

# Determination of Heavy Metals in Cannabis and Hemp Products Following AOAC Method for ICP-MS

Routine monitoring of As, Cd, Hg, Pb, and other elements using an Agilent 7850 ICP-MS



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## Introduction

The analysis of metals in cannabis has been difficult for many labs because of a lack of official methods in the industry. In August 2021, AOAC adopted an ICP-MS method for the determination of arsenic (As), cadmium (Cd), mercury (Hg), and lead (Pb) in a variety of cannabis and cannabis-derived products. The new method is adopted as an Official Method of Analysis in First Action status (1) and will be tracked for a maximum of two years. If the method is shown to be reproducible, it will be recommended for Final Action status. This AOAC method has undergone rigorous assessment by the AOAC Expert Review Panel (ERP) and achieved consensus through AOAC members.

The new AOAC method specifies microwave acid digestion of homogenized cannabis or hemp samples, followed by quantitative analysis by ICP-MS. The 'big four' elements, As, Cd, Hg, and Pb, can be harmful, so are regulated in most countries and states where cannabis has been legalized for medicinal or recreational use. In common with the pharmaceutical industry, the cannabis industry must control contaminants in final products, with control limits supported by robust testing protocols. Plants can accumulate trace metals and other elements from soil or water. To ensure compliance, producers should therefore analyze cannabis plant materials – as well as final, manufactured cannabis-based products – as part of the testing program.

Method development for the AOAC method was performed on an Agilent 7850 ICP-MS. The same type of ICP-MS instrument was also used in this study to measure As, Cd, Hg, and Pb in a range of cannabis samples in accordance with the AOAC method. The AOAC Standard Method Performance Requirements (SMPR) also allow for the determination of the optional additional elements antimony (Sb), barium (Ba), chromium (Cr), copper (Cu), nickel (Ni), silver (Ag), selenium (Se), and zinc (Zn). The 7850 ICP-MS provides fast multi-element analysis with good control of spectral overlaps and measurement over a wide dynamic range. This means it is easy for these additional elements to be included in the ICP-MS method without the need for modified instrument settings.

The quality of the data was assessed through the measurement of four food standard reference materials (SRMs) and recoveries of low, medium, and high-level spikes of As, Cd, Hg, and Pb in cannabis samples.

## Experimental

### Instrumentation

The 7850 ICP-MS, which includes the Ultra High Matrix Introduction (UHMI) system and ORS<sup>4</sup> collision/reaction cell, was used for the analysis. Sampling was performed using an Agilent SPS 4 autosampler. The 7850 ICP-MS was configured with the standard sample introduction system consisting of a MicroMist glass concentric nebulizer, quartz spray chamber, and quartz torch with 2.5 mm id injector. The interface consisted of a nickel-plated copper sampling cone and a nickel skimmer cone. Instrument operating conditions are listed in Table 1.

UHMI adds an additional argon gas flow to dilute the sample aerosol before it reaches the torch, reducing the need for conventional liquid-dilution, as well as significantly increasing plasma robustness. The automated and fully calibrated aerosol dilution capability of UHMI enables samples with percent level total dissolved solids (TDS) to be analyzed routinely over extended periods of time. The plasma settings and UHMI dilution factor are autotuned as appropriate for the target sample types. To account for all the challenging and different cannabis matrices included in this study, the UHMI dilution factor was set to 4x.

All analytes were measured with the ORS<sup>4</sup> cell operating in helium (He) collision mode, which reduces common polyatomic interferences using kinetic energy discrimination (KED). He KED mode allows the same cell conditions to be used for multiple elements in varied sample types, simplifying method development and routine operation. He KED also gives access to confirmatory isotopes, and the ability to do full mass screening for additional elemental contaminants.

