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Journal

Chemical research in toxicology, 34(6)

ISSN

0893-228X

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Publication Date

2021-06-01

DOI

10.1021/acs.chemrestox.1c00070

Supplemental Material

<https://escholarship.org/uc/item/7rg2p1h2#supplemental>

Peer reviewed

Impact of e-liquid composition, coil temperature, and puff topography on the aerosol chemistry of electronic cigarettes

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Abstract E-cigarette aerosol is a complex mixture of gases and particles with a composition that is dependent on the e-liquid formulation, puffing regimen, and device operational parameters. This work investigated mainstream aerosols from a 3rd generation device, as a function of coil temperature (315 – 510 °F, correspond to 157 – 266 °C), puff duration (2 – 4 s), and the ratio of propylene glycol (PG) to vegetable glycerin (VG) in e-liquid (100:0 – 0:100). Targeted and untargeted analyses using liquid chromatography high-resolution mass spectrometry, gas chromatography, in-situ chemical ionization mass spectrometry, and gravimetry was used for chemical characterizations. PG and VG were found to be the major constituents (> 99%) in both phases of the aerosol. Most e-cigarette components were observed to be volatile or semivolatile under the conditions tested. PG was found almost entirely in the gas phase, while VG had a sizable particle component. Nicotine was only observed in the particle phase. The production of aerosol mass and carbonyl degradation products dramatically increased with higher coil temperature and puff duration, but decreased with increasing VG fraction in the e-liquid. An exception is acrolein, which increased with increasing VG. The formation of carbonyls was dominated by the heat-induced dehydration mechanism in the temperature range studied, yet radical reactions also played an important role. The findings from this study identified open questions regarding both pathways. The vaping process consumed PG significantly faster than VG under all tested conditions, suggesting that e-liquids become more enriched in VG and the exposure to acrolein significantly increases as vaping continues. It can be estimated that a 30:70 initial ratio of PG:VG in the e-liquid becomes almost entirely VG when 60-70% of e-liquid remains during the vaping process at 375 °F (191 °C). This work underscores the need for further research on the puffing lifecycle of e-cigarettes.

For TOC only

1. Introduction

Electronic (e-) cigarettes are battery-operated devices used to “vape” or aerosolize “e-liquid” consisting of propylene glycol (PG), vegetable glycerin (VG), nicotine, and optional flavor compounds.¹⁻⁵ The global market share of e-cigarettes is rapidly growing,⁶⁻¹³ and e-cigarette use among young people has become a significant public health concern.¹⁴⁻¹⁷ Of U.S. high school students and middle school students, 27.5% and 10.5%, respectively, self-reported usage for one or more days during the past 30 days in 2019.¹⁸ The design of the e-cigarette¹⁹⁻²¹ has rapidly evolved from 1st generation “cig-a-like” pods with disposable, prefilled, e-liquid cartridges and fixed operational parameters (notably voltage and power, and correspondingly, coil temperature of the device), to 3rd generation “mods” with a refillable e-liquid tank and adjustable device operational parameters. More recently, 4th generation “mod-pod” hybrids with fixed power output have been released. Approximately 80% of e-cigarette users primarily use 3rd or 4th generation devices today.²²⁻²⁴

E-cigarette gas and particle emissions are composed of aerosolized PG, VG, optional flavors, and nicotine from the e-liquid, as well as free radicals, and a variety of carbonyls or hydroxycarbonyls (e.g., formaldehyde, acetaldehyde, hydroxyacetone, acrolein) formed by thermal degradation during the e-liquid heating process.^{1, 2, 5, 25-36} Recent evidence suggests hydroxycarbonyls may be more abundant than anticipated, but their impacts on health remain poorly understood.³⁷ With the ability to change vaping parameters (e.g., puff duration, puff frequency, device power, etc.), coil material, and e-liquid formulations in 3rd and 4th generation devices, there exists a multitude of use combinations that can influence the composition of the inhaled e-cigarette aerosol. In particular, aerosol composition and gas/particle partitioning could greatly influence the risk of chemical exposure and aerosol deposition in the human respiratory tract.³⁸⁻⁴² However, the ways in which e-liquids form aerosol components under different vaping parameters have not been fully elucidated in the literature.

Coil temperature and e-liquid composition will directly affect e-cigarette aerosol emissions, as heating e-liquid solutions with metal coils results in thermal degradation reactions and changes in aerosol concentration.^{5, 29, 31, 43} Coil surface area is also an important parameter that could affect thermal decomposition rates in various coil designs.²⁰ The majority of published studies have correlated e-cigarette emissions to device voltage and power, but not directly to the vaping coil

temperature that governs the thermal degradation process.⁴⁴⁻⁴⁷ For example, Korzun et al.⁴³ inferred coil temperature by airflow rate, and found higher temperatures led to higher concentrations of formaldehyde and acetaldehyde by promoting the degradation of higher-molecular-weight products such as hydroxyacetone and glycoaldehyde in the product mixture. Uchiyama et al.³¹ evaluated the phase distribution for a number of compounds, and found the formation of degradation products from vaping exponentially increased when the device power exceeded 40 W. However, a direct comparison between such studies is challenging. This is because the actual coil temperature is synergistically influenced by many factors, some of which are inherent to the coil, while others are a result of the conditions of operation. For example, different coils may have different resistances due to material and structural variance. Furthermore, coil temperature may also be influenced by e-liquid composition, which changes the viscosity and heat capacity, or by air flow rates in the device, as faster air flow rates have higher cooling effects.^{43, 48, 49} Thus, a single vaping device may produce different temperature ranges for the same voltage input upon minor alterations in operational scenarios.⁵⁰ In addition, the aerosol emissions will change as a result of the users' puffing regimen.^{28, 51-54} Bitzer et al.⁵⁵ showed puff volume and duration influence the per-puff yield of nicotine, carbonyls, aerosols, and free radicals. Beauval et al.⁵⁶ also found modifications in puffing conditions lead to significant variations in the carbonyl composition of e-cigarette aerosols.

PG and VG are known to be the major contributors to the aerosol particle phase. However, there remain a number of questions concerning the fractions of PG and VG in the total e-liquid that convert to degradation products, the specific chemical mechanisms of transformation, and the ways in which e-cigarette chemical components partition between phases in response to changing vaping parameters.^{57, 58} Thus, a systematic understanding of how the carbon mass balance and chemistry of the vaping process respond to changing e-liquid formulation, major puffing parameters, and actual coil temperatures is critically needed. Monitoring coil temperature instead of voltage/power as a standard evaluation metric may provide greater fundamental insights into the chemistry. However to do so, the coil temperature will need to be directly measured during each puff, as the temperature-controlled programs of e-cigarette devices may not be a true reflection of the actual coil temperature.⁵⁰

In the present study, a broad chemical analysis suite, volatility-based aerosol sampling, and direct measurement of coil temperatures were employed to study the aerosol emissions from a 3rd generation e-cigarette device at various coil temperatures, puff durations, and PG:VG ratios in the e-liquid solution. Flavoring compounds were deferred for future research. The loss of mass from the e-liquid conversion to aerosols was compared with independent measurements in the particle and gas phases for carbon mass closure analyses.

