APPLICATION NOTE

Residual Solvents analysis of cannabinoid products by Headspace GC-MS

AN139v2; SCION Instruments

Introduction

Due to the legalization of cannabis in multiple countries for medicinal and recreational use, there has been an increased demand for quality control of hemp and marijuana products. This is to ensure the product labels accurately reflect the characteristics and quality of new products entering the market.

Cannabis products have many requirements for testing, from potency analysis (cannabinoids), terpenes, residual solvents and pesticides.

This application note will study the analysis of residual solvents in cannabinoid products. Solvents are organic, volatile compounds that are used frequently for extracting cannabinoids from marijuana.

In industrial processes often traces of the solvents remain in the product. These are known as residual solvents and can cause health risks to end users. Therefore it is very important to monitor these components to assure the quality of the product and prevent health risks after the consumption of marijuana.

SCION Instruments has an extended portfolio for cannabis testing, including cannabis potency analysis performed on GC with a Flame Ionization Detector (FID, AN163), Mass Spectrometry (MS, AN142) or using a High Performance Liquid Chromatography (HPLC, AN145). In addition, our portfolio contains Terpene analysis with GC-FID (AN133) and Terpene analysis with GC-MS with Headspace (AN136).

This application can be performed on either the SCION Instruments 8300 GC or 8500 GC platform with 8700 Single Quad Mass Spectrometer (SQMS) and the SCION HT3 Headspace autosampler (HS), shown in Figure 1.

Figure 1 SCION Instruments 8300-GC and 8700-SQMS with the SCION HT3 Headspace Autosampler

This application will focus on the 20 most commonly used solvents for the extraction of cannabis, these are shown in Table 1.

Table 1: most commonly used solvent components and their risk classes

No.	Component	Class	No.	Component	Class
1	Methanol	2	11	Chloroform	2
2	Pentane	3	12	Cyclohexane	2
3	Ethanol	3	13	Benzene	1
4	Ethyl Ether	3	14	1,2-Dichloroethane	1
5	Acetone	3	15	Heptane	3
6	2-Propanol	3	16	Trichloroethylene	2
7	Acetonitrile	2	17	Toluene	2
8	Methylene chloride	2	18	p-Xylene	2
9	Hexane	2	19	m-Xylene	2
10	Ethyl Acetate	3	20	o-Xylene	2

The class of solvent is determined by a risk assessment.[1] Class 1 are solvents that are known to have unacceptable toxicity and should be avoided, class 2 are solvents to be limited and class 3 are solvents with low toxic potential.

Experimental

This residual solvent application is performed on the SCION Instruments 8300 GC analyzer equipped with an 8700 SQMS and HT3 Headspace sampler. Table 2 details the instrument method parameters used throughout the application.

Table 2: Instrumentation operating conditions GC, MS and HS

Part	Settings
Injector	200°C Split ratio 150:1
Column	SCION-624MS
Carrier Gas	Helium 1.6 mL/min
Oven Program	35°C (hold 1.0 min), 15°C/min to 180°C (hold 0 min), 30°C/min to 240°C (hold 0.5min)
Run Time	24 min
Software	MS workstation, HT3 Teklink

MS Part	Settings	HT3 Part	Settings
MS transfer line temp	250°C	Oven temperature	80°C
Ion source temp	200°C	Transfer line temperature	140°C
Ionization mode	EI	Sample temperature	80°C
Scan start	1.25min	Sample equilibrium time	12 min
Scan mode	Full Scan, range 50 – 500 a.m.u.	-	-

Calibration samples were prepared for the components at concentrations between 0.5 and 25 µg/mL.

A Quality Control (QC) sample was also prepared at a concentration of 7.5 µg/mL for all components. The QC sample was used to determine the recovery and repeatability of each component and thus evaluate the suitability of the method.

Sample preparation is dependant on the sample matrix. For example, hemp oil and capsules contain the same target compounds but require different sample preparation. To all samples 1mL of saturated Sodium Sulphate ('salting out') has been added to increase the sensitivity and headspace efficiency.

