) | 0.079-ND | ND-0.00720 (ND-0.000366) | 0.00720-ND |
| Uchiyama22     | 9 commercial brands of e-cigarettes | ND-5.20 | 0.03-13.61 | ND-4.11 | ND-79.0 | n/a | ND-0.04 | n/a | n/a | n/a | n/a |
| Geiss1         | 6 commercial products           | 0.013-0.350 | 0.0025 | 0.024-1.559 | 0.0046-0.279 | 0.013-0.374 | n/a | n/a |
| Flora2         | 11 European nicotine brands    | 0.0073-0.0907 | 0.00046 | 0.0046-0.279 | 0.013-0.374 | n/a | n/a |
| Kosmider3      | 10 commercially available nicotine solutions and 3 control solutions | 0.0013-0.0071 | ND | 0.0032-0.0039 | ND | n/a | n/a |
| Jaccard25      | 1R6F Reference Cigarette (CI smoking regime) | 1601 μg/cig | 173 μg/cig | 104 μg/cig | 55 μg/cig | n/a | n/a | n/a |

Table 4. EVALI Case-Related Product Results by the Product Type

| product type | n | detects | range (μg) | mean ± stdev (μg) | range (μg) | mean ± stdev (μg) | range (μg) | mean ± stdev (μg) | range (μg) | mean ± stdev (μg) | range (μg) |
|--------------|---|---------|------------|-------------------|------------|-------------------|------------|-------------------|------------|-------------------|------------|
| THC          | 34 | 29 | 0.0856-2.58 | 0.591 ± 0.537 | 0.000646 | 0.135 ± 0.263 | 0.00213-0.108 | 0.0256 ± 0.0267 | 8 | 0.533-1.85 | 1.26-4.35 |
| nicotine     | 10 | 10 | 0.301-5.59 | 1.59 ± 1.48 | 0.0383-1 | 0.360 ± 0.330 | 0.00168-0.00549 | 0.00272 | 0.00145 | 0.930-1.93 | 5.00-1.17 |
| none         | 1 | 1 | 0.414 | n/a | 0 | 0.805 | 0 | 0 | n/a | 2.22 | n/a |

*Positive detections within the calibration range only; one THC product produced aerosol emission of acetaldehyde above the calibration range.*
Some differences in carbonyl deliveries were noted when comparing individual products, and these are most clearly seen in Figure 1. The box plots displayed in Figure 1 show EVP results where each target analyte is plotted relative to its product active ingredient type. In the box plots, the individual results are represented by circles, and the mean for each product active ingredient type is indicated by a cross. Plot (a) shows all results, plot (b) shows a closeup view of the nicotine and THC results, and plot (c) shows the crotonaldehyde results.

**Figure 1.** Box plots showing carbonyl aerosol deliveries stratified by the product type. Plot (a) shows all results, plot (b) shows a closeup view of the nicotine and THC results, and plot (c) shows the crotonaldehyde results.
category is represented by an “X.” Among the nicotine products, the highest results for both acetaldehyde and formaldehyde (both outliers as shown in Figure 1a) came from the same product. Among the THC products, the highest formaldehyde and acrolein results also came from the same product. This product also produced the second highest crotonaldehyde result and an acetaldehyde result that was above the upper limit of our reportable range (>15 μg). The one product without any active ingredients detected had measurable levels of acetaldehyde and formaldehyde, but no acrolein or crotonaldehyde. In the box plot presentation of Figure 1, we can see that while acetaldehyde and acrolein are higher in the nicotine products as a whole than THC products, there is an overlap in the aerosol deliveries between the two product types. The formaldehyde results are much higher for nicotine products than the THC products analyzed; however, the mean delivery is similar. As seen in the box and whiskers plot of Figure 1a, there was one outlier formaldehyde result among the THC products that drives up the mean value. While the acetaldehyde level is in the range of both THC and nicotine product types, the formaldehyde result was quite high. In general, carbonyls were detected in the aerosols from all types of products independent of the active ingredient. A primary limitation in this EVALI study was related to the nature of the emergency response. Sampling was limited by the number of products available for carbonyl aerosol analysis, and replicate analyses were not possible as samples had to be extracted in the same manner, as described above, to be used as quality-control (QC) samples. Additionally, a matrix-based QC pool was generated by spiking known amounts of standard solution into a pooled matrix extract generated from commercially available nicotine EVPs. All QC samples were analyzed in duplicate.

