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Article

A Rapid and Sensitive Chemical Screening Method for E-Cigarette Aerosols Based on Runtime Cavity Ringdown Spectroscopy

Ruwini D Rajapaksha,[$] Mina W. Tehrani,[$] Ana M. Rule,[*] and Charles C. Harb

Cite This: https://doi.org/10.1021/acs.est.0c07325

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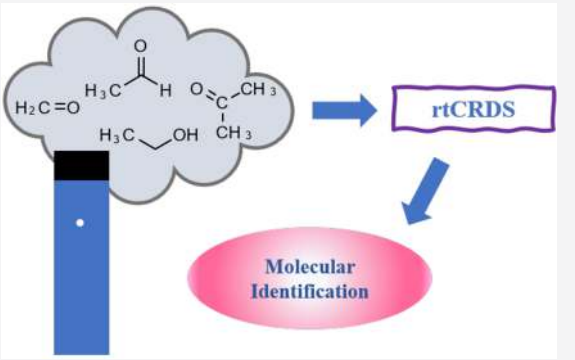
ABSTRACT: Growing demand of Juul and other electronic cigarettes, despite critical knowledge gaps about their chemical composition, has led to concerns regarding their potential health effects. We introduce a novel analytical approach, runtime cavity ringdown spectroscopy (rtCRDS) for rapid detection of oxidative products in e-cigarette aerosols, to facilitate the study of aerosol from a single puff of e-liquid. We report a systematic investigation of three flavors of commercial Juul pods (Virginia tobacco, mango, and menthol) and known commercial e-liquid ingredients (propylene glycol (PG), vegetable glycerin (VG), nicotine, ethyl maltol, benzoic acid, and nicotine benzoate) vaped using Juul devices. Juul e-liquids and neat chemical additives spiked into a 30:70 PG/VG solution were vaped and their aerosols were collected in 1-L Tedlar gas bags and analyzed using rtCRDS. Acetaldehyde, formaldehyde, and acetone were identified as primary oxidative products in aerosolized PG/VG. Ethanol was detected as a major constituent of the three commercial Juul flavors. Spectral intensities of carbonyl compounds increased with the addition of spikes, benzoic acid, ethyl maltol, and nicotine to PG/VG, suggesting that oxidative product generation increases with common additives. The method of direct, rapid analysis of e-cig aerosols introduced here can be used to complement traditional methods in vaping exposures.



KEYWORDS: *Juul, e-Cigarette aerosols, Runtime cavity ringdown spectroscopy, Molecular fingerprinting*

INTRODUCTION

Electronic cigarette (e-cig) use is on the rise around the world, with Juul dominating the US market since 2018.[1] Juul devices use "pods" filled with liquids (e-liquids) containing flavorants and nicotine benzoate salt in a propylene glycol (PG) and glycerol (vegetable glycerin, VG) base. Juul and other e-cig devices work by heating e-liquid with a metallic or ceramic coil to generate a fine aerosol, which is inhaled by the user. In combination with appealing flavorings, the nicotine content of Juul, higher than that of previous generations of e-cigs, has led to addiction to nicotine products among youth.[1] In response to the rapid rise in popularity of Juul, many studies have been published on the potential for toxicant exposure and adverse health effects in users. Of particular concern are oxidative products such as carbonyl compounds and free radicals, which may form as thermal degradation or other transformation products of PG, VG, and flavoring compounds, and have been linked to tobacco-related respiratory diseases and cancers.[2]

Previous investigations of carbonyl compound products in e-liquids have primarily been based on derivatization methods and chromatographic separation.[3] Aside from one investigation of carbon monoxide,[4] no studies to our knowledge have used infrared or laser-based optical spectroscopy to characterize oxidative products in e-cig aerosol, despite the low cost, speed, and excellent sensitivity and specificity of this technology. Importantly, the high sensitivity of laser optical spectroscopy enables the characterization of e-cig aerosol with the resolution of a single puff, providing insight into puff-to-puff variability.

