# Analysis of 21 Residual Solvents from Cannabis Matrix by FET Headspace on a Zebron™ ZB-624*PLUS*™ GC Column

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## Introduction

The Zebron ZB-624*PLUS* GC column is shown to meet the many challenges of residual solvent testing of cannabis products under stringent State of California requirements. These include: (1) High separation of 21 residual solvent analytes of highly variable polarity and boiling point at both high and low levels, (2) Good separation of closely eluting solvent pairs, and (3) High reproducibility of peak shape and retention time over multiple analyses owing to the high temperature stability of the ZB-624*PLUS* column which allows high temperature column bakeout to remove cannabinoid and matrix residues. However, even with the best GC column, the low-level analysis of residual solvents from cannabis products is highly matrix dependent.

## Materials and Methods

### Standard Preparation

200 µL of N, N- Dimethlyacetamide (DMAc) is first added to a 2 mL amber vial fitted with a Mininert® valve (Supelco, Bellefonte, PA). 500 µL of California Residual Solvent Mix #2 (Emerald Scientific, San Luis Obispo, CA) was added, making sure to re-seal the Mininert valve upon addition of each component. Next,1000 µL of California Residual Solvent Mix #1 (Emerald Scientific, San Luis Obispo, CA) was added to the vial and vortexed. This mix is "Standard 1" and was used to prepare subsequent Standards 2, 3, 4, 5 through semi-serial dilution.

### Headspace Autosampler Conditions

**Vial:** Verex™ Headspace Vial
**Description:** 23 x 75 mm, 20 mL
**Part No.:** AR0-3260-13
**Vial Seal:** 20 mm, PTFE/Silicone, Magnetic (AR0-5255-12)
**Instrument:** Thermo Scientific® TriPlus™ 500
**Vial Incubation Temperature:** 170 °C
**Vial Incubation Time:** 8 min
**Loop Temperature:** 180 °C
**Loop Pressure:** 7.5 psi
**Loop Equilibration Time:** 0.01 min
**Injection Mode:** Standard
**Injection Time:** 0.10 min

### GC-MS Conditions

**Column:** Zebron ZB-624*PLUS*
**Dimension:** 30 meter x 0.25 mm x 1.40 µm
**Part No.:** 7HG-G040-27
**Injection:** Split 38:1 @ 250 °C
Split Flow: 75 mL/min
Purge Flow: 5 mL/min
**Recommended Liner:** Zebron PLUS Liner (Compatible with Agilent® and Thermo Scientific GC instrument), 4 mm ID Single Taper, Wool on Bottom
**Liner Part No.:** AG2-0A11-05
**Carrier Gas:** Helium @ 1.3 mL/min (Constant Flow)

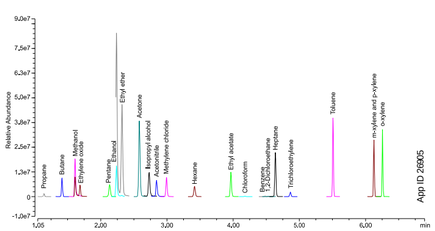
**Oven Program:**

| Ramp(°C/min) | Temp (°C) | Time(min) |
|---|---|---|
| - | 35 | 2.0 |
| 7.3 | 58 | 0.0 |
| 11.3 | 115 | 0.0 |
| 25.2 | 300 | 8.9 |

**Detector:** Thermo Scientific ISQ™ GC-MS/MS
**Detector Temperature:** 300 °C

## Results

**Figure 1.** Separation of Residual Solvents with Clear Resolution and Peak Symmetry on a Zebron ZB-624*PLUS* GC Column.




## Results

**Figure 2.** Separation of Residual Solvents at Low LOD on a Zebron ZB-624*PLUS* GC Column.

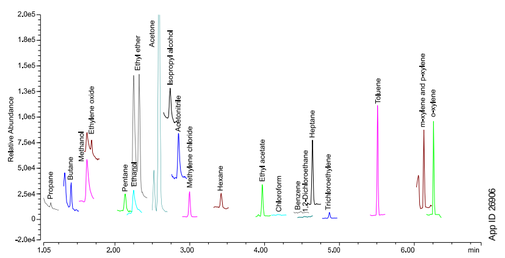



**Figure 3.** Reproducible Peak Shape and Retention of Residual Solvents Between 11 and 196 Injections of Residual Solvents on a Zebron ZB-624*PLUS* GC Column.