CONCLUSIONS

We developed and validated a quantitative method for measuring carbonyls in aerosol emissions produced by both polar (nicotine) and nonpolar (THC) EVPs. Concurrent trapping and DNPH derivatization on the sorbent provided an efficient collection procedure with minimal sample loss. The levels of carbonyls observed in the EVALI case-related products were within the range of those observed in other studies of EVPs, and differences were observed when comparing carbonyl levels between different product types. Acetaldehyde and acrolein levels were higher in nicotine products while THC products were more likely to be higher in crotonaldehyde. Mean formaldehyde deliveries were similar in both nicotine and THC products. The overall carbonyl levels observed in the EVALI case-associated EVPs were lower than those found in mainstream smoke produced by combustible tobacco products but comparable to that measured in EVPs by other researchers.

EXPERIMENTAL SECTION

Materials. Rezorian sorbent-style cartridges containing 350 mg of high-purity silica coated with 2,4-DNPH were purchased from Sigma Aldrich (St. Louis, MO). A made-to-order calibration standard was purchased from O2Si Smart Solutions (Charleston, SC) containing target analytes in acetonitrile at the following concentrations: formaldehyde (5000 mg/L), acetaldehyde (5000 mg/L), acrolein (500 mg/L), and crotonaldehyde (125 mg/L). An isotopically labeled analog solution was also purchased from O2Si Smart Solutions with the following concentrations in acetonitrile: formaldehyde-d$_{1}$-DNPH (1000 mg/L), acetaldehyde-d$_{1}$-DNPH (1000 mg/L), acrolein-2,4-DNPH-3,5,6-d$_{3}$ (100 mg/L), and crotonaldehyde-2,4-DNPH-3,5,6-d$_{3}$ (25 mg/L). Ammonium acetate (molecular biology grade) was purchased from Sigma Aldrich.

Calibration Curve and Quality-Control Sample Preparation. Calibration spiking solutions were prepared by diluting the calibration standard solution in acetonitrile to create individual solutions of varying concentrations. These solutions were spiked directly onto the Rezorian cartridges and extracted in the same manner as the analytical samples prepared in the same manner as the analytical samples to ensure that the derivatization of the standards was the same as the known vaporized products. A 300 μL aliquot of the calibration spiking solution was spiked directly onto a cartridge for each calibration level. The on-cartridge amounts ranged from 0.05–15 μg (formaldehyde and acetaldehyde), 0.005–1.5 μg (acrolein), and 0.00125–0.375 μg (crotonaldehyde). Immediately after spiking, the cartridges were re-capped and allowed to equilibrate. Each cartridge was extracted within 10 min of spiking. Positive pressure was used to push the cartridge contents out into a vial containing 10 mL of an extraction solution (acetonitrile containing internal standard). The cartridge body was also added to the vial and capped. The vials were then placed on a rotary shaker for 15 min at 180 rpm. After shaking, a 600 μL aliquot of each calibrator solution was placed into a 2 mL autosampler vial containing 900 μL of 10 mM ammonium acetate. Additional sample spikes were prepared in the same manner, as described above, to be used as quality-control (QC) samples. Additionally, a matrix-based QC pool was generated by spiking known amounts of standard solution into a pooled matrix extract generated from commercially available nicotine EVPs. All QC samples were analyzed in duplicate.