In this study, we introduce a novel, advanced laser-based analytical approach as a qualitative screening technique: runtime cavity ringdown spectroscopy (rtCRDS). rtCRDS is an emerging analytical technique used to detect trace levels of chemicals in air, whether in gas or particle phase.[5−9] rtCRDS measures the rate of photon decay in a high-finesse optical resonator providing the highest selectivity toward chemical detection. To enhance the sensitivity of detection, CRDS utilizes pulsed quantum cascade lasers (QCLs) operating in mid- and long-infrared (IR) ranges. Mid-IR rtCRDS is a powerful chemical detection platform and next-generation chemical detection system that can be used in many research areas such as environmental science, exposure assessment, and clinical diagnosis. QCLs operating in mid-IR possess low energy and excite the analytes to their fundamental vibration

Received: October 30, 2020
Revised: March 24, 2021
Accepted: May 6, 2021

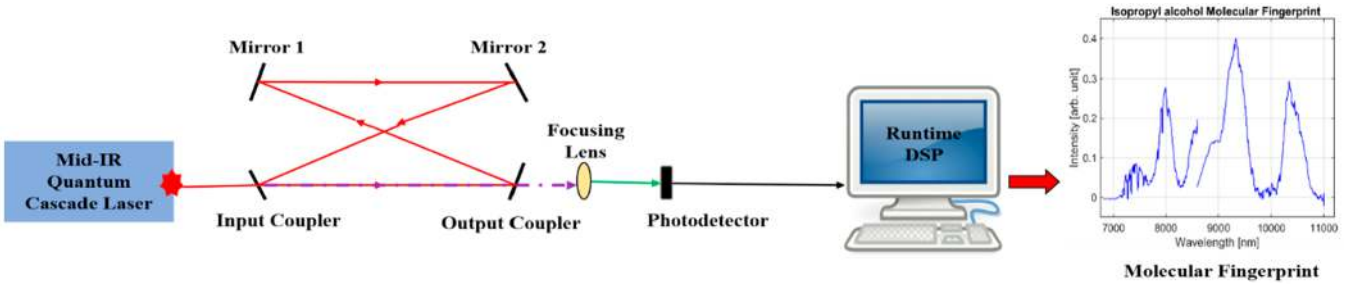


Figure 1. Optical diagram for runtime cavity ringdown spectroscopy (rtCRDS) and molecular fingerprinting process.

bands which yield clean, unique spectra compared to higher-energy UV−vis or near-IR ranges. The fundamental vibrational transition spectrum of a molecule enables selective, rapid identification in the form of its unique spectral signatures, so-called molecular fingerprints (MF). The data analysis algorithm employed by rtCRDS identifies analytes based on a ≥ 90% match with chemicals in our database, or for the most abundant chemicals (up to three chemicals with 75% match), identification is based on a mixtures analysis approach that has been previously described in optical spectroscopy.[10,11]

The RingIR *Agnoscis AG-4000* (RingIR Inc., NM) pulsed laser multiplexed rtCRD spectrophotometer, designed for rapid chemical detection using molecular fingerprinting, was used in this study. The instrument features RingIR patented direct optical absorption CRD technology,[12] which utilizes broad wavelength scanning QCLs operating uninterruptedly over the 6.8 to 11 μm mid-IR wavelength range and reaching as low as high parts-per-trillion (>100 ppt) levels with low false positives (<0.01%). The molecular fingerprints of pure chemical standards, analyzed previously, are stored in a chemical database and used to identify chemicals rapidly. Currently, the device can detect and positively identify over 80 chemicals, including explosives, toxic gases, terpenes, cannabinoids, and illicit drugs. Adiagram demonstrating the working principle of rtCRDS is shown in Figure 1, and the details of RingIR patented CRDS scheme can be found in the literature.[12] Herein, we report utilization of rtCRDS for chemical identification in single puffs of aerosolized Juul e-liquids.

This study constitutes a systematic investigation of aerosolized products of Juul e-liquid ingredients and chemical species present in commercially available flavored Juul pods. Juul reports nicotine, propylene glycol (PG), vegetable glycerin (VG), flavors, and benzoic acid as the main ingredients in Juul pods.[13] Nicotine, benzoic acid, PG, VG, and ethyl maltol, a common flavoring ingredient, were analyzed to create molecular fingerprints for comparison with the chemicals in RingIR's molecular fingerprint database.