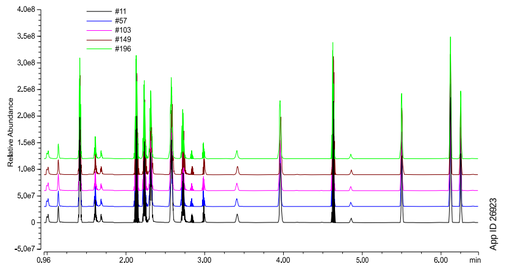
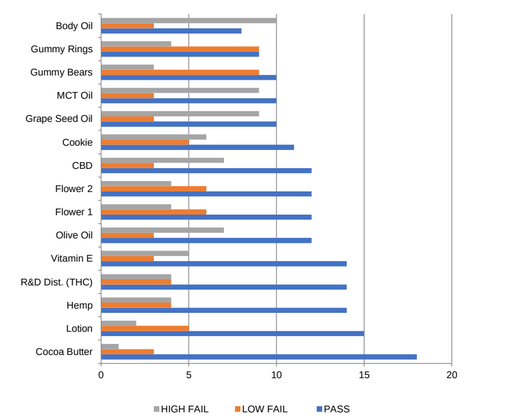
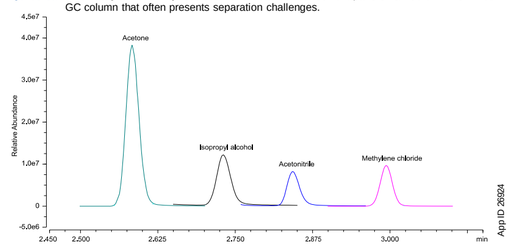



**Figure 4.** Matrix Pass/Fail Rates for Low-Level Spikes of 21 Analytes into 15 Matrices.

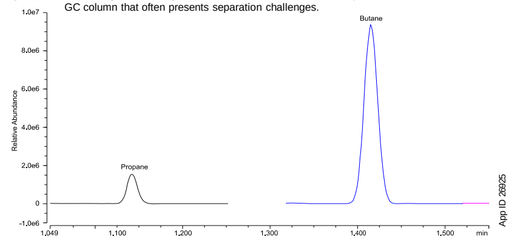



## Results

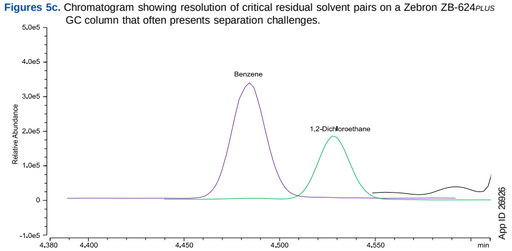
**Figures 5a.** Chromatogram showing resolution of critical residual solvent pairs on a Zebron ZB-624*PLUS* GC column that often presents separation challenges.



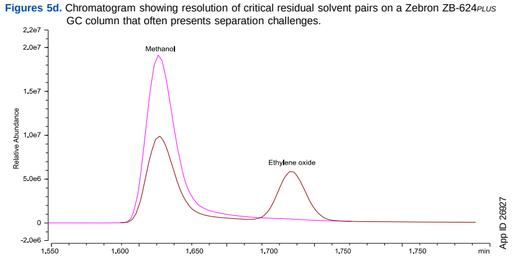

**Figures 5b.** Chromatogram showing resolution of critical residual solvent pairs on a Zebron ZB-624*PLUS* GC column that often presents separation challenges.




**Figures 5c.** Chromatogram showing resolution of critical residual solvent pairs on a Zebron ZB-624*PLUS* GC column that often presents separation challenges.




**Figures 5d.** Chromatogram showing resolution of critical residual solvent pairs on a Zebron ZB-624*PLUS* GC column that often presents separation challenges.