Vaping and Sample Collection. EVPs were analyzed on an automated CETI-8 linear vaping machine equipped with push-button actuators (Cerulean, Milton Keynes, UK). Prior to vaping, a series of 25 clearing puffs were performed to warm up the machine and ensure that the system was clear of any residual aerosol. Puff volumes were checked with a calibrated soap bubble flow meter, and any adjustments were made if necessary. The EVPs were connected to the vaping machine with Rezorian cartridges attached in-line behind the Cambridge filter pad holder capturing both the vapor and particle phases. A set of seven EVPs were vaped per run, and the remaining port was used as a blank control (a Rezorian cartridge was attached, but no EVP was connected). Product aerosols were generated using the CORESTA recommended method 81 for analyzing e-cigarettes (55 mL puff volume, 3 s puff duration, 30 s puff interval, square puff profile). A total of 15 puffs were collected for each product. Immediately after vaping, the Rezorian cartridges were removed and capped, and the EVP devices were weighed to assess for e-liquid loss. All cartridges (blank and unknowns) were extracted, as described above, for the calibration standards.

High-Performance Liquid Chromatography–Tandem Mass Spectrometry Analysis. Samples were analyzed using an Agilent 1260 HPLC System (Agilent Technologies, Wilmington, DE) paired with a 5500 Triple Quad mass spectrometer with a turbo spray ion source (SCIEX, Framingham, MA). Target analyte separation was performed using an Acquity UPLC BEH C18 column (1.7 μm particle
size, 2.1 mm I.D. × 50 mm, Waters, Milford, MA) with a Vanguard BEH C18 precolumn (1.7 μm particle size, 2.1 mm I.D. × 5 mm, Waters). Water with 10 mM ammonium acetate (A) and acetonitrile (B) was used as mobile phases. A 5 μL sample injection was used, and the column temperature was maintained at 35 °C. The mobile-phase gradient elution went from 60%/40% A/B to 30%/70% A/B over 6.2 min with a total run time of 10 min. Dwell times of 25 ms were used for all analytes, and the transitions monitored are listed in Table 5. In

Table 5. Multiple Reaction Monitoring (MRM) Transitions Monitored for Target Analytes

| Compound          | Quantitation (Da) | Confirmation (Da) | Internal Standard (Da) |
|-------------------|-------------------|-------------------|------------------------|
| Formaldehyde−DNPH | 209.1 → 163.1     | 209.1 → 151.0     | 211.0 → 151.0          |
| Acetaldehyde−DNPH | 223.1 → 151.0     | 223.1 → 163.0     | 227.0 → 151.0          |
| Acrolein−DNPH     | 235.1 → 163.0     | 235.1 → 158.0     | 238.0 → 161.0          |
| Crotonaldehyde−DNPH | 249.1 → 181.0 | 249.1 → 172.0     | 252.0 → 175.0          | 252.0 → 184.0

addition to calibrators and samples, blank samples were analyzed from various stages in the sample preparation procedure to assess for background levels and assure that detected carbonyls came from EVP emissions. Solvents, Rezorian cartridges, and the sample blank from the vaping run were assessed for carbonyl content daily.

Chromatographic data were analyzed using Analyst software (SCIEX). Integrated peaks were examined for shape, and all peaks were baseline-resolved. No manual integration was necessary. For each analyte, two sets of ion transitions (quantitation and confirmation) were monitored to ensure correct identification. Calibration curves were generated by plotting the response area ratio of the native peak area to the internal standard peak area (native area/internal standard area) vs the calibration standard amount using linear regression and 1/x weighting.

**Application: EVALI Products.** A set of 77 EVPs collected from 37 EVALI case patients was examined for aerosol carbonyl content. The products examined included a mixture of complete vaping devices including their liquids, vaping tanks, or cartridges containing liquid (but no battery), and in most cases, just the vaping liquid itself (no tank/cartridge or battery). Every effort was made to use the complete product as received when possible. In the case where a product could be analyzed as received, it was operated at its highest voltage setting. In the case where we only had the tank/cartridge or the liquid itself, the liquid was transferred to a commercially available device that was operated at its highest battery voltage setting (4 volts). All EVPs were weighed before and after vaporizing to determine the product mass lost (PML), and only those with a loss of 6.5 mg (two standard deviations below average for deliveries of functional devices) or greater were considered to have functioned properly, and therefore, the analysis of vapor for the carbonyl content was carried out. Out of the 77 EVPs examined, 45 passed the requirements for product operation and aerosol generation, including normal analytical QC/QC review. The liquids contained in these products were also analyzed for the following active ingredients: nicotine (Nic), cannabidiol (CBD), and Δ9-tetrahydrocannabinol (THC). Products examined were categorized based on their active ingredient, and the thresholds used for product class determination were >0.3% for THC, >0.2% for nicotine, and >1% for CBD. Thus, among the 45 products examined, 34 were THC products, 10 were nicotine products, and none were CBD products. One product was found to contain no appreciable amount of THC, nicotine, or CBD.