MATERIALS AND METHODS

Materials. A Juul e-cigarette device (3.7 V battery) was used to vape all samples (Juul Laboratories, San Francisco, CA). Three commercial Juul e-liquid pods (1.6 Ω coil) were purchased via Juul's website and analyzed: Virginia Tobacco, Mango, and Mint. E-liquid base solutions for spike experiments were prepared from propylene glycol (Sigma-Aldrich, Darmstadt, Germany) and ultrapure 99.5% glycerol (Thermo Fisher Scientific, Waltham, MA). Additives ethyl maltol (Thermo Fisher Scientific), (−) nicotine tartate (Thermo Fisher Scientific), and benzoic acid (Sigma-Aldrich) were spiked into the laboratory e-liquid base. Laboratory-prepared PG/VG and spike solutions were vaped using refillable, Juul-compatible pods (Blankz, online retailer, 1.4 Ω coil), filled to 0.7 mL. Blankz cartridges are not manufactured by Juul and their electrical properties and wick, coil, and other materials may differ from those of Juul pods, potentially affecting aerosol generation and characteristics. Juul batteries have an electronic power regulation system that limits power output ensuring both Juul and Blankz pods work at the same power. Table 1 summarizes the tested solutions and compositions.

Table 1. Compositions of Analyzed Samples and Additive Spikes

Solution	Composition
Propylene glycol (PG)	Pure
Vegetable glycerin (VG)	99.5%
PG/VG mixture	3 mL PG and 7 mL VG
Benzoic acid in PG/VG mixture	44.9 mg
Ethyl maltol in PG/VG mixture	3.3 mg
Nicotine in PG/VG mixture	59.2 mg
Benzoic acid, nicotine and ethyl maltol in PG/VG mixture	20 mg of each additive
Virginia tobacco flavor	Commercially available pods with 5% nicotine by weight
Mango flavor	Commercially available pods with 5% nicotine by weight
Mint flavor	Commercially available pods with 5% nicotine by weight

Three levels of nicotine salt content commonly used in commercial e-liquids were also investigated. Varying masses of nicotine and benzoic acid, combined to form nicotine benzoate salt, were spiked into a 30:70 PG/VG solution (Table 2) and vaped in Blankz pods.

Aerosol Generation and Collection. Each Juul or Blankz pod was inserted into a charged Juul device, and the mouthpiece was connected to a 16 cm tubing piece (4.8 mm internal diameter, Masterflex L/S 15, Vernon Hills, IL, USA). Aerosol was generated using a peristaltic pump (drive no. 07522−20 and head no. 77200−62, Cole-Parmer, Vernon

Table 2. Composition of Spikes of Three Levels of Nicotine Benzoate into PG/VG[a]

Nicotine strength (w/w)	Nicotine (mg)	Benzoic acid (mg)	30:70 PG/VG solution (mg)
2%	19.8	15.3	964.9
4%	39.2	29.8	930.6
5%	50.01	37.8	911.9

[a]Total mass for each spiked sample was 1.0 g.

https://doi.org/10.1021/acs.est.0c07325
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Hills, IL, USA), which activated the Juul device and drove the aerosol from the e-cigarette mouthpiece through the tubing into a Tedlar gas bag (Dupont, Wilmington DE). The puff topography used was based on the International Organization for Standardization 20768:2018 method[14] but with a higher puff volume to compensate for the observed relatively weak aerosol generation of the Juul device compared to previous generation devices. Puff duration was 4 s, with a 30 s interpuff interval and a flow rate of 1.1 L/min, to give a volume of 73.33 mL per puff. The aerosol generation setup used is shown in Figure 2.

Figure 2. Setup for aerosol generation from a Juul device and collection into a 1L Tedlar gas bag using a peristaltic pump.