2. Experimental Procedures

2.1 E-cigarette sample generation and extraction.

E-cigarette aerosols were generated using a 3rd generation Evolv DNA 75 Color modular vaping device (Evolv LLC., Hudson, Ohio) with replacement single mesh vaping coils (SS316L, FreeMax Technology Inc., Shenzhen, China) that have a coil resistance of *ca.* 0.12 Ohm. The stainless steel coil was selected as only limited coil materials (e.g., nickel, titanium, stainless steel) are appropriate for temperature control.⁵⁰ The device (**Fig. 1**) has a rechargeable battery with a variable output voltage (0.2 – 9 V) and power (0 – 75W), an atomizer coil assembly, a refillable e-liquid tank that enables e-liquid with variable formulations to be tested, and a push button to initiate puffing. The

device was robotically operated by a custom linear actuator (TE-2e, Teague Enterprises Inc., Woodland, CA) during the puffing process, which enabled precise control of the puff rate (1 – 6 puffs/minute) and puff duration (2 – 4 s) with a $\pm 3\%$ standard deviation (1σ). Evolv Escribe software (Evolv LLC., Hudson, Ohio) was used to set the power and temperature conditions to achieve the desired coil temperature (**Fig. S1**), as measured by a flexible Kapton-insulated K type thermocouple (Oakton instrument Inc., Vernon Hills, IL) in contact with the center of the coil surface, and output to a digital readout. The puff flow rate was 1.186 ± 0.002 L/min, and the corresponding puff volume for a 3-s puff was 59.3 ± 0.1 mL, as quantified by a primary flow calibrator (A.P. Buck Inc., Orlando, FL). The puff volume and duration selected for this study is

Figure 1. Device and sampling set up. The total aerosol and the particle fraction of total aerosol (captured by a 0.2-um pore hydrophilic-surface PTFE filter) were analyzed independently. The difference is termed the volatile/semi-volatile fraction in the gas phase.

consistent with the CORESTA e-cigarette testing protocol (3 ± 0.1 s, 55 ± 0.1 mL).⁵⁹ However, puff volume larger than 100 mL and puff duration longer than 3 s have been observed in some vaping scenarios.^{60,61} For example, Robinson et al.⁶² found a typical case of puff topography with 3.7 s puff duration and 144 mL puff volume. Thus, this highlights a limitation of the current study when extrapolated to various vaping scenarios, as an increase in the puff volume will increase the formation of aerosol and thermal degradation compounds.⁵⁵ The puffing protocol for the puff duration study is not based on volume, but used a variable puff duration at a fixed flow rate. **Table 1** shows the experimental conditions used in this work. Pure VG, PG, and nicotine (> 99 % purity, Sigma Aldrich) were used to generate e-liquids at the ratios and concentrations shown in **Table 1**.

Table 1. Experimental conditions for e-cigarette aerosol sample generation. Coil temperatures were measured by a thermocouple and controlled to within a standard deviation of 5 °F (3 °C), variable temperatures correspond to 157, 191, 216, 246, 266 °C.

Parameters	Variable settings	Fixed settings
Coil temperature (°F)	315, 375, 420, 475, 510	PG:VG 30:70, nicotine 3 mg/mL, 3 s puff
PG:VG ratio	100:0, 70:30, 50:50, 30:70, 0:100	Temperature 375 °F, nicotine 3 mg/mL, 3 s puff
Puff duration (s)	2, 3, 4	Temperature 375 °F, PG:VG 30:70, nicotine 3 mg/mL

Particles were collected on a hydrophilic polytetrafluoroethylene (PTFE) membrane filters (Omnipore, 0.2 μ m pore size, Millipore Sigma Inc., Burlington, MA). PTFE and other types of filters have been used in sample collection for e-cigarette research.⁶³⁻⁶⁵ As hydrophobic filters were found to be incompatible with the polar compounds in e-cigarette aerosol,⁶⁵ the hydrophilic PTFE filters were chosen for use because they have broad compatibility with both polar and nonpolar functional groups. Both the gas phase of total aerosol stream and the particle filters (**Fig. 1**) were analyzed for mass and chemical composition. The total mass lost from the e-liquid due to vaping was determined gravimetrically on a microbalance (Shimadzu Corp., 0.0001 g precision, calibrated by weight standards) by weighing the e-liquid compartment immediately before and after puffing 10 puffs, and dividing by the number of puffs at different experimental conditions. The standard deviation of the gravimetric analysis after triplicate measurements was determined to be ~ 20%, mainly due to variations in puffing. The composition of gas phase PG/VG, was analyzed by chemical ionization triple-quadrupole mass spectrometer (CIMS); a detailed description can be found in **Section 2.4**. The particle mass on the filter was analyzed after each collection on the microbalance, also performed in triplicate. The total mass of molecules residing

in the gas phase was determined as the difference between the total mass of e-liquid lost and the mass of the particles collected.

E-cigarette aerosols are known to be semivolatile at room-temperature, i.e., the chemicals can exist in both gas and particle phases under various conditions (slight temperature and humidity variance, condensable surface area, dilution air, etc.), and are highly unstable mixtures that undergo continuously change of size, number concentration and chemical composition by coagulation, evaporation/condensation of individual components, wall deposition and potentially water uptake.^{66,67} Thus, there is no perfect sampling protocol for such a dynamic mixture. Sampling with particle filters may either underestimate or overestimate total nonvolatiles. Underestimation may occur if fine particles break through the filter. Overestimation could result if the filter has a higher surface area than in realistic vaping scenarios, or if the filter is saturated with an organic film, into which the semivolatiles can partition during sampling. Our particle size distribution analysis with a scanning mobility particle sizer (SMPS, TSI Inc) that measures a size range of 0.014 - 0.671 μm diameter (**Fig. S2**) showed that particle breakthrough for Omnipore filter at a 0.2- μm pore size may not be significant for this work. However, the diameter of aerosol will go through a size change process caused mainly by coagulation and evaporation that could occur during the aerosol collection and measurement steps.⁶⁶ Zhang et al.⁶⁸ found that the count median diameter (CMD) of e-cigarette aerosols is 120 – 180 nm when counted immediately after emission from the e-cigarette. The CMD changes to 400 nm for the measurement of droplets at steady-state. Furthermore, we confirmed that the collection efficiency for the filter was > 97.5% based on consecutive collections in series. Thus, we believe this method minimized the possible underestimations of the particle phase. We then tested a denser structure or higher surface area particle filtering material. A high-flow (no pressure drop) High Efficiency Particulate-free Air (HEPA) capsule (Pall Corp., 121144) upstream of our chemical analyses removed 99.9% of all particles (**Fig. S2**). However, the HEPA capsule also removed 50-100% of gaseous formaldehyde, hydroxyacetone, acetone, acetaldehyde, and dihydroxyacetone gas standards that were evaporated and diluted directly into a 100-L Teflon FEP bag using chemical standards, which would overestimate the particle phase.