**DISCLAIMER**

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The use of trade names is for identification only and does not imply endorsement by the Centers for Disease Control and Prevention, the Public Health Service, or the U.S. Department of Health and Human Services.

**AUTHOR INFORMATION**

**Corresponding Authors**

Megan McGuigan — Division of Laboratory Sciences, National Center for Environmental Health, U.S. Centers for Disease Control and Prevention, Atlanta, Georgia 30341, United States; orcid.org/0000-0002-9340-9299; Email: MMcguigan@cdc.gov

Liza Valentin-Blasini — Division of Laboratory Sciences, National Center for Environmental Health, U.S. Centers for Disease Control and Prevention, Atlanta, Georgia 30341, United States; Email: lbv5@cdc.gov

**Authors**

Gala Chapman — Division of Laboratory Sciences, National Center for Environmental Health, U.S. Centers for Disease Control and Prevention, Atlanta, Georgia 30341, United States

Erica Lewis — Division of Laboratory Sciences, National Center for Environmental Health, U.S. Centers for Disease Control and Prevention, Atlanta, Georgia 30341, United States

Clifford H. Watson — Division of Laboratory Sciences, National Center for Environmental Health, U.S. Centers for Disease Control and Prevention, Atlanta, Georgia 30341, United States

Benjamin C. Blount — Division of Laboratory Sciences, National Center for Environmental Health, U.S. Centers for Disease Control and Prevention, Atlanta, Georgia 30341, United States; orcid.org/0000-0003-4788-8169

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.1c06321

**Notes**

The authors declare no competing financial interest.

**REFERENCES**

1. Kruiseman, E. J. Z.; Havermans, A.; Pennings, J. L. A.; de Graaf, K.; Boesveldt, S.; Talhout, R. Comprehensive overview of common e-liquid ingredients and how they can be used to predict an e-liquid’s flavour category. Tob. Control 2021, 30, 185–191.

2. Shao, X. M.; Friedman, T. C. Pod-mod vs conventional e-cigarettes: nicotine chemistry, pH, and health effects. J. Appl. Physiol. 2020, 128, 1056–1058.

3. Nicol, J.; Fraser, R.; Walker, L.; Liu, C.; Murphy, J.; Proctor, C. J. Comprehensive chemical characterization of the aerosol emissions of
a vaping product based on a new technology. *Chem. Res. Toxicol.* **2020**, *33*, 789–799.

(4) Geiss, O.; Bianchi, I.; Barrero-Moreno, J. Correlation of volatile carbonyl yields emitted by e-cigarettes with the temperature of the heating coil and the perceived sensorial quality of the generated vapors. *Int. J. Hyg. Environ. Health* **2016**, *219*, 268.

(5) Li, Y.; Burns, A. E.; Tran, L. N.; Abellar, K. A.; Poindexter, M.; Li, X.; Madl, A. K.; Pinkerton, K. E.; Nguyen, T. B. Impact of e-Liquid Composition, Coil Temperature, and Puff Topography on the Aerosol Chemistry of Electronic Cigarettes. *Chem. Res. Toxicol.* **2021**, *34*, 1640–1654.

(6) Uchiyama, S.; Tomizawa, T.; Inaba, Y.; Kunugita, N. Simultaneous determination of volatile organic compounds and carbonyls in mainstream cigarette smoke using a sorbent cartridge followed by two-step elution. *J. Chromatogr. A* **2013**, *1314*, 31–37.