Some components like cyclohexane have a high partition coefficient (K), A higher K-value means the compound has better affinity to the sample matrix instead of the gas phase. In order to lower the K-value, matrix modification techniques have to be used. "Salting out" is one of the most common techniques, but also changing the phase ratio can decrease K and increase sensitivity. Figure 2 shows the effect of the addition of the saturated salt.

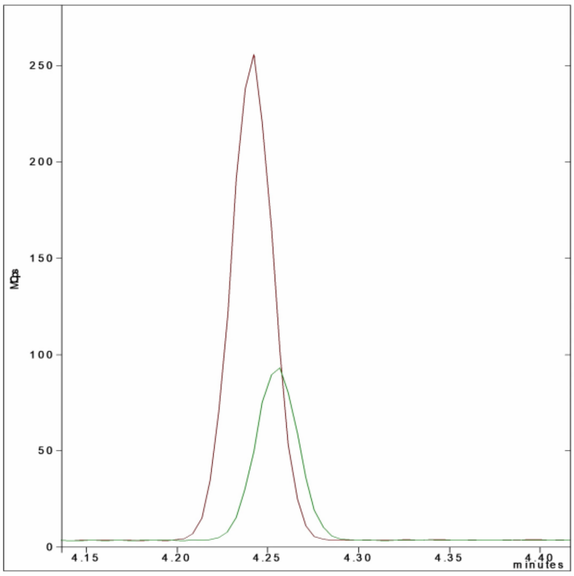


Figure 2: The response of cyclohexane with (red) and without (green) the addition of salt.

The identity of all target compounds were confirmed using the NIST library integrated within SCION's MS workstation software.

Results

The calibration curves for the Residual solvent standards were prepared from 0.5 µg/mL up to 25 µg/mL. Figure 3 shows an example of the calibration curves for the components Acetone, Hexane and Toluene.

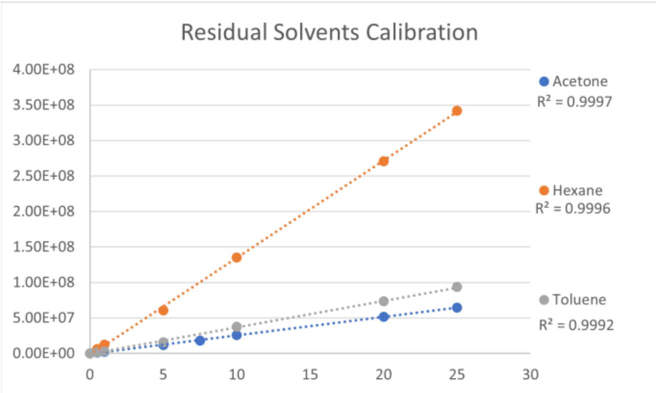


Figure 3. Three example calibration curves of the residual solvents standards.

For all components a correlation coefficient (R^2) of 0.999 or higher was achieved, which is an excellent result with many regulations requiring an R^2 value of only ≥0.98. The assay accuracy and precision was determined by injecting the QC sample 7 times.

Assay accuracy (recovery) assay precision (repeatability) are shown in Table 3. Recovery was shown to be close to the expected value for each component and well within the 70 – 130% which is often considered acceptable for method validation.

Repeatability was found to be between 1.6 and 6.5% for all components, which is acceptable for trace analysis.

Table 3: Summary of Results – Linearity, QC recovery and repeatability

No.	Component	R^2	Repeatability (%)	QC (µg/mL)
1	Methanol	0.9997	6.5	7.6
2	Pentane	0.9990	5.4	7.0
3	Ethanol	0.9994	5.7	7.1
4	Ethyl Ether	0.9991	5.7	7.1
5	Acetone	0.9997	3.3	7.4
6	2-Propanol	0.9994	3.0	7.5
7	Acetonitrile	0.9992	3.2	7.5
8	Methylene chloride	0.9993	3.1	7.2
9	Hexane	0.9996	4.8	7.4
10	Ethyl Acetate	0.9994	3.1	7.2
11	Chloroform	0.9991	3.1	7.4
12	Cyclohexane	0.9996	2.8	7.4
13	Benzene	0.9992	3.5	7.5
14	1,2-Dichloroethane	0.9995	3.0	7.4
15	Heptane	0.9995	1.6	7.6
16	Trichloroethylene	0.9991	4.4	7.3
17	Toluene	0.9992	5.4	7.4
18	p-Xylene	0.9991	5.4	7.5
19	m-Xylene	0.9991	3.8	7.5
20	o-Xylene	0.9988	3.9	7.5