For the purpose of this work, particles that are trapped by hydrophilic PTFE filter are termed the “nonvolatile (NV)” or “particle” fraction and the difference between the total aerosol and the NV

fraction is termed the “volatile/semivolatile” or “gas” fraction. Although particles are termed nonvolatile, it does not mean that they cannot partition to the gas phase under conditions different than the ones we tested (e.g., with a dilution stream of gas). Likewise, semivolatiles emitted in the gas phase directly from the mainstream can condense onto surfaces (e.g., respiratory passageways) that have higher condensable surface area than used in our study.

2.2 Particle-phase PG, VG, and nicotine characterized by GC-MS. The particle filters were analyzed by an Agilent 6890N gas chromatograph coupled to an Agilent 5973N quadrupole mass spectrometer (GC-MS, Agilent Technologies Inc., Santa Clara, CA). Filters were extracted by a 10-mL 1:1 mix of methanol and ethyl acetate (Fisher Scientific Inc., Hampton, NH). The method for the analysis of PG, VG, and nicotine was adapted from Williams et al.⁶⁹ The components were separated on a DB-wax capillary column (30 m, 0.25 mm ID, 0.25 μ m film, Agilent Technologies Inc., Santa Clara, CA) with ultra-high purity (UHP) grade Helium at a constant flow of 1.1 mL/min. The temperature program was 50 °C (0.5 min), 8 °C/min to 160 °C, 5 °C/min to 170 °C, then 170 °C (15 min). Electron impact mass spectra for PG, VG, and nicotine were > 90% matched to the National Institute of Standards and Technology (NIST) database. PG, VG, and nicotine standards (purity $\geq$ 99%, Sigma-Aldrich Inc.) were used for GC-MS calibration (**Fig. S3**).

2.3 Carbonyls and organic acids characterized by high performance liquid chromatography-high resolution mass spectrometry (HPLC-HRMS). Details of the identification and quantification methods have been previously described in detail.³⁷ Briefly, carbonyls are derivatized *in-situ* into hydrazones with 2, 4-dinitrophenylhydrazine (2,4-DNPH) cartridges (Supelco Inc., 350 mg DNPH) and extracted with 2 mL acetonitrile (Fisher Scientific Inc., LC-MS grade, Hampton, NH) prior to analysis. Consecutive sampling with three DNPH cartridges in series showed that >98.4% of carbonyls were captured in the first cartridge. Consecutive solvent extractions of DNPH cartridges for samples confirmed that > 97% of both DNPH and its hydrazones were extracted after the first 2-mL volume of acetonitrile. Carbonyl-DNPH extracts were analyzed for molecular composition using an Agilent 1100 HPLC with an Agilent Poroshell EC-C18 column (2.1 $\times$ 100 mm, 2.7 μ m, 120 Å) coupled to a linear-trap-quadrupole Orbitrap (LTQ-Orbitrap) mass spectrometer (Thermo Corp., Waltham, MA) at a mass resolving power of $\sim$ 60,000 $m/\Delta m$ at m/z 400. All analyses were performed in triplicate. A total of 30 puffs were collected for each analysis, which was verified to be within the linear dynamic range of the

measurement (**Fig. S4**). Concentrations of formaldehyde, acetaldehyde, acetone, acrolein, and propionaldehyde in e-cigarette aerosols were quantified by analytical standards (**Fig. S4**), and those of other carbonyls were quantified using theoretical calculations of relative sensitivity in the ESI negative mode ionization (**Fig. S5**).³⁷ The $\pm 1\sigma$ uncertainty of the analysis is 10-20% when using analytical standards and 30-50% when using the theoretical model. The HPLC-HRMS data for carbonyls derivatized as hydrazones were corrected to remove the mass contribution of DNPH.

2.4 Volatile/semivolatile PG and VG characterized by chemical ionization triple-quadrupole mass spectrometer (CIMS). The volatile/semivolatile concentrations of PG and VG were quantified by custom trifluoromethanolate (CF_3O^-) CIMS at a 5-min time resolution, which analyzes the *in-situ* mixing ratios of polar volatiles in the gas phase.⁷⁰⁻⁷³ One puff was introduced into a Teflon pillow bag that was filled with 100 L of ultra-zero air via a calibrated mass flow controller. The CIMS flow tube diluted the mixture by a factor of 9 with UHP nitrogen. The particulate fractions of aerosols are lost through the flow introduction method to the CIMS, which uses a small pinhole orthogonal to a fast straight flow. The ionization mechanism for PG and VG in the negative mode is cluster formation ($\text{M} + \text{CF}_3\text{O}^-$). Direct calibration is not possible due to lower Teflon permeation efficiencies and unavailability of fourier-transform infrared (FT-IR) spectra for PG and VG; thus, quantification of PG and VG was performed based on ethylene glycol as a proxy calibrant. The ethylene glycol sensitivity was obtained by gravimetric measurements of a permeation tube of the pure standard with a stable permeation rate over several months, achieved by constantly flowing 25 sccm of UHP nitrogen past the permeation tube in a custom flow chamber kept in a 40 °C bath. The effect of an additional hydroxy ($-\text{OH}$) group and methyl ($-\text{CH}_3$) group on the CIMS sensitivity was estimated based on the sensitivities of other calibrant compounds (e.g., formic acid vs. acetic acid, and hydroxymethylhydroperoxide vs. methylhydroperoxide). Analytical uncertainties of 40-50% were estimated based on the range of possible sensitivities, with PG having lower uncertainty. The CIMS signal for PG and VG were normalized by the reagent signal before applying their sensitivities, then dilution-corrected to obtain the gas-phase mixing ratios in the bag. Multiplying by the exact volume of gas in the bag gave the quantity in one puff.

