# Screening Thermal Degradation of E-cigarette Flavorants: A PY-GC-MS Approach

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## Introduction

Electronic nicotine delivery systems (ENDS) use heat to transfer flavor chemicals into the aerosol phase. Because the heating process can affect these chemicals, evaluating the toxicological impact of the inhaled aerosol is challenging. Screening a flavorant for its thermal stability prior to inclusion in an e-liquid formulation using thermal conditions that generate a similar degradation profile would facilitate the identification of thermally unstable compounds. This work describes an analytical methodology employing Pyrolysis-Gas Chromatography-Mass Spectrometry (PY-GC-MS) to investigate the thermal behavior of prospective e-liquid flavor compounds under thermal conditions relevant to ENDs.

In order to establish that thermal conditions in the PY-GC-MS generated a similar thermal profile to that of a JUUL2 device, the thermal degradation profile of a custom e-liquid was run in the PY-GC-MS across a range of temperatures and puffed in a JUUL2 device. Based on the consistent formation of key aerosol-related degradation products in both the PY-GC-MS and the JUUL2 system, conservative pyrolysis conditions were determined for subsequent compound screening.

## Methodology

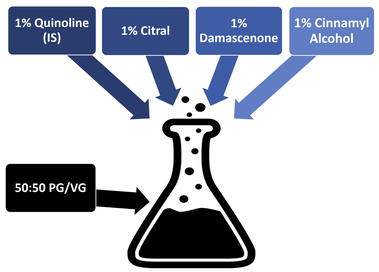
### GC-MS Settings

| Parameter | Description |
|---|---|
| Instrument | Agilent 7890B GC System<br>5977 MS Detector |
| Injection Volume | 1 µL |
| Injection Mode | Split (50:1) |
| Inlet Temperature | 260°C |
| GC Column | Restek Stabilwax MS (30 m x 250 µm x 0.25 µm |
| Flow Rate | 1 mL/min |
| Oven Program | Initial 40°C (hold 1 min)<br>Ramp 5°C/min to 110°C<br>Ramp 10°C/min to 250 (hold 10 min) |
| Source Temperature | 230°C |
| Transfer Line Temperature | 250°C |
| Quadrupole Temperature | 150°C |
| Method Run Time | 40 min |

### Pyrolyzer Settings

| Parameter | Description |
|---|---|
| Instrument | CDS Pyroprobe 6200 |
| Chamber Top Temperature | 180°C |
| Chamber Bottom Temperature | 180°C |
| Pyrolysis Temperature | 300°C |
| Chamber Hold Time | 30 s |
| Valve Oven Temperature | 300°C |
| Transfer Line Temperature | 300°C |

### Pyrolysis Heater Calibration

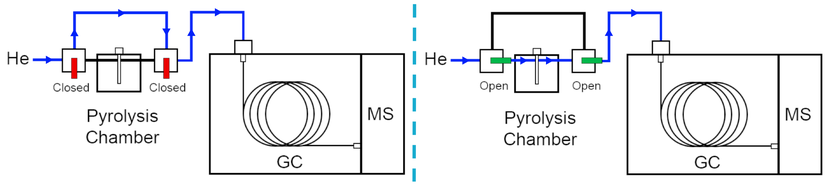



**Schematic 1.** Custom e-liquid mix containing 50:50 PG/VG, 1% citral, 1% damascenone, 1% cinnamyl alcohol and 1% quinoline (IS).

To ensure that the thermal conditions in the pyrolysis chamber were comparable to those in a JUUL2 device, a custom e-liquid containing 50:50 propylene glycol (PG) to vegetable glycerin (VG) with 1% by weight each of citral, damascenone, and cinnamyl alcohol, with quinoline at 1% as an internal standard, was utilized. This e-liquid was puffed using intense conditions (6 second puff, 110 cc, 30 second interval) and the resulting aerosol was analyzed using GC-MS. The response ratios of the target compounds, their reaction products, and thermal degradants relative to the internal standard were determined. The same e-liquid mixture was analyzed in the PY-GC-MS system across a range of set temperatures. The analyte-to-internal standard ratios for compounds found in the JUUL2 analysis were directly compared to the same compounds in the PY-GC-MS analysis. Based on the similarity in response ratios, a pyrolysis temperature and time were determined to conservatively mirror the thermal conditions in a JUUL2 device.