From the linearity the theoretical limit of detection (LOD) and limit of quantitation (LOQ) were calculated according to equations:

1) $LOD = 3.3 * \left(\frac{\sigma}{S}\right).$

2) $LOQ = 10 * \left(\frac{\sigma}{S}\right).$

Where σ is the standard deviation of the response and S is the slope of the calibration curve.

Results for the theoretical LOD, LOQ and the amounts found in the hemp sample for each component are found in Table 4.

Table 4: Summary of Results – LOD, LOQ, and amount found in hemp oil sample.

No.	Component	LOD (µg/mL)	LOQ (µg/mL)	Amount Found in Sample (µg/mL)
1	Methanol	0.59	1.79	<LOD
2	Pentane	1.18	3.58	<LOD
3	Ethanol	0.81	2.45	ND
4	Ethyl Ether	1.09	3.31	ND
5	Acetone	0.62	1.87	ND
6	2-Propanol	0.85	2.59	27
7	Acetonitrile	0.93	2.82	ND
8	Methylene chloride	0.93	2.83	ND
9	Hexane	0.69	2.10	ND
10	Ethyl Acetate	0.87	2.62	ND
11	Chloroform	1.10	3.33	ND
12	Cyclohexane	0.76	2.31	ND
13	Benzene	1.02	3.10	ND
14	1,2-Dichloroethane	0.85	2.59	ND
15	Heptane	0.82	2.50	ND
16	Trichloroethylene	1.08	3.28	ND
17	Toluene	1.05	3.18	ND
18	p-Xylene	1.12	3.40	ND
19	m-Xylene	1.12	3.40	ND
20	o-Xylene	1.31	3.96	ND

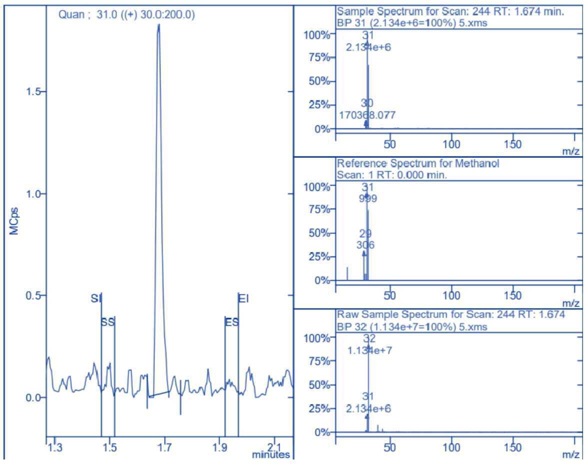
ND = Not detected

The analysis of the hemp oil shows that the sample contained 2–propanol and traces of both methanol and pentane (<LOD). All other measured residual solvents were not detected.

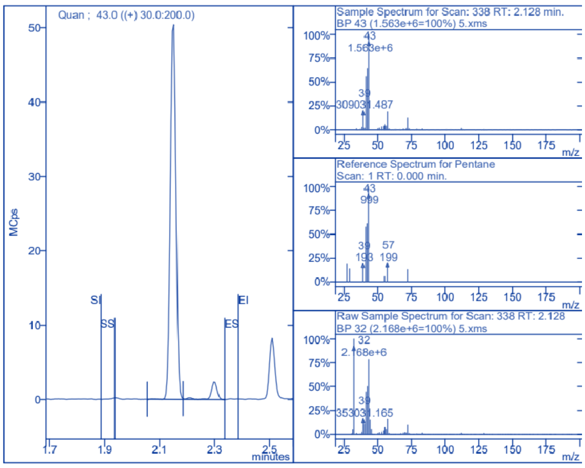
Pentane and 2-propanol are class 3 solvents, which carry a daily exposure limit of 50mg per day.[1] It is therefore highly unlikely that using this hemp oil would exceed this limit. This means the product is safe for human use. SCION recommends checking local regulatory limits for residual solvents prior to analysis.