Spectrophotometric Analysis. Immediately (<10 s) after aerosol collection, the Tedlar gas bag was attached to the RingIR AG-4000 spectrophotometer and the aerosol sample was introduced into the optical cavity. Condensation in the Tedlar bag was not observed between the time of aerosol collection and introduction into the instrument. Five sets of spectral data were captured for each sample and the average was used to plot the IR spectrum of each sample. Distinct molecular fingerprint spectra were found for each individual additive and compared with the RingIR chemical database for chemical identification. The RingIR molecular fingerprint database is based on IR spectra of molecules in the 6.8−11 μm mid-IR range. Each molecule has a unique fingerprint in this region that can be used for identification.

After introduction of the sample and sweeping of the lasers across their wavelength range, the AG-4000 transforms raw detector data into a power spectral density matrix. This matrix is then decomposed to determine the sample's wideband absorption and generate a spectrum. Because measurements are taken at atmospheric pressure, the spectrum of the sample includes effects of the background atmosphere. To compensate, the AG-4000 then divides the spectrum of the sample with a previously measured background spectrum to create a unique molecular fingerprint for the unknown sample.

The ability to rapidly catalog fingerprints allows the AG-4000 to quickly build reference libraries of many different chemical vapors tested in controlled laboratory settings. These libraries can then be used to reliably match with unknown samples. To identify an unknown aerosol's molecular fingerprint, the AG-4000 calculates the Pearson correlation coefficient between the sample's fingerprint vector and that of the library's entries to find the best match. This correlation metric is scale- and offset-invariant, so differences in concentration or background between the sample and reference do not affect the matching reliability.

RESULTS AND DISCUSSION

Single puffs of ten samples of PG, three samples of VG, 30 samples of PG/VG, and three samples of PG/VG spiked with three additives in Juul (nicotine, ethyl maltol, and benzoic acid) were analyzed, and molecular fingerprint spectra were obtained.

Analysis of Neat PG, VG, and PG/VG and Variability between Single Puffs. The molecular fingerprint of PG aerosol primarily indicated the presence of acetaldehyde. Many research studies have reported acetaldehyde as a major emission product of e-cig aerosol,[15−17] and higher acetaldehyde content of neat PG aerosol compared to VG or PG/VG together has specifically been reported.[18] Our observation supports these findings to suggest that a major source of acetaldehyde in Juul aerosol is the oxidation of PG. The observed molecular fingerprint for PG aerosol and the molecular fingerprint of acetaldehyde at 1 ppm are shown in Figure 3. In measurements of 10 single puffs of neat PG, variation in absorption intensity was 31 to 47% (RSD) (SI Figure S1).

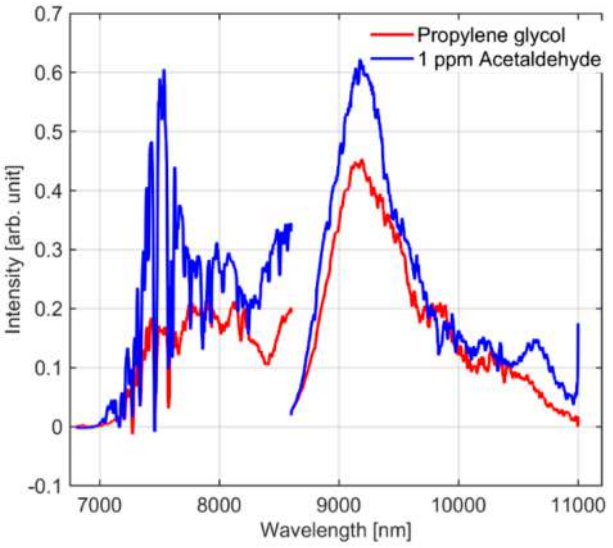

Figure 3. An example of the molecular fingerprint of PG aerosol (single puff) vaped by a Juul device and the molecular fingerprint for a 1 ppm acetaldehyde solution.

The analysis of aerosols collected from a single puff of VG did not show any carbonyl emission and matched with the molecular fingerprint spectrum of water (Figure S2 in Supporting Information). At least two previous studies have characterized the water content of e-cigarette devices, not including Juul, and found up to 35% water content in some e-

https://doi.org/10.1021/acs.est.0c07325
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liquids.[19,20] Both PG and VG are humectants which draw and retain moisture from the ambient air, and VG has the higher hygroscopicity of the two compounds.