## Results

**Table 1.** Analytical Figures of Merit of the Residual Solvent Method on a Zebron ZB-624*PLUS* GC Column.

| Analyte | Retention Time (min) | EI Mass Fragments (m/z) | %RSD Peak Area (n=6) | Calibration Range (units) | Coefficient of Determination |
|---|---|---|---|---|---|
| **Propane** | 1.15 | 29.2, 38.1, 39.1, 41.1, 42.1 | 5.79 | 0.0111 to 182118 | 0.998623583 |
| **Butane** | 1.42 | 29.2, 39.1, 41.1, 42.1, 43.1, 58.1 | 3.04 | 0.0283 to 1513111 | 0.99959537 |
| **Methanol** | 1.62 | 29.2, 31.1, 32.1 | 5.86 | 0.0195 to 2544192 | 0.998637504 |
| **Ethylene oxide** | 1.69 | 29.2, 42.1, 43.1, 44.1 | 2.88 | 0.0039 to 663053 | 0.999656857 |
| **Pentane** | 2.13 | 41.1, 42.1, 43.1, 57.1, 72.1 | 0.81 | 0.0233 to 1230316 | 0.99997221 |
| **Ethanol** | 2.26 | 31.1, 45.1, 46.1 | 1.43 | 0.0198 to 2751018 | 0.999915227 |
| **Ethyl ether** | 2.33 | 29.2, 31.1, 45.1, 59.1, 74.1 | 1.36 | 0.0132 to 6299258 | 0.999922411 |
| **Acetone** | 2.6 | 42.1, 43.1, 58 | 2.81 | 0.0301 to 7727685 | 0.999674714 |
| **Isopropyl alcohol** | 2.75 | 29.2, 43.1, 45.1, 59.1 | 0.93 | 0.0275 to 2344812 | 0.999964032 |
| **Acetonitrile** | 2.86 | 38.1, 39.1, 40.1, 41.1, 42.1 | 4.18 | 0.0309 to 632698 | 0.999263719 |
| **Methylene chloride** | 3 | 49, 51, 83.9, 86, 88 | 3.69 | 0.0039 to 1933879 | 0.999440936 |
| **n-Hexane** | 3.42 | 41.1, 43.1, 56.1, 57.1, 86.1 | 3.81 | 0.0015 to 1048053 | 0.999405304 |
| **Ethyl acetate** | 3.98 | 43.1, 43.1, 45.1, 61.1, 70.1, 88 | 1.32 | 0.0108 to 2188014 | 0.999927263 |
| **Chloroform** | 4.19 | 47, 83, 84.9, 86.9, 116.9, 117.9, 118.9 | 1.21 | 0.0002 to 45637 | 0.999938319 |
| **Benzene** | 4.49 | 74, 76, 77.1, 78.1, 79.1 | 2.01 | 0.0002 to 60489 | 0.999797066 |
| **1,2-Dichloroethane** | 4.54 | 62, 64, 98, 100 | 0.78 | 0.0002 to 33851 | 0.99996857 |
| **Heptane** | 4.65 | 41.1, 43.1, 56.1, 57.1, 70.1, 71.14.87 | 4.19 | 0.0181 to 3329474 | 0.999217892 |
| **Trichloroethylene** | 4.87 | 95, 97, 129.9, 131.9, 133.9 | 2.51 | 0.0007 to 428642 | 0.999741161 |
| **Toluene** | 5.52 | 39.1, 65.1, 91, 92.1 | 0.86 | 0.0049 to 5750500 | 0.999968735 |
| **m-Xylene and p-Xylene** | 6.14 | 78.1, 91.1, 103.1, 105.1, 106.1, 107.1 | 4.06 | 0.0112 to 3850165 | 0.999262251 |
| **o-Xylene** | 6.27 | 78.1, 91.1, 103.1, 105.1, 106.1, 107.1 | 4.02 | 0.0054 to 4266483 | 0.999281869 |

## Discussion

Shown in **Figures 1-3**, is the symmetric peak shape and high resolution of 21 residual solvent components. Low-level standards exhibit sharp peaks and low baseline noise, providing high resolution of critical analyte pairs (**Figures 5a-d**). Method robustness is demonstrated by analyzing multiple real samples, followed by standard injection showing consistent retention, peak shape and resolution. Also demonstrated (**Figure 4**) is the real-world challenge of recovering low-level residual solvents from complex cannabis matrices.

## Conclusion

This GC-MS/MS method, based upon the unique separation properties of the Zebron ZB-624*PLUS* GC column, provides separation of 21 regulated residual solvents in diverse cannabis matrices. In addition to resolving critical solvent pairs, the Zebron ZB-624*PLUS* GC column provides thermal stability with low bleed and long-term chromatographic stability, thus allowing confident low-level detection of residual solvents in cannabis matrices that are notoriously difficult to analyze.





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