The limitation of this technique for e-cigarette aerosols is that semivolatiles may evaporate from particles during the dilution process. Thus, the technique may overestimate the

volatile/semivolatile fractions in comparison to the filter method. Thus, we limited the interpretations of CIMS to the following: (1) observations of gaseous nicotine, which may be observed in the positive mode as a protonated ion if it existed in the mixture (we did not observe this signal); (2) a rough mass balance closure — estimations of whether the gaseous fraction (gravimetric difference between total mass loss from the e-liquid and the particulate fraction) can be attributed to PG, VG, or other compounds such as hydroperoxides and organic acids that the CIMS can quantify well; and (3) the relative abundance of PG and VG compared to carbonyls, such as hydroxyacetone, that the CIMS also detects with high sensitivity.

3. Results and Discussion

Figure 2. The relationship between the production of particle mass and **a)** measured coil temperatures, or **b)** temperatures set by the Evolv software for four different coils using e-liquid with a 30:70 PG:VG ratio by volume and 3 mg/mL nicotine.

3.1. Coil temperature The particle mass was strongly correlated to the measured coil temperature (**Fig. 2a**, $R^2 \sim 0.8$), and was independent of coil identity. In contrast, the production of particle mass was not well-correlated to the temperature set by the Evolv program when different coils were used from the same manufacturer, model, and batch (**Fig. 2b**). Repeated replacement of the coil in the device was also found to change the measured temperature response for the same power and temperature settings. Our findings demonstrated significant variations were present between different coils.⁵⁰ The particle mass range of 0.9 – 17.2 mg/puff for the temperatures examined in this study was within the range studied by Gillman et al. (1.5 – 28 mg/puff) for five different devices.⁴⁴ The exponential dependence shown **Fig. 2a** is in large measure consistent with the few

limited studies of particle production with device power, which generally show a positive relationship, albeit with limited data points.^{46, 74} A more thorough comparison of the present findings to others is challenging, as coil temperatures are typically not reported in the literature.

The production of carbonyls from vaping (**Fig. 3**) had a strong dependence on coil temperature and, in general, a vertical offset around zero (i.e., they were not formed without heat). Hydroxyacetone (**Fig. 3B**) was the only compound observed with a substantial concentration at a coil temperature of 315 °F (157 °C). This finding is consistent with Sleiman et al.,⁵ who reported hydroxyacetone exists in PG/VG e-liquid without thermal degradation, as a possible minor impurity. In general, we found exponential relationships between carbonyl formation and temperature, which reflect that of particle mass production, and are consistent with Arrhenius kinetics given that the formation of carbonyls is a chemical process.⁷⁵⁻⁷⁷ All data for carbonyls and organic acids (also captured by the DNPH cartridge) are reported in **Table S1 – S3**. The temperature dependencies for formaldehyde, hydroxyacetone, acetaldehyde, acrolein, and propionaldehyde (**Fig. 3A, B, C, F, G, and H**) were more steeply exponential than those observed for others. The trends for acetone, dihydroxyacetone, and glyceraldehyde (**Fig. 3E, G, I**) were

Figure 3. The production of representative carbonyl compounds and various coil temperatures.

nearly linear (or at least, within the linear part of the exponential curve that would manifest when a greater temperature range is used). We believe the different response curves were due to the different chemical pathways forming specific carbonyls.

Two major pathways have been proposed for the thermal degradation of PG and VG in e-cigarette devices, including heat-induced dehydration (**Scheme 1a**)^{2, 5, 78, 79} and H-abstraction by radicals

a) Dehydration mechanism

b) Radical reaction mechanism

Scheme 1. Proposed mechanism of PG and VG degradation in the e-cigarette device from (a) heat induced dehydration and (b) radical reaction pathways, with further oxidation and bond cleavage to form final products. Legend key: 1) acetone, 2) propionaldehyde, 3) hydroxyacetone, 4) formaldehyde, 5) acetaldehyde, 6) 1-hydroxypropanal, 7) acrolein, 8) methylglyoxal, 9) lactaldehyde, 10) glyceraldehyde, 11) glyoxal, 12) dihydroxyacetone, 13) glycolaldehyde.

such as OH (**Scheme 1b**),^{25,28,80,81} both followed by further oxidation and bond cleavage. The more exponential temperature-dependent carbonyl compounds (e.g., formaldehyde, acetaldehyde, acrolein, hydroxyacetone, 1-hydroxypropanal) are formed primarily through heat-induced dehydration pathways since they are directly affected by heat. The carbonyls formed from the radical reaction pathway (e.g., dihydroxyacetone and glyceraldehyde, **12** and **10** in **Scheme 1**) have trends that are more linear because they only have a secondary dependence on heat; their direct dependence is on radical concentrations. Bitzer et al.⁸² found that the formation of free radicals from e-cigarettes is linear within the temperature range (315 – 510 °F, correspond to 157 – 266 °C) of the present study. Thus, the radical-derived products will mirror this temperature dependence. It is not clear from Bitzer et al. or our data what temperature inflection point will cause a more exponential formation of radicals, as higher temperatures are outside the range for our device. However, computational modeling data predict radical formation may start dominating at 680 °F (360 °C) for VG.⁸³ Acetone (**1**), in particular, has a linear temperature trend, even though it can be formed through the same PG dehydration pathway (**Scheme 1a**) as propionaldehyde (**2**). Acetone is a minor product of PG dehydration due to the selectivity of the rearrangement of the propylene oxide intermediate, as the energy barrier for acetone is significantly higher (> 8 kcal/mol) than for the main product, propionaldehyde.⁷⁹ Thus, either radical-initiated reaction from PG may dominate over the dehydration, which is unlikely based on known rates,⁸⁴ or other unknown radical mechanisms exist from VG.

The linear temperature dependences of dihydroxyacetone (**12**) and glyceraldehyde (**10**) support that they are from the same radical pathway of VG (**Scheme 1b**). Furthermore, the product ratio between them, a factor of 2-3 in favor of dihydroxyacetone, is consistent with the thermodynamic stability of alkyl radicals,⁸⁵⁻⁸⁷ wherein a secondary alkyl radical that eventually forms dihydroxyacetone is thermodynamically preferred compared to the primary alkyl radical that will form glyceraldehyde.

The compounds 1-hydroxypropanal (**6**) and lactaldehyde (**9**) coeluted in the chromatography because they are isomeric with very similar polarity. While 1-hydroxypropanal can only be formed by VG by heat-induced dehydration, lactaldehyde can only be formed by PG from radical reaction. We show later, in the e-liquid formulation data (**Fig.5**) that 1-hydroxypropanal is more efficiently produced than lactaldehyde. This conforms with the overall exponential temperature trend that is

more consistent with heat-induced dehydration, as 1-hydroxypropanal is a hydroxyacetone coproduct from the hydroxypropylene oxide intermediate in VG dehydration (**Scheme 1a**).