In addition to the quantitative analysis of the AOAC method elements, IntelliQuant data was also acquired during the quantitative analysis to provide semiquantitative results for other elements. IntelliQuant results are based on a two-second full mass spectrum scan obtained in He mode (2). The periodic table "heat map" view of the IntelliQuant QuickScan data provides a quick and simple overview of the concentration of up to 78 elements within the sample. IntelliQuant allows the analyst to see the complete elemental content for the samples, without the need to calibrate for every element. IntelliQuant results also allow the analyst to see a report of the total matrix solids (TMS) content of each sample within a few seconds (ICP-MS MassHunter software version 5.1 or later). The TMS report is useful for method development and troubleshooting, particularly when a lab is analyzing new sample types.

Some plant materials can accumulate high enough levels of less typical elements to cause unexpected and unusual interferences. One example is if the rare earth elements (REEs) are present at high enough concentration in a sample they can form doubly charged ion (REE<sup>2+</sup>) interferences. Since a quadrupole separates ions based on their mass-to-charge ratio ( $m/z$ ), doubly charged ions appear at half their true mass, where they can overlap other analytes. For example, <sup>150</sup>Nd<sup>2+</sup> and <sup>150</sup>Sm<sup>2+</sup> overlap singly charged As<sup>+</sup> at  $m/z$  75, and <sup>156</sup>Gd<sup>2+</sup> and <sup>156</sup>Dy<sup>2+</sup> overlap singly charged selenium (Se<sup>+</sup>) at  $m/z$  78. Routine method setup using ICP-MS MassHunter can automatically apply 'half-mass correction', which corrects any potential REE<sup>2+</sup> interferences, ensuring accurate analysis of trace As and Se (3).

**Table 1.** Agilent 7850 ICP-MS operating conditions.

Parameter	Value
RF Power (W)	1600
Sampling Depth (mm)	10
Carrier Gas (L/min)	0.80
Dilution (UHMI) Gas (L/min)	0.15
UHMI Setting	4
Helium Cell Gas (mL/min)	4.3
KED (V)	3.0

*Shaded parameters were automatically optimized during start up for the UHMI conditions.*

**Table 2.** Types of cannabis and hemp samples that are within scope for analysis by the AOAC ICP-MS method. The samples in bold italics were used in the spiking study.

Sample Category	Sample
Inhaled	<b><i>Hemp flower</i></b>
	Cannabinoid (CBD) vape oil
	Hemp isolate extract
Oral	Full spectrum softgel capsules
	Full spectrum tincture
	Isolate tincture
	CBD coffee grounds
	<b><i>Hemp butter</i></b>
	Hemp seed oil
	CBD beef jerky
	CBD hard candy
	CBD pineapple drink
Topical	Full spectrum balm
	<b><i>Pain relief cream</i></b>
	CBD balm
	CBD topical oil
	Hemp soap
Manufacturing	Hemp biomass
	Spent hemp biomass
	Trichomes
	<b><i>CBD crude extract</i></b>
	CBD distillate
	CBD isolate

### Standard Reference Materials (SRMs)

To verify the sample preparation digestion process and the accuracy of the ICP-MS method, four National Institute of Standards and Technology (NIST) SRMs were analyzed. The SRMs included NIST 1547 Peach Leaves, NIST 1573a Tomato Leaves, NIST 1575 Pine Needles, and NIST 1515 Apple Leaves.

### Samples

The AOAC method is suitable for the analysis of the range of cannabis and hemp-based products that are listed in Table 2. A sample from each category was analyzed in this study, including hemp flower, hemp butter, pain relief cream, and CBD crude extract.

### Standard and sample preparation

Calibration standards were prepared using a mix of 1% HNO<sub>3</sub> and 0.5% HCl. It is recommended to include HCl in samples for ICP-MS analysis, as this acid helps to stabilize several critical analytes including Hg. Hg was calibrated from 0.01 to 10 ppb. All remaining elements were calibrated from 0.1 to 100 ppb.