Previous studies have associated several carbonyl compounds of concern, namely acrolein, with VG and found that acrolein can be formed directly from VG double dehydration.[18] The lack of detection of carbonyl compounds in our study could be due to the lower maximum temperature of Juul devices, capped at approximately 215 °C, compared with other e-cigarette devices used in previous studies.[21] Previous studies have established that the thermal decomposition of PG and VG increases with temperature,[22] and levels of carbonyl compounds in e-cigarettes are influenced by coil temperature and PG/VG ratio among other factors.[23] Indeed, a previous study found lower levels of formaldehyde, acrolein, and other carbonyl compounds in Juul device aerosols compared with other e-cig devices.[21] Acrolein, in particular, has been reported to be abundant at high temperatures and powers, and PG has been suggested to decompose at much lower temperatures than VG[24] and be more susceptible to thermal decomposition.[3,25] Further, VG has a high boiling point (290 °C) compared to water, potentially causing evaporative cooling as water boils off first to prevent the generation of oxidative products from the heating of VG.

The analysis of a PG/VG 30:70 mixture showed a distinct molecular fingerprint spectrum compared to PG and VG individually and vaping PG/VG visually appeared to generate a larger volume of aerosol in the collection bag. The observed molecular fingerprint of three puffs of PG/VG mixture was compared with molecular fingerprints in the RingIR database and matched with acetaldehyde and formaldehyde (Figure 4).

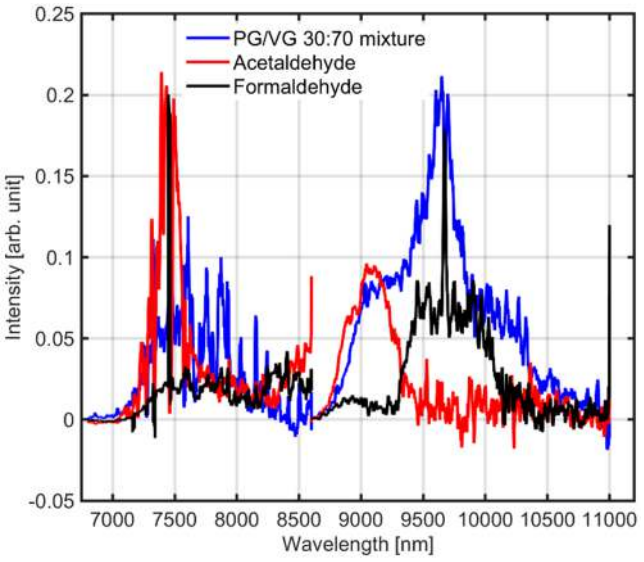

Figure 4. Molecular fingerprint spectrum of aerosols collected from three puffs of propylene glycol and vegetable glycerin 30:70 mixture and molecular fingerprint spectra of acetaldehyde and formaldehyde.

Acetaldehyde and formaldehyde are the two major carbonyls that have been reported in e-cig aerosols in one study measured at concentrations of the same order of magnitude as nicotine.[18]

Considerable variability between single puffs of PG/VG (30:70) was found in the analysis of the first 30 puffs from a Blankz pod in a Juul device (Figure S3). Characteristic wavelengths were selected to represent acetaldehyde (9060.3 nm) and formaldehyde (9674.0 nm), and corresponding absorption intensity was plotted for 30 puffs. As expected, absorption intensities of the two compounds were strongly correlated (R = 0.95). For both compounds, relative standard deviations of absorption intensities over 30 puffs were >100%, and no linear trend in intensity as a function of puff number was observed ($R^2 \ll 0.1$). The highest variation is seen within the first ten puffs for acetaldehyde (RSD = 189%) and formaldehyde (RSD = 216%). The high variability observed between puffs demonstrates an inconsistency of aerosol delivered by the Juul device and/or Blankz cartridge as well as analytical variability, highlighting that the methodology developed here is suitable for qualitative analysis and chemical identification only.