(7) Flora, J. W.; Wilkinson, C. T.; Wilkinson, J. W.; Lipowicz, P. J.; Skapars, J. A.; Anderson, A.; Miller, J. H. Method for the Determination of Carbonyl Compounds in E-Cigarette Aerosols. *J. Chromatogr. Sci.* **2017**, *55*, 142–148.

(8) Goniwicz, M.; Knysak, J.; Gawron, M.; Kosmider, L.; Sobczak, A.; Kurek, J.; Prokopowicz, A.; Jablonska-Czapla, M.; Rosik-Dulewska, C.; Havel, C.; Jacob, P.; Benowitz, N. Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tob. Control* **2014**, *23*, 133–139.

(9) Kosmider, L.; Sobczak, A.; Fik, M.; Knysak, J.; Zaciera, M.; Kurek, J.; Goniwicz, M. L. Carbonyl compounds in electronic cigarette vapors: effects of nicotine solvent and battery output voltage. *Nicotine Tob. Res.* **2014**, *16*, 1319–1326.

(10) Troutt, W. D. Didonato MD Carbonyl compounds produced by vaporizing cannabis oil thinning agents. *J. Altern. Complementary Med.* **2017**, *23*, 879–884.

(11) Braymiller, J. L.; Barrington-Trimis, J. L.; Leventhal, A. M.; et al. Assessment of Nicotine and Cannabis Vaping and Respiratory Symptoms in Young Adults. *JAMA Netw. Open* **2020**, *3*, No. e2030189.

(12) Meehan-Atrash, J.; Luo, W.; McWhirter, K. J.; Strongin, R. M. Aerosol Gas-Phase Components from Cannabis E-Cigarettes and Dabbing: Mechanistic Insight and Quantitative Risk Analysis. *ACS Omega* **2019**, *4*, 16111–16120.

(13) Harmful and Potentially Harmful Constituents in Tobacco Products and Tobacco Smoke; Established List, 77 FR 20034 (April 3, 2012).

(14) Belki, K.; Uchiyama, S.; Ohta, K.; Inaba, Y.; Nakagome, H.; Kunugita, N. Carbonyl compounds generated from electronic cigarettes. *Int. J. Environ. Res. Public Health* **2014**, *11*, 11192–11200.

(15) Spencer, A.; Lauterbach, J. H. Generation of acetalddehyde and other carbonyl compounds during vaporization of glycerol and propylene glycol during puffing of a popular style of e-cigarette, in 54th Meeting of the Society of Toxicology, 2015. Abstract 188.

(16) Fowles, J.; Dybing, E. Application of toxicological risk assessment principles to the chemical constituents of cigarette smoke. *Tob. Control* **2003**, *12*, 424–430.

(17) Stephens, W. E. Comparing the cancer potencies of emissions from vapourised nicotine products including e-cigarettes with those of tobacco smoke. *Tob. Control* **2018**, *27*, 10–17.

(18) Miller, J. H.; Gardner, W. P.; Gonzalez, R. R. UHPLC separation with ms analysis for eight carbonyl compounds in mainstream tobacco smoke. *J. Chromatogr. Sci.* **2010**, *48*, 12–17.

(19) Intorp, M.; Purkis, S.; Wagstaff, W. Determination of Carbonyl Compounds in Cigarette Mainstream Smoke. The CORESTA 2010 Collaborative Study and Recommended Method. *Contrib. Tob. Res.* **2013**, *25*, 361–374.

(20) Intorp, M.; Purkis, S.; Whittaker, M.; Wright, W. Determination of “Hoffmann Analytes” in Cigarette Mainstream Smoke. The Coresta 2006 Joint Experiment. *Contrib. Tob. Res.* **2009**, *23*, 161–202.

(21) Ding, Y. S.; Yan, Z.; Wong, J.; Chan, M.; Watson, C. H. In Situ Derivatization and Quantification of Seven Carbonyls in Cigarette Mainstream Smoke. *Chem. Res. Toxicol.* **2016**, *29*, 125–131.