## Results

### "PyLock" Method vs. Normal Pyrolysis Method




**Schematic 2.** The initial, "locked" state (left): The pyrolysis chamber is sealed off allowing the sample to heat and pyrolyze under a static helium atmosphere. The "open" state (right): the valve opens, restoring helium flow and sweeping the resulting pyrolyzates from the chamber into the GC-MS for analysis.

In the standard pyrolysis configuration, a sample is placed into the pyrolysis chamber and rapidly heated to a set temperature for a specific time. During the heating process, a constant flow of helium through the pyrolysis chamber sweeps compounds into the GC-MS for analysis. In initial experiments using this standard pyrolysis approach, little or no temperature dependence was observed in the formation of thermal degradants, despite increasing the pyrolyzer temperature to over 500°C. This was attributed to the helium flow through the pyrolysis chamber, which removed volatile compounds from the heated region before they could be adequately exposed to the final pyrolysis temperature. To rectify this issue, the helium flow was diverted around the pyrolysis chamber during heating. This modified approach, or "pylock" method, allows the sample to be heated to the target temperature under a static atmosphere, enabling the flavorant compounds to pyrolyze effectively. Once the desired pyrolysis time is complete, the helium flow is restored, and the resulting degradation products enter the GC inlet for analysis. This refined methodology ensures that the observed compounds are true pyrolyzates, providing a more accurate representation of the thermal decomposition process.

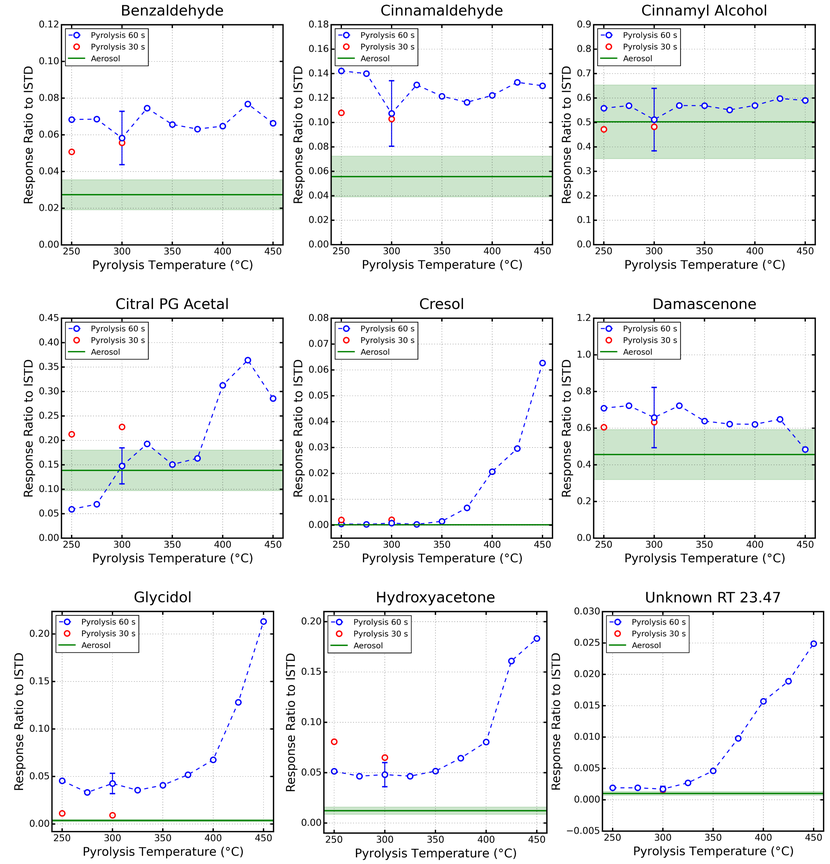



**Figure 1.** Py-GC-MS response ratios for nine analytes, comparing pyrolysis times of 30 s and 60 s across various temperatures. Aerosol results are shown for reference with ±.30% uncertainty.