A variety of cannabis and cannabis-containing samples were purchased in North Carolina, USA. To obtain a representative sample for microwave digestion, it is important to ensure that the solid samples are homogenized, while non-solid samples can be digested as received. The samples (approximately 0.5 g of cannabis plant or cannabis product) were weighed into TFM (modified PTFE) MARSXpress Plus vessels (CEM). To ensure complete digestion of all the varied and potentially complex cannabis sample matrices, 9 mL HNO<sub>3</sub> and 1 mL HCl were added. A MARS 6 microwave digestion system (CEM) was used to digest the samples and a method blank using the program given in Table 3. The digested samples were diluted to 50 mL with reagent water. The acid concentrations in the final sample digests are higher than the levels used for the calibration standards. However, these acid levels were found to give reliable digestion of all the sample matrices and good chemical stability for all the analytes.

UHMI enables high and variable sample matrices to be run against simple (not matrix-matched) calibrations. Any small differences in sample transport and nebulization were automatically corrected by the internal standards.

The SRMs were prepared using the same method to verify that the digestion was complete and to confirm the quantitative recovery of the analytes. Four samples (see Table 2) were prepared in triplicate and spiked at low, medium, and high-levels with an Agilent Environmental Mix Spike solution (part number 5183-4686) before digestion. Three separate preparations of a Fortified Method Blank (FMB) were also prepared for each of the spike levels.

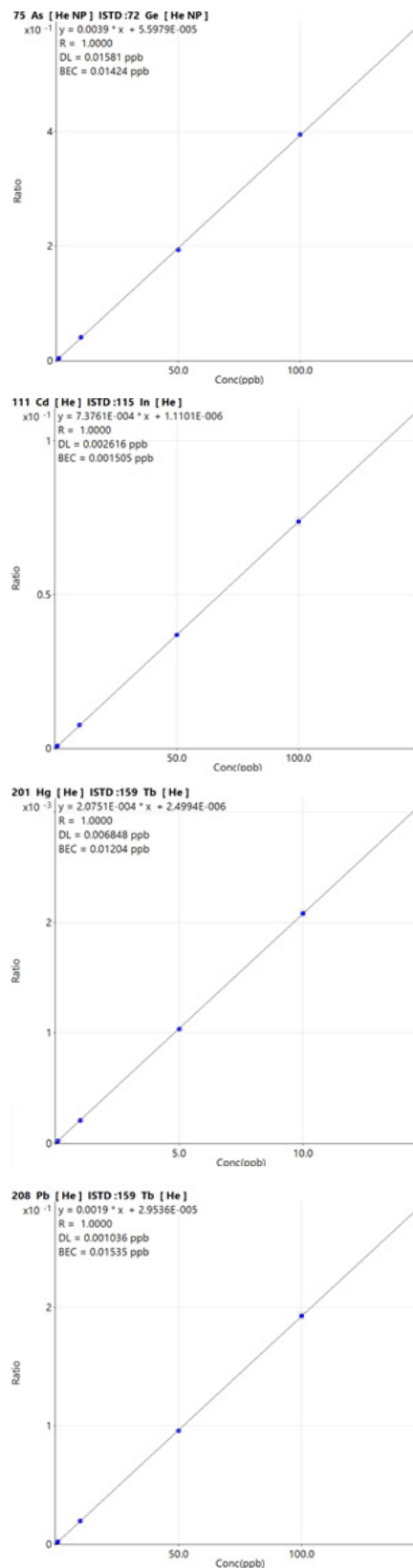
**Table 3.** A typical microwave digestion program for the preparation of cannabis samples.

Example Digestion	
Sample weight	0.5 g
HNO <sub>3</sub>	9 mL
HCl	1 mL
<b>Oven Program</b>	
Ramp (to 210 °C)	20 min
Hold (at 210 °C)	15 min
Cool down	10 min
<b>Final Dilution</b>	
Reagent water	Add to 50 g
Total dilution factor	100 x

### Calibration and calibration verification

Representative calibration curves for As, Cd, Hg and Pb are shown in Figure 1. All show excellent linearity across the calibration range.

A summary of the calibration data for As, Cd, Hg, and Pb, including detection limits (DLs) and background equivalent concentrations (BECs) is given in Table 4. The Limits of Quantitation (LOQ) were calculated from 3 x standard deviation (low-level spike) x 100 (dilution factor). The LOQs were within the AOAC SMPR of ≤10 ppb in the original sample.



