Oregon Residual Solvent Analysis Method for Cannabis/Hemp using a Shimadzu GCMS-SQ and Headspace Injections

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Introduction

The State of Oregon mandates the analysis for Residual Solvents in Hemp and Cannabis products. 35 solvents are being monitored, with limits varying from 2 ppm (by weight) for benzene, to 5000 ppm for butane. These solvents are commonly used in manufacturing processes for extraction and concentration of THC or CBD. They can be analyzed by GC and GCMS using a method similar to USP 467, which is used for the same purpose in pharmaceutical manufacturing. Different inlets have been devised, with static headspace becoming very popular, while the detection is either by FID or by MS. The most commonly used column is of the Rxi-624 Sil MS type. The headspace autosampler has heat ahead capability, which speeds up the processing of the samples.

Instrument and Method

A Shimadzu GCMS QP-2010SE was utilized, with a HS-20 headspace autosampler in static mode. The method parameters are reported in the table below.

Headspace	**HS-20 Loop Model**
Operation Mode	Static headspace with heat-ahead
Sample	150uL sample volume 20mL headspace vial
Equilibration	15.00 minutes at 120°C
Sample Loop	0.2mL Loop Vial pressure 125KPa, Pressurizing Time 1.50 min Loop load time 0.20 min, equilibration 0.20 min Injection time 0.20min
Sample Line Temperature	150°C
Transfer Line Temperature	150°C
Gas Chromatograph	**GC-2010 Plus**
Injection	Split injection from HS-20, with 50:1 split ratio
Column	Rxi-624 Sil MS 30.0m x 0.25 mm x 1.40 um Helium carrier gas Constant linear velocity, 39.9cm/sec Column Flow 1.24mL/min Purge flow 0.0mL/min
Oven Program	30°C, hold 3.0 min 10°C /min to 140°C, hold 0.0 min 45°C /min to 200°C , hold 1.0 min Total GC run time 16.33 min Total GC cycle time: 25.00 mins
Detector	**GCMS-QP2010 SE**
Operation Mode	Selected Ion Monitoring Mode (SIM)
Ion Source	200°C, EI mode, 70eV
Solvent Cut Time	0.1 min
MS Interface	300°C

Table 1: Acquisition parameters for the headspace GCMS residual solvent method for Oregon.

Measurements

The measurements were conducted in three different groups, displayed in Figure 1; the respective SIM channels used are plotted as well. The standards preparation followed a 10-fold serial dilution from 150 ug, using butyl acetate as the dilution solvent.

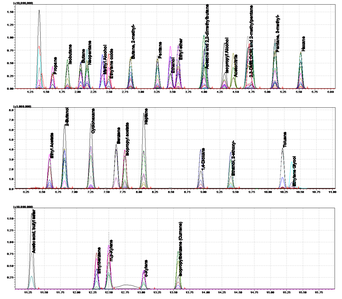

Figure 1: Plot of SIM acquisition for 35 residual solvents at 150 ug each in the headspace (representing less than 0.1% in a 200 mg sample).

Results and Discussion

Specific analytes such as benzene which has the lowest screening limit in the OR method were calibrated and determined to levels well below the limit. Figure 2 demonstrates benzene content of approximately 300 ng in the headspace of the vial, which represents 0.3 ppm by weight for a 200 mg sample, with full evaporation assumed.

Benzene

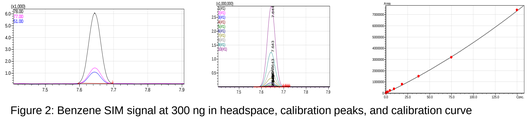

Figure 2: Benzene SIM signal at 300 ng in headspace, calibration peaks, and calibration curve

Other analytes of typical interest such acetonitrile and methanol are shown in Figure 3 at similar levels, as well as in the full range of calibration (0.293 ug to 150 ug).

Acetonitrile

Methanol

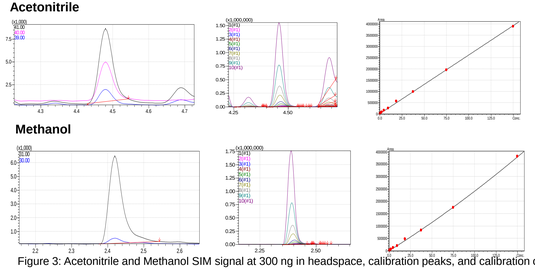

Figure 3: Acetonitrile and Methanol SIM signal at 300 ng in headspace, calibration peaks, and calibration curve

Ethylene glycol is an analyte that can sometimes be difficult to determine; the determination level (LOD) achieved with this method is 4 ug in 200 mg, which is about 30 times better than the screening level. The lowest level of detection is shown in Figure 4.