Figure 4 shows example chromatograms of the present residual solvents in the hemp oil sample.

Methanol



Pentane



2-Propanol

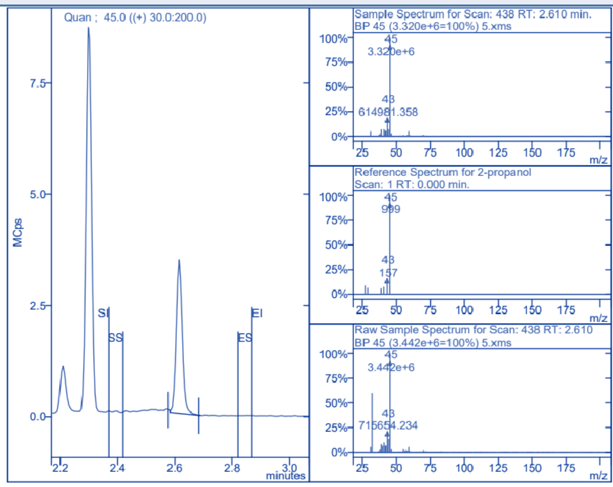


Figure 4: Example chromatograms of residual solvents found in the hemp oil sample.

Conclusion

The SCION 8300 GC platform equipped with a split/spitless injector, SCION-624MS column and 8700 SQMS along with the HT3 Headspace sampler is the ideal solution for analysing residual solvents in cannabis products in a qualitative and quantitative way.

The developed method is well suited for the analysis of residual solvents. Research has shown that the addition of saturated salt is important to improve sensitivity at lower concentration levels.

The incorporation of the NIST Library search tool within SCION MSWS software allows for easy identification of unknown components.

The hemp oil sample analysed for this application was shown to contain 2-propanol at a concentration of 27 µg/mL, this is well below the US daily exposure limit of 50 mg, meaning the product is safe for use by humans.

The recent growth within the cannabis market has led to increased regulatory scrutiny.

This will mean that accurate quantification of cannabis components including residual solvents will continue to become more important as regulations across the world inevitably become more stringent.

Order Information

Ordering Information for the 8300 GC

Part	Part Number
8300-GC with 8700-MS-SQ EI Select, with S/SL inlet (120V)	SCIONSQ83SEL311
8300-GC with 8700-MS-SQ EI Select, with S/SL inlet (230V)	SCIONSQ83SEL312
HT3 Headspace Autosampler 230V.	SC149300100
SCION MSWS software	394195791
NIST 20 MS Library and Search Program for MSWS	4121057

Suggested Consumables

Part	Part number
15% Graphite/85% Vespel Ferrule 1/16" with 0.4 mm hole pk/10	41312148
BTO Septa 9 mm, pk/50	CR298713
10µL fixed needle syringe, 5 cm, 0.47 mm OD, 26 g conical needle	41312133
Vial, 9-425 Screw Thread, 2 mL Clear Glass 12x32 mm Flat Base with Label. pk/100	41311000
SCION-624MS column 30m x 0,25mm x 1,40 µm	SC32591
78.5mm x 6.3mmOD x 4mmID; S/SL Recessed Gooseneck Qwool with o ring, pk/5	41312106

For ordering info on the SCION 8500 GC, which offers greater functionality with the option of up to 4 detectors (including MS), please contact your local SCION sales representative. SCION offers other MS options such as the 8700 SQ Premium and 8900 TQ, as well as additional spectral libraries such as NIST and Wiley.

References

1.HTTPS://WWW.USPNF.COM/SITES/DEFAULT/FILES/USP_PDF/EN/USPNF/GENERALCHAPTER467CURRENT.PDF

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