There are a number of compounds, such as formaldehyde (**4**), hydroxyacetone (**3**), and acrolein (**7**), that can be formed from either heat-induced dehydration of VG or radical pathways from both PG and VG. The exponential temperature dependence data suggest that the heat-induced dehydration pathway is more efficient for **3**, **4**, and **7** under the studied conditions. Our data agree with the modeling work of Buhler et al.,⁸³ which predicts a preference for VG dehydration at the lower temperatures employed in the present study and a preference for radical chemistry at higher temperatures (e.g., above 680 °F, corresponds to 360 °C). It is unlikely that vaping devices will reach the temperatures that favor predominant radical chemistry for VG. Thus, our findings demonstrate that heat-induced dehydration of VG will dominate most vaping scenarios. Based on the significant abundance of dihydroxyacetone (**12**) and glyceraldehyde (**10**), however, it is clear that radical chemistry for VG in e-cigarette vessels is not negligible.

With regard to phase partitioning, most of the simple carbonyls including formaldehyde, acetaldehyde, acetone, and acrolein can be considered volatile or semivolatile and exist primarily in the gas phase, as they were not captured by the hydrophilic PTFE filter. Nearly 100% of the mass was recovered after the filter. These data are not shown, as a more thorough study on phase partitioning is forthcoming. In contrast, hydroxyacetone was captured at ~ 20% in the particle phase. The differences between simple and hydroxylated carbonyls is likely due to hydrogen bond interactions with PG and VG in the particles, which will keep a fraction of hydroxycarbonyls from partitioning to the gas phase.⁸⁸⁻⁹¹ We emphasize that these phase partitioning results apply to the mainstream aerosol that is directly released from the device, and gas/particle partitioning may change toward more evaporation or condensation on surfaces as the aerosol travels in the respiratory system.⁶⁶

The partitioning of carbonyl compounds between the gas and particle phase is influenced by many factors (e.g., relative humidity, temperature, collection method) and has been subject of numerous studies in cigarette smoke. For example, John et al.⁹² found the fraction of particulate formaldehyde ranges from 35% - 61% at temperatures of 298 – 323 K. Acetaldehyde is found mainly in the gas phase (98%), and the acrolein concentrations in the particle phase ranges from 0% - 33% in different studies.⁹³⁻⁹⁵ Uchiyama et al.³¹ recently studied the phase distribution for

select carbonyl compounds. They reported approximately half of the formaldehyde in the particle phase, whereas our PTFE filters did not trap formaldehyde. Formaldehyde is a well known volatile organic compound with a very high vapor pressure (> 0.8 atm at -20 °C;⁹⁶ thus, it should be in the gas phase at room temperature in the carbonyl form. However, it can also exist in aqueous-like solutions to some extent as methanediol, which will lower its vapor pressure. When we collected formaldehyde gas with our high-flow HEPA filter, we captured $\sim 90\%$ of formaldehyde. It is possible the Cambridge filter pads used by Uchiyama et al.³¹ had a surface area between our HEPA filter and hydrophilic PTFE filter, that there was substantial organic loading on their filter (i.e., if a high number of puffs was collected), or that the commercial e-liquid used in their work contains some water, which helps formaldehyde condense. Similarly, Uchiyama et al.³¹ reported most of the hydroxyacetone is in the particle phase, while we captured only 20% on the filter. The limited volatility results for carbonyls in the present study are consistent with calculations by Pankow et al.^{97, 98} for gas/particle partitioning in electronic cigarettes.

Another discrepancy arose in the total mass of carbonyl compounds, where the Uchiyama work reported much higher carbonyl formation (in the mg/puff range) than found in the present and other studies (e.g., Geiss et al.⁹⁹ and references therein), including those that used flavored e-liquid.¹ The reasons for these discrepancies are unclear. However, our results for nicotine are consistent with Uchiyama et al.³¹, who reported it exclusively in the particle phase. Prior research found that nicotine is almost entirely in the particle phase of cigarette smoke, and the partitioning coefficient of nicotine between the gas and particle phase is related to the pH of the aerosol, as nicotine can exist in both free base form and protonated form.^{100, 101} Lisko et al.¹⁰² found that the pH of e-liquids with PG and VG is pH ~ 6 , suggesting that most of the nicotine in our study will be protonated, which will suppress its partitioning into the gas phase. El-Hellani et al.¹⁰³ found that some flavored e-liquids have high pH, such that a significant fraction of nicotine may exist as free base for some commercial e-liquids.

3.2. E-liquid formulation

Table 2. Total mass of e-cigarette aerosol and particle phase composition from e-liquids of different PG/VG ratios and temperatures.^(a)

PG:VG ratio	Temp. (°F)	Total mass (mg/puff)	Particle mass (mg/puff)	Particle PG (mg/puff)	Particle VG (mg/puff)	Nicotine (mg/puff)	Particle PG (%)	Particle VG (%)	Nicotine (%)
100:0	375	150 ± 34	17.5 ± 1.8	17.3 ± 1.4	N.D.	0.07 ± 0.01	99 ± 1/-8	---	0.4 ± 0.1
70:30	375	121 ± 27	16.2 ± 1.6	9.1 ± 0.9	6.3 ± 0.8	0.04 ± 0.01	56 ± 6	39 ± 5	0.25 ± 0.06
50:50	375	50 ± 12	6.9 ± 0.7	2.7 ± 0.3	3.7 ± 0.6	0.01 ± 0.002	40 ± 2	54 ± 9	0.15 ± 0.03
30:70	375	26 ± 6	3.9 ± 0.4	0.8 ± 0.2	3.0 ± 0.3	0.007 ± 0.002	20 ± 4	76 ± 9	0.17 ± 0.03
0:100	375	19 ± 4	3.0 ± 0.3	N.D.	2.9 ± 0.3	0.01 ± 0.002	---	96 ± 4/-9	0.3 ± 0.07
30:70	525	135 ± 28	14.1 ± 1.4	2.9 ± 0.3	11.2 ± 1.9	0.01 ± 0.002	20 ± 2	78 ± 13	0.08 ± 0.02

^(a) Nicotine concentration was 3 mg/mL in all e-liquids. N.D. = not detected. The uncertainty in the control of measured coil temperature is ± 5 °F (3 °C). Temperature 375, 525 °F correspond to 191, 274 °C.