Analysis of PG/VG Spiked with Nicotine, Benzoic Acid, and Ethyl Maltol. Relevant masses of three common e-cig additives (nicotine, benzoic acid, nicotine benzoate, and ethyl maltol) were individually spiked and dissolved in a 30:70 PG/VG mixture, vaped, and analyzed with a single puff. The matches of molecular fingerprints of the additives in PG/VG are shown in Figure 5. Acetone was the only carbonyl compound detected in the ethyl maltol and 2% nicotine (Figure S4) spikes. Acetaldehyde was detected in the spikes of benzoic acid, 4% nicotine, and 5% nicotine, while formaldehyde was also detected in the 4% and 5% nicotine spikes (Figure 5 and Figure S4). The ethyl maltol spike was additionally matched with pure ethyl maltol. We observed higher spectral intensities for spiked samples compared to PG/VG alone. This may be due to the increase of oxidative products in the vapor phase due to the increase of vapor pressure in these mixtures. These results suggest that the additives studied increase the generation of the oxidative products acetone, acetaldehyde, and formaldehyde and that the addition of nicotine has the strongest effect. The finding of increased acetaldehyde and formaldehyde in aerosols of PG/VG solutions due to high (4−5%) nicotine levels is in contrast with earlier studies that did not find strong or significant effects of nicotine with oxidative product generation in comparison with PG/VG composition and device power.[19,23] Our data additionally suggests carbonyl emissions may be modulated by nicotine and benzoic acid levels. Previous studies have found that benzoic acid, although a carboxylic acid, does not generate oxidative degradation products when heated up to 300 °C, which exceeds the temperature reached by the Juul device.[26] Therefore, benzoic acid itself is not likely to be the source of the increase in carbonyl compounds observed in these spiked samples. In contrast to previous studies that have reported that oxidative product formation (free radicals[27] and acetaldehyde[23]) is responsive to flavorant concentration, we found that only acetone was produced as a result of vaping ethyl maltol spiked into PG/VG. The observation that formaldehyde and acetaldehyde are generated only at higher nicotine spike concentrations may be explained in part by different mechanisms of formation of these three oxidative products. A study by Diaz et al. (2010) suggested that acetone forms via the dehydration of propylene glycol, while acetaldehyde and formaldehyde can be generated by propylene glycol oxidation.[28] Our current study suggests that dehydration might be the dominant transformation undergone by propylene glycol at lower nicotine levels, while oxidation increases with higher levels; however, more investigation is needed to explore this finding.