Ethylene Glycol

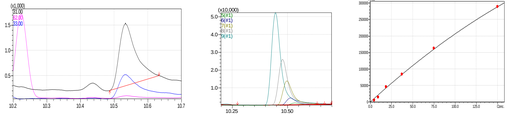

Figure 4: Ethylene Glycol SIM signal at 4 ug in headspace, calibration peaks, and calibration curve

The groups of analytes referred to by the method, such as butanes, pentanes, hexanes, and xylenes are shown in Figure 5, 6, 7, and 8 as well. The level shown is about 10 ug for all of these.

Butane and Isobutane

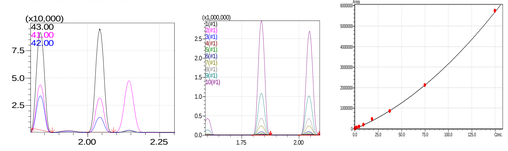

Figure 5: Butane and Isobutane SIM signal at 10 ug in headspace, calibration peaks, and calibration curve

2,2-methylpropane

2-methylbutane

Pentane

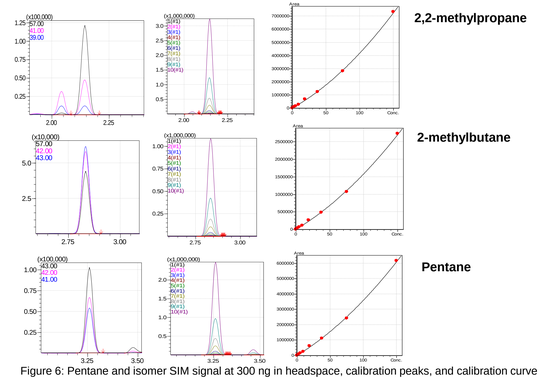

Figure 6: Pentane and isomer SIM signal at 300 ng in headspace, calibration peaks, and calibration curve

2,2-dimethylbutane

2,3-dimethylbutane and 2-methylpentane

3-methylpentane

Hexane

m,p-xylene

o-xylene

Ethylbenzene

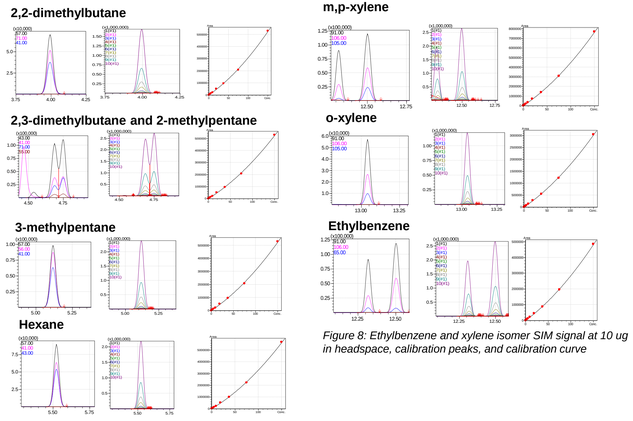

Figure 7: Hexane and isomer SIM signal at 10 ug in headspace, calibration peaks, and calibration curve

Figure 8: Ethylbenzene and xylene isomer SIM signal at 10 ug in headspace, calibration peaks, and calibration curve

Table 2 shows the analytes that the State of Oregon requires for determination in the Residual Solvents analysis, including the screening limit (in micrograms) for a sample of 200 mg, as well as the LOD (for low concentration analytes) and saturation levels (for high concentration analytes).

Analyte	Screening Level (ug)	LOD by this method (ug)	Saturation Level (ug)
Propane	1000	N/A	2000
Isobutane	1000	N/A	2000
Butane	1000	N/A	2000
2,2-dimethylpropane	1000	N/A	2000
Methanol	600	N/A	2000
Ethylene Oxide	10	0.1	N/A
2-methylbutane	1000	N/A	2000
Pentane	1000	N/A	2000
Ethanol	1000	N/A	2000
Ethyl ether	1000	N/A	2000
2,2-dimethylbutane	58	0.1	N/A
Acetone	1000	N/A	2000
Isopropyl Alcohol	1000	N/A	2000
Acetonitrile	82	0.1	N/A
2,3-dimethylbutane	58	0.1	N/A
Methylene Chloride	120	0.1	N/A
2-methylpentane	58	0.1	N/A
3-methylpentane	58	0.1	N/A
Hexane	58	0.1	N/A
Ethyl Acetate	1000	N/A	2000
2-butanol	1000	N/A	2000
Tetrahydrofuran	144	1	N/A
Cyclohexane	776	0.1	N/A
Benzene	0.4	0.05	N/A
Isopropyl acetate	1000	N/A	2000
Heptane	1000	N/A	2000
1,4-Dioxane	76	0.5	N/A
2-ethoxyethanol	32	0.5	N/A
Toluene	178	0.1	N/A
Ethylene glycol	124	4	N/A
Ethylbenzene	434	0.5	N/A
m,p-Xylene	434	0.5	N/A
o-Xylene	434	0.5	N/A
Isopropylbenzene (cumene)	14	0.5	N/A

Table 2: Screening levels for OR assuming 200 mg sample compared to performance data of this method