The total aerosol mass production, particle mass production, and composition of the aerosol are affected by the PG:VG ratio in the e-liquid due to the fact that VG and PG have different vaporization, aerosolization, and/or degradation rates at any particular temperature. When the VG content increased in the e-liquid mixture, a decrease was found for the production of total aerosol mass and corresponding particle mass (**Table 2**). This has also been observed elsewhere.¹⁰⁴⁻¹⁰⁶ The trend held for all of the major components of the particle phase as well, including PG, VG, and nicotine. Clearly, PG is easier to aerosolize than VG. This is due to the differences in chemical structure, and correspondingly, viscosity, vapor pressure, and boiling point. VG has one more OH group than PG, which results in stronger hydrogen bond intermolecular forces in the e-liquidsolution. The order of magnitude higher viscosity of VG at room temperature,^{107, 108} requires more energy for vaporizing the solution.¹⁰⁹ Moreover, the coil temperatures in **Table 2** already surpass the boiling point of PG (372.2 °F, corresponds to 189 °C) but are below the boiling point of VG (557.6 °F, corresponds to 292 °C). This is consistent with the high aerosol production when pure PG was used,¹¹⁰ and the high PG fraction in the gas phase (discussed later, in **Section 3.4**.) The difference in total aerosol mass when vaping pure PG versus pure VG e-liquids at 375 °F (191 °C, 150 mg/puff vs. 19 mg/puff, **Table 2**) suggests that PG was lost from the e-liquid at 8 times the rate of VG. This observation was corroborated in the mixed e-liquid (PG:VG = 30:70) using the gaseous CIMS and particle filter GC-MS data for PG and VG. The combined analytical uncertainties from CIMS (gas phase data) and CG-MS (particle phase data) are larger than for the

pure gravimetric analysis, but also suggested a significant acceleration of PG loss compared to VG by a factor of ~9.

Figure 4. The absolute concentrations of representative carbonyl compounds and nicotine observed in aerosols from vaping e-liquid at various PG:VG ratios at a coil temperature of 375 °F (191 °C).

Figure 4 shows representative carbonyl compounds (**Fig. 4A-H**) and nicotine (**Fig. 4I**) emitted from vaping e-liquid with different PG:VG ratios. Generally, carbonyl and nicotine concentrations decrease as the VG percentage increases in the mixture; although the hydroxycarbonyls do not decrease as dramatically as the simple carbonyls. This is likely due to the lower total aerosol and particle mass production overall as VG content increases in the e-liquid (**Table 2**). A notable exception is acrolein (**Fig. 4G**), which is the only compound whose formation increased with increasing VG, even as total aerosol mass decreased. Thus, for the 100% VG e-liquid, acrolein was one of the most concentrated carbonyls inhaled, and its relative production exceeded that of formaldehyde. The enhancement of acrolein between 30:70 and 0:100 PG:VG e-liquid was a factor of 7 – 30 considering all analytical and sampling uncertainties from concentration error bar (**Fig. 4F**). This was higher than the VG increase would predict, suggesting that the intermolecular interactions of PG and VG in the e-liquid may alter the thermal degradation chemistry.

Mechanistic differences were more apparent when carbonyl formation was normalized by the total aerosol mass (**Fig. 5**). The normalized trends reverse the absolute trends for some compounds, such as hydroxyacetone (**Fig. 5B**). Although hydroxyacetone can be generated from both PG (through radical reaction) and VG (through dehydration), the increase in relative aerosol fraction of hydroxyacetone with higher VG percentage in the e-liquid suggests that it is more efficiently formed from VG through the dehydration mechanism. This is consistent with the previous discussion that the heat-induced pathway is much more favorable for VG at the vaping temperatures we tested, and supports the exponential temperature dependence of hydroxyacetone (**Fig 3B**). Likewise, formaldehyde emissions were inversely proportional to VG content (**Fig 4A**), but increased slightly when normalized by aerosol mass (**Fig 5A**). Formaldehyde can originate from both PG and VG and from either thermal or radical pathways. The data suggest that it is formed at similar efficiencies from both precursors, perhaps slightly favoring VG, which is consistent with more pathways available from VG (**Scheme 1**).

Figure 5. The production yield percent of representative carbonyl compounds and nicotine, as normalized by total aerosol mass, from vaping e-liquid at various PG:VG ratios at a coil temperature of 375 °F (191 °C).

The relative production trends clearly showed that PG decomposition was responsible for all of the propionaldehyde (**Fig. 5H**) and most of the acetaldehyde (**Fig. 5C**), while VG decomposition was responsible for all of the dihydroxyacetone (**Fig. 5E**) and nearly all of the acrolein (**Fig. 5G**).

The VG source of acrolein is well-studied, and is leveraged in the conversion of biomass to fuels.¹¹¹ Although acrolein can be formed by PG, it is a secondary product of a minor compound that is formed by the primary alkyl radical intermediate instead of secondary (**Scheme 1b**), which limits the importance of the PG source. The isomeric lactaldehyde and 1-hydroxypropanal (co-eluted) likely had opposite trends that overlapped since they are solely formed by PG and VG, respectively (**Scheme 1**). Given the higher formation of the sum of lactaldehyde and 1-hydroxypropanal with increased VG percentage (**Fig. 5D**), it appears that the formation of 1-hydroxypropanal from VG dominates over lactaldehyde formation from PG. These data support the exponential temperature trends (**Fig. 3D**) of the lactaldehyde/1-hydroxypropanal pair, given that 1-hydroxypropanal is formed via heat-induced dehydration from VG.

So far, most of the data are consistent with PG/VG mechanisms from the literature as shown in **Scheme 1**. However, notable deviations may exist for acetaldehyde and acetone. Acetaldehyde is thought to be a coproduct of formaldehyde in the VG dehydration,²⁵ which would elevate it to be a major VG product, yet it appeared to be formed almost exclusively from PG (**Fig. 5C**). From PG, there was a suggested acetaldehyde source via radical reaction, instead of heat-induced dehydration. Thus, there was no reason to expect such a large abundance, or an exponential temperature curve (**Fig. 3C**). These observations, together with the fact that propionaldehyde (the main PG dehydration product expected from **Scheme 1** was observed in quite low abundance, suggests that there is at least one missing PG dehydration pathway to form acetaldehyde. We rule out the idea that PG radical reaction may be more efficient than dehydration, as the OH rate coefficient of PG is slightly lower than VG in aqueous solution.⁸⁴ The results for acetone were also interesting (**Fig. 5F**). Acetone is known to be formed by PG; however, the data suggest that it can be formed by both PG and VG at roughly equal efficiencies. The temperature results (**Fig. 3E**) also suggest a radical mechanism is dominant for acetone formation. Combined with the relative production trends, it would suggest that a radical formation mechanism from VG is missing from **Scheme 1**. We are not aware of any proposed mechanism in the literature stemming from VG, especially one that is radical-initiated. The nicotine percentage in the particle phase (0.15% - 0.4%) at the same vaping temperature (375 ± 5 °F, corresponds to 191 ± 3 °C) fluctuated with different PG:VG ratios (100:0 – 0:100). The nicotine concentration range observed in the particle phase is comparable to that in the original e-liquid (0.24% - 0.29%). These results are consistent with those of Baassir et al.¹⁰⁴ and the trials organized by the Cooperation Centre for Scientific Research

Relative to Tobacco (CORESTA).¹¹² A 3-mg/mL concentration of nicotine in the e-liquid translated to 1.2 – 3.4 mg/mL nicotine in the particle phase, with the lowest nicotine percentage for the 50:50 mixture and increasing in both directions (**Fig. 5I**). More research is needed to understand the robustness of, and underlying reasons for, this trend and whether it is conserved with different nicotine content in the e-liquid. Approximately 0.3 mg/mL nicotine was observed in the total aerosol compared to 3 mg/mL used in e-liquid.