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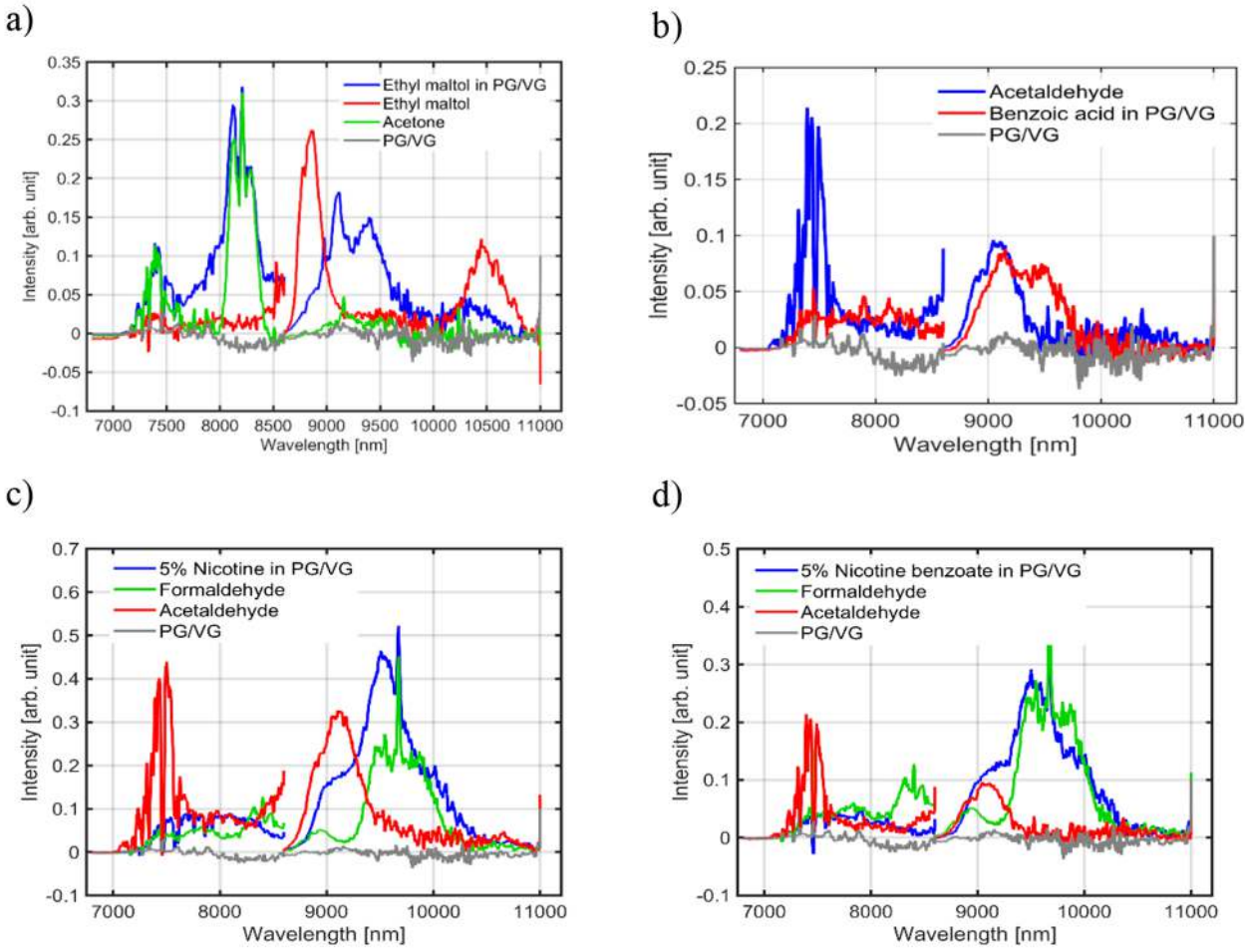

Figure 5. Molecular fingerprint of aerosols of additive spikes into 30:70 PG/VG matched with pure chemicals in database: (a) ethyl maltol in PG/VG, pure ethyl maltol, acetone, and PG/VG; (b) benzoic acid in PG/VG, acetaldehyde, and PG/VG; (c) 5% nicotine in PG/VG, acetaldehyde, formaldehyde, and PG/VG; (d) 5% nicotine benzoate in PG/VG, formaldehyde, acetaldehyde, and PG/VG.

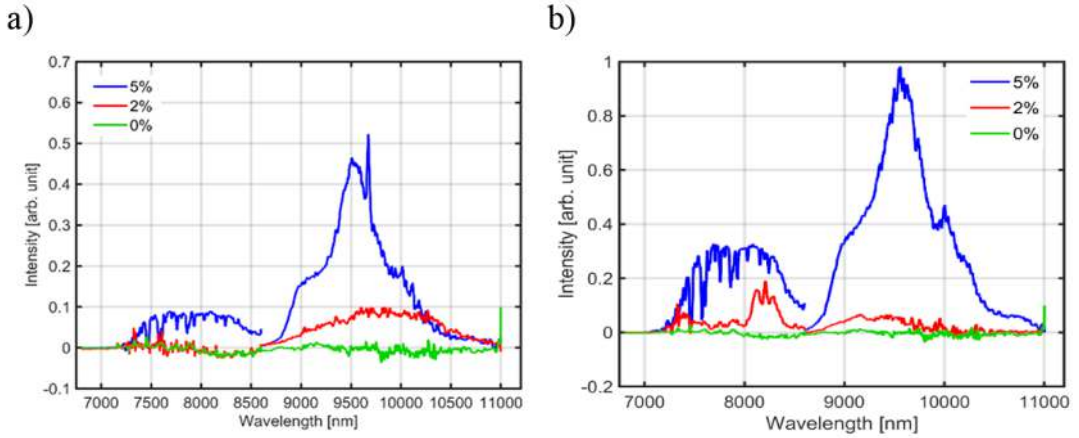

Figure 6. Molecular fingerprint spectra of aerosols collected from single puffs of 0, 2, and 5% (a) nicotine and (b) nicotine benzoate salt dissolved in a 30:70 PG/VG mixture.