| Flavor Compound | CAS # | Purity (%) | Peak Area > 0.01% [1] | | Peak Area > 0.1% [2] | |
|---|---|---|---|---|---|---|
| | | | Intact Transfer % | Number of Chemicals Identified | Intact Transfer % | Number of Chemicals Identified |
| 1-Decanol | 112-30-1 | 99.7 | 94.7 | 18 | 95.1 | 5 |
| 1-Heptanol | 111-70-6 | 99.9 | 97.3 | 25 | 97.8 | 5 |
| 1-Nonanol | 143-08-8 | 99.3 | 88.9 | 11 | 89.1 | 5 |
| 1-Octanol | 111-87-5 | 99.2 | 91.1 | 40 | 91.6 | 19 |
| 2-Isopropyl-4-methylthiazole | 15679-13-7 | 99.8 | 91.1 | 41 | 91.8 | 12 |
| 2-Methyl-4-propyl-1,3-oxathiane | 67715-80-4 | 99.3 | 92.8 | 36 | 93.4 | 17 |
| 2-Octanol | 123-96-6 | 99.5 | 95.2 | 10 | 95.2 | 7 |
| 2-Pentanone | 107-87-9 | 99.9 | 97.2 | 25 | 97.6 | 10 |
| 5,6,7,8-Tetrahydroquinoxaline | 34413-35-9 | 99.3 | 94.8 | 24 | 95.5 | 7 |
| 6-Methyl-5-hepten-2-ol | 1569-60-4 | 99.2 | 86.5 | 72 | 88.0 | 16 |
| Allyl cyclohexanepropionate | 2705-87-5 | 99.3 | 92.1 | 20 | 92.6 | 10 |
| Benzyl isovalerate | 103-38-8 | 99.8 | 85.9 | 23 | 86.3 | 15 |
| Cinnamyl acetate | 103-54-8 | 99.4 | 83.6 | 25 | 83.9 | 12 |
| cis-3-Hexenyl 3-methylbutanoate | 35154-45-1 | 99.7 | 97.4 | 30 | 98.1 | 5 |
| Diphenyl ether | 101-84-8 | 99.9 | 98.6 | 6 | 98.8 | 3 |
| Ethyl (2E,4Z)-decadienoate | 3025-30-7 | 95.9 | 80.7 | 41 | 81.0 | 13 |
| Mango furanone | 14400-67-0 | 99.3 | 83.9 | 41 | 84.5 | 15 |
| Massoia lactone | 54814-64-1 | 96.3 | 59.3 | 67 | 59.9 | 43 |
| Succinic acid | 110-15-6 | 99.4 | 0.0 | 5 | 0.0 | 5 |
| trans-2-Hexen-1-ol | 928-95-0 | 98.7 | 74.3 | 57 | 75.3 | 16 |

**Table 1.** Py-GC-MS results for flavor compounds. This table presents the name, CAS #, and purity for each compound. Key results include the Calculated Intact Transfer %, which indicates thermal stability, and the # of compounds ID'd, which represents the number of identified degradation products, reaction products or impurities from pyrolysis.
[1] Analysis includes all peak areas that are 0.01% or greater of the main component's peak area.
[2] Analysis includes all peak areas that are 0.1% or greater of the main component's peak area.

## Conclusions

This work establishes a robust PY-GC-MS methodology to screen flavor compound thermal stability, with conditions selected to produce a degradation profile similar to a JUUL2 device. This was achieved at 300°C with a 30-second hold time. A key innovation was the "pylock" method, developed to ensure proper thermal degradation by preventing the premature transfer of volatile compounds to the GC.

Screening of 20 compounds revealed a wide range of thermal stability, with intact transfer percentages from 0.0% to 98.8% and the number of identified degradation products ranging from 3 to 72. While most compounds showed high stability, the method effectively identified those with lower thermal stability, such as massoia lactone, and compounds that underwent complete degradation, such as succinic acid.

The study also highlights the role of analytical sensitivity; the 0.01% peak area threshold provided a more detailed profile of degradation products, while the 0.1% threshold was a valid option for general assessment due to similar intact transfer percentages. In conclusion, this methodology is an effective and repeatable tool for the rapid screening of e-liquid components, informing formulation decisions and aiding in the development of products with reduced toxicological risk.

**References:**
1. Yu, C.; Liang, M.; Dai, S.-Y.; Cheng, H.-J.; Ma, L.; Lai, F.; Liu, X.-M.; Li, W.-G. Thermal stability and pathways for the oxidation of four 3-phenyl-2-propene compounds. *RSC Adv.* **2021**, *11*, 32654–32670.
2. Oldham, M. J.; Jeong, L.; Gillman, I. G. An Approach to Flavor Chemical Thermal Degradation Analysis. *Toxics* **2024**, *12*, 16.



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