3.3. Puff Duration

Figure 6 shows that the mass of the particles and representative carbonyl compounds generally increased with puff duration, as expected. Given the simultaneous increase in both particle mass and carbonyl mass with puff duration at the same flow rate, which would increase the puff volume, the carbonyl mass yield as normalized by aerosol mass would more or less be invariable. Both linear and non-linear fits would have yielded acceptable correlation coefficients within the

Figure 6. Particle mass (blue filled squares) and representative carbonyl compounds produced during vaping with various puff durations, at a 375 °F (191 °C) coil temperature and 30:70 PG/VG e-liquid ratio by volume. A non-linear best fit relationship for particle mass is shown.

studied range of only three data points. As puff durations in realistic use cases are unlikely to exceed this range,¹¹³ we did not test further. The relative increase between carbonyl compounds were roughly the same, within uncertainty. These results agree with Son et al.,^{28, 114} who found that increases in puff duration will increase the formation of carbonyl compounds, OH radicals, and nicotine.

3.4. Mass Balance Closure and Volatility

Most of the aerosol mass ended up in the gas phase (84 - 88 %, **Fig. 7**), i.e., not captured on the hydrophilic PTFE filter, regardless of the temperature or PG:VG ratio tested (**Table 2**). It is challenging to understand how the carbon mass from the e-liquid loss was distributed in the gas phase because there is no conventional analytical technique to quantify PG and VG in the gas phase due to the semivolatile nature of these compounds. The results from CIMS (**Fig. S6**), demonstrated that the majority of the gas phase was PG and VG instead of unknown compounds (e.g., peroxides, CO, CO₂, etc.) that are not well-measured by targeted techniques. This is consistent with findings that CO and CO₂ are not abundant e-cigarette emissions.^{115, 116}

The CIMS spectra also showed that PG and VG were orders of magnitude larger in concentration than hydroxycarbonyls, a result that is consistent with the carbonyl-DNPH analysis. For the 30:70 PG:VG condition at 375 °F (191 °C) coil temperature, the sum of PG (22.5 ± 8 mg/puff) and VG (4 ± 2 mg/puff) obtained by CIMS in the gas phase accounted for the missing mass that was not captured by the particle filter (22 ± 5 mg/puff) within uncertainty (**Fig. 7**). As discussed in **Section 2.4**, CIMS may overestimate semivolatile distribution in the gas phase due to evaporation during the sample dilution (which was necessary as the instrument is highly sensitive). However, it is clear from the CIMS spectra that the gas phase was dominated by mainly PG (even after accounting for the higher sensitivity of CIMS to VG).

Figure 7. Distribution of total mass loss from the e-liquid as nonvolatile (NV) particles captured by a filter or volatile/semivolatile (V/SV) compounds at different PG:VG ratios and a measured coil temperature of 375 °F (191 °C), 3 s puff duration and 3 mg/ml nicotine concentration. For the 30:70 PG:VG ratio sample (insert), the V/SV fraction was measured by CIMS to be primarily PG, and the nonvolatile (NV) fraction was measured by GC-MS to be primarily VG. The measured V/SV mass closed the balance of mass determined from gravimetric analysis.

GC-MS analysis of filters also showed that PG and VG were dominant components in the particle phase, with nicotine making up much less than 1%. In the 30:70 sample (**Fig. 7**, insert), approximately three-fourths of the particulate fraction was VG and three-fourths of the gaseous fraction was PG. The particle-phase composition roughly mirrored the e-liquid composition (note that a 30:70 volume ratio of PG:VG translates to a 26:74 ratio by mass according to their densities). The particle phase content of nicotine at 2.2 mg/mL was also similar to the e-liquid composition. Our particle-phase results are consistent with other accounts that PG, VG, water and nicotine are the main components of e-cigarette droplets,^{57, 58, 117} and that nicotine is a small fraction of the total aerosol and only found in the particle phase (regardless of whether free-base or nicotine salts were used).^{118, 119} Thermal degradation products of nicotine (e.g., nicotyrine, nornicotine) have been reported in other works,^{3,32} but were not found in the present study even though the GC-MS method we used can detect nicotine products.

3.5. Health Impacts

It can be assumed that regular e-cigarette users intake a median of 200 puffs per day.¹²⁰ This translates to an exposure dose of approximately 4.5 g PG/day and 0.8 g VG/day through inhalation of e-cigarette aerosols produced from vaping 30:70 PG:VG e-liquid at a coil temperature of 375 °F (191 °C) for a duration of 3 seconds. Although the PG exposure is fairly high compared to other aerosol components, animal and human studies demonstrate that PG has low toxicity even at relatively high doses.¹²¹⁻¹²³ Mild sensory and respiratory irritation effects may result at concentrations of > 871 mg/m³ for particle plus gas phase PG,¹²³ which translates to ~ 17.5 g/day exposure assuming 20 m³ air intake per day for a 70 kg adult.¹²⁴ VG has similarly weak irritation effects, which is supported by the German occupational exposure limit (MAK) of 200 mg glycerin/m³ to protect against sensory irritation effects in the workplace.¹²⁵

In contrast, the thermal degradation products, such as carbonyls, are a concern for potential risk of acute and chronic adverse human health effects despite their low absolute concentration in our study (< 0.5% by mass under all tested conditions). Carbonyls may be further enhanced in flavored e-liquid,¹ and may approach or exceed unhealthy doses for toxicological exposure with or without additional flavors. Formaldehyde, acetaldehyde, and acrolein are classified as known or probable human carcinogens.¹²⁶ The more abundant hydroxycarbonyls in e-cigarette aerosols, such as hydroxyacetone, do not have available toxicology data. Carbonyls are also found in combustible

cigarettes, so it is informative to discuss carbonyl exposure risk compared to combustible cigarettes and normalized to nicotine, as e-cigarette users have been reported to self-titrate for nicotine intake.^{13, 127}

Ashton et al.¹²⁸ reported a mean nicotine production of 1.4 mg/cigarette (The maximum legal content for nicotine is 1.0 mg/cig in the European Union),⁶⁰ and cigarette smokers can consume a range of 1 – 30 cigarettes per day (average 15 cig/day);^{129, 130} With an observed formaldehyde/nicotine ratio range of 11 – 90 µg/mg in the coil temperature range of 315 – 510 °F (157 – 266 °C), there exists vaping conditions in this study that exceed the 37 µg/mg of formaldehyde/nicotine in combustible cigarettes.¹³¹ However, we found that the acetaldehyde/nicotine ratio (6 - 66 µg/mg), acrolein/nicotine ratio (1 – 20 µg/mg), and propionaldehyde/nicotine ratio (1 – 9 µg/mg), at the coil temperature range of 315 – 510 °F (157 – 266 °C) and the 30:70 PG:VG e-liquid composition, were all lower than combustible cigarettes (580 µg/mg for acetaldehyde, 62 µg/mg for acrolein, and 59 µg/mg for propionaldehyde).