As Juul and other products typically contain nicotine benzoate salts rather than free-base nicotine, we analyzed the vaped aerosols of three levels of nicotine benzoate salt spiked into a 30:70 PG/VG solution. Similar molecular fingerprint spectra were obtained at all levels, but a 2-fold increase of intensities were observed for 5% nicotine benzoate compared with 5% free-base nicotine (Figure 6).

Identification of Ethanol in commercial Juul e-Liquids. Three flavored samples of commercial Juul pods were investigated: Virginia Tobacco, Menthol, and Mango. The commercial samples showed distinct molecular fingerprints from those of the PG/VG and spiked samples and suggested that these Juul pods contain ethanol as a primary constituent. All three samples resulted in similar molecular

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fingerprint spectra and matched with ethanol molecular fingerprint in the RingIR chemical database (Figure 7). It is

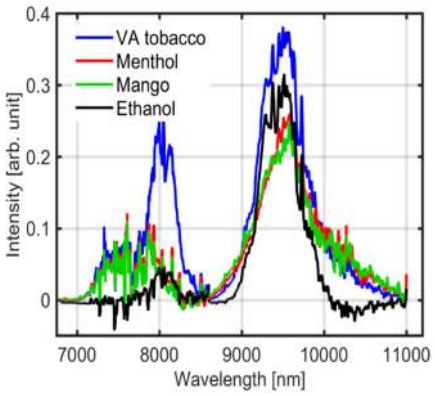

Figure 7. Molecular fingerprint spectra of aerosols collected from single puffs of Juul Virginia Tobacco, Menthol, and Mango flavors, superimposed with the molecular fingerprint for ethanol.

likely that slight variations in spectral signatures are due to differences in concentration of ethanol in the collected aerosols. The absorption intensity was variable (40% RSD) but appeared to stabilize at the end of 10 puffs (Figure S5). Ethanol was not found in the analysis of PG/VG or nicotine, ethyl maltol, or benzoic acid spikes, indicating that additional ingredients are the source of ethanol in Juul e-liquids. Previous studies have found that ethanol is added to e-liquids directly or used as a solvent for flavoring compounds.[18,29] Frequent inhalation of e-cig aerosol could result in rapid absorption of ethanol into the bloodstream with potential and unanticipated chronic health effects and should be investigated further.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.est.0c07325.

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■ AUTHOR INFORMATION

Corresponding Author

Ana M. Rule − *Department of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland 21205, United States;* orcid.org/0000-0003-2328-0749; Email: arule1@jhu.edu

Authors

Ruwini D Rajapaksha − *RingIR, Albuquerque, New Mexico 87102, United States;* orcid.org/0000-0003-3411-1676

Mina W. Tehrani − *Department of Environmental Health and Engineering, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland 21205, United States*

Charles C. Harb − *RingIR, Albuquerque, New Mexico 87102, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.est.0c07325

Author Contributions

[$]The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript. These authors contributed equally.

Funding

Research reported in this publication was supported by the FDA Center for Tobacco Products and National Institute of Environmental Health Sciences of the National Institutes of Health under Award Number R01ES030025. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Notes

The authors declare the following competing financial interest(s): Mina Tehrani and Ana Rule declare that they have no competing conflict of interest. Ruwini Rajapaksha works for -and Charled Harb is CEO of RingIR, who manufactures and markets the rtCRDS instrument that was used in the analysis.

■ ABBREVIATIONS

rtCRDS, runtime cavity ringdown spectroscopy; PG, propylene glycol; VG, vegetable glycerin; QCL, quantum cascade laser

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https://doi.org/10.1021/acs.est.0c07325
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