At a VG content of 100% in the e-liquid, exposure to VG products (**Fig. 4**) such as hydroxyacetone, 1-hydroxypropanal, and acrolein become increasing important. At 100% VG, the acrolein/nicotine ratio range increased by a factor of 20 (range 17 – 408 µg/mg) compared to the 30:70 e-liquid at the same coil temperature range of 315 – 510 °F (157 – 266 °C), which exceeds the acrolein/nicotine ratio in combustible cigarettes (50 - 70 µg/mg)^{131 132} under some temperature conditions. A Chronic Reference Exposure Levels (chREL) value of 0.35 µg/m³ was set by the California Office of Health Hazard Assessment (OEHHA) for acrolein. If this is multiplied by 20 m³ inhaled volume of per day for a 70 kg adult,¹²⁴ then a threshold of 7 µg/day may be considered safe for chronic exposure. However, at 100% VG, the acrolein e-cigarette exposure that is equivalent to replacing only 1 cigarette/day exceeds chREL threshold at all tested temperatures. Given the lower aerosol and nicotine production at high VG ratios in the e-liquid (**Table 2**), users may increase temperatures, puff duration, or puff frequencies to achieve higher aerosolization rates, which will significantly increase carbonyl exposure.

Although e-liquids with 100% VG can be readily found commercially, they also may be formed during the dynamic vaping process. Our data suggest, because the total e-liquid mass loss from PG was 8 times that of VG (**Table 2**, total aerosol mass), the e-liquid will be more enriched in VG as vaping continues. This will shift the e-cigarette aerosol composition toward VG and its degradation

products, particularly acrolein, as VG enrichment occurs. Relative formation of formaldehyde will stay fairly uniform as VG enrichment occurs. Likewise, total aerosol mass and total nicotine will decrease during the lifespan of the e-liquid. We can build a simple model (**Fig. S7**) to predict the e-liquid mass remaining when 100% enrichment occurs. The model assumes that, as the PG and VG ratio changes during vaping, the total amount of e-liquid lost also changes in accordance with the total aerosol data (**Table 2**, with a fit function of $f(\text{PG}\%) = 16.92e^{(0.0231 \times \text{PG})}$). Thus, for an 8:1 aerosolization ratio (by mass) for PG:VG, and for a 30:70 (by volume) ratio PG:VG mixture, it can be estimated that approximately 30-40% of e-liquid mass will be consumed by the time the e-liquid reaches 100% VG (**Fig. S7**). In other words, the e-liquid will be entirely VG well before the e-liquid reservoir is depleted. The predicted percent of e-liquid remaining at full VG enrichment in the model is fairly insensitive to starting volume in the e-liquid but is sensitive to starting PG:VG ratio and temperature, as expected. Thus, a user may be inhaling high relative concentrations of acrolein (**Fig. 5G**) and other predominant VG products in the aerosol for a significant amount of time during the e-liquid cartridge or reservoir lifespan.

4. Conclusion

The vaping process for e-cigarettes is complex and dynamic, possibly more so than currently appreciated. Coil temperature, puff duration, and PG:VG ratio all significantly affect both the aerosol production and the composition. Most of the mass that was lost from the e-liquid could be accounted for as PG and VG. Furthermore, volatile/semivolatile compounds dominated the total aerosol. Caution should be exercised when collecting particles with dense filter material or with overloaded filters for studying the particle phase, as the semivolatiles can be trapped and interpreted as particulates. In general, the chemical mechanisms for forming carbonyls appear to be well understood, and consistent with the numerous insights gained from interpreting the carbonyl mass yield as normalized by aerosol mass. Some exceptions include acetone, for which there may be a radical pathway from VG not currently accounted for, and acetaldehyde, for which there may be a thermal pathway from PG. The thermal pathways appeared more efficient under the temperature conditions tested. Importantly, the user's exposure to toxic carbonyls such as acrolein may change during the vaping process, and the user may be exposed to high relative content of VG and its degradation products as the e-liquid is depleted. These findings support the need for further research into aerosol composition and toxicology as a function of the e-cigarette

puffing lifecycle, in addition to e-liquid composition, puffing regimen, and vaping device operational conditions.

Supplemental materials

Supporting information is available for the following: Temperature and power change during the vaping process monitored both by software and thermocouple; particle size distribution data, concentration standard curves for carbonyl-DNPH hydrazones, PG, VG and nicotine; linear dynamic range for HPLC-HRMS analyses of the number of puffs collected; the linear relationship between calculated ΔG_d and sensitivities of 13 carbonyl-DNPH hydrazones in ESI negative mode in solution phase; CIMS spectra of the gas phase; model output for percent mass of e-liquid vaped during VG enrichment; tables showing the carbonyl and organic acid concentrations at all experimental conditions.

Author Contributions TBN and YL designed the experiments, YL and AEB carried out the experiments. All authors contributed original data and data analyses. TBN and YL prepared the draft manuscript. All co-authors have reviewed and edited the manuscript.

Acknowledgements This work was supported by the University of California Tobacco-Related Disease Research Program grant #27IR-0049, the National Heart, Lung, and Blood Institute grant R01 HL144384, and the California Agricultural Experiment Station grant CAD-ETX-2345-H through the USDA National Institute of Food and Agriculture.

Conflicts of Interest One of the authors (AKM), in addition to an appointment at the University of California, Davis, is employed by a scientific consulting firm, Cardno ChemRisk, which provides scientific advice to the government, corporations, law firms, and various scientific/professional organizations. Cardno ChemRisk has been engaged by various electronic nicotine delivery system (ENDS) and e-liquid manufacturers to provide general consulting and expert advice on scientific matters in litigation and in the context of regulatory requirements. This article was prepared and written exclusively by the authors without review or comment by any outside organization.

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