**Figure 1.** Calibration curves for As, Cd, Hg, and Pb, showing good linearity (R = 1.0000) across the calibration range.

**Table 4.** Calibration data, DLs, BECs, and LOQs for As, Cd, Hg, and Pb.

Mass	Element	R	DL (ppb)	BEC (ppb)	Limit of Quantitation (LOQ), µg/kg
75	As*	1.000	0.0158	0.0142	9.18
111	Cd	1.000	0.0026	0.0015	6.25
201	Hg	1.000	0.0068	0.0120	2.16
206, 207, 208**	Pb	1.000	0.0010	0.0150	7.85

\*Data for As using half mass correction

\*\*Pb results were based on the sum of the signals measured at mass 206, 207, and 208.

## Results and discussion

### Method accuracy

To check the effectiveness of the sample digestion process and the accuracy of the ICP-MS method, each of the four NIST SRMs was prepared in triplicate. Each of the three preparations of the SRMs was analyzed three times using the 7850 ICP-MS. As shown in Table 5, the mean concentrations were in good agreement with the certified concentrations, where values were provided, meeting the AOAC method SMPR acceptance criteria of 80–120%. Blank cells indicate the absence of a certified or reference value.

**Table 5.** Mean concentrations (ppm) of three repeat measurements of four plant-based SRMs, including comparison with reference values, and recoveries for certified elements. Blank cells indicate the absence of a reference or certified value.

Element	NIST 1547 Peach Leaves				NIST 1573a Tomato Leaves			
	Measured Conc (ppm, µg/kg)*		Certified Conc (mg/kg)	Recovery (%)	Measured Conc (ppm, µg/kg)*		Certified Conc (mg/kg)	Recovery (%)
	Mean	SD			Mean	SD		
<b>75 As</b>	<b>0.06</b>	<b>0.01</b>	<b>0.06</b>	<b>99</b>	<b>0.109</b>	<b>0.021</b>	<b>0.112</b>	<b>97</b>
<b>111 Cd</b>	<b>0.025</b>	<b>0.001</b>	<b>0.026</b>	<b>96</b>	<b>1.39</b>	<b>0.01</b>	<b>1.52</b>	<b>91</b>
<b>201 Hg</b>	<b>0.034</b>	<b>0.003</b>	<b>0.031</b>	<b>108</b>	<b>0.032</b>	<b>0.002</b>	<b>0.034</b>	<b>96</b>
<b>Pb**</b>	<b>0.78</b>	<b>0.02</b>	<b>0.87</b>	<b>90</b>	<b>0.555</b>	<b>0.098</b>		
52 Cr	1.04	0.08	1 <sup>R</sup>	(104)	2.09	0.51	1.99	105
55 Mn	95.4	3.3	98	97	238.67	34.91		
59 Co	0.068	0.004	0.07 <sup>R</sup>	(97)	0.504	0.014	0.57	88
60 Ni	0.79	0.01	0.69	114	1.50	0.03	1.59	94
63 Cu	3.31	0.08	3.7	89	4.25	0.34	4.7	90
66 Zn	16.38	0.56	17.9	92	26.19	0.27	30.9	85
78 Se	0.108	0.032	0.12	90	0.062	0.009	0.054	114
107 Ag	0.006	0.000			0.023	0.002	0.017 <sup>R</sup>	(135)
137 Ba	128	4	124	103	60.07	0.56	63 <sup>R</sup>	(95)
Element	NIST 1575 Pine Needles				NIST 1515 Apple Leaves			
	Measured Conc (ppm, µg/kg)*		Certified Conc (mg/kg)	Recovery (%)	Measured Conc (ppm, µg/kg)*		Certified Conc (mg/kg)	Recovery (%)
	Mean	SD			Mean	SD		
<b>75 As</b>	<b>0.047</b>	<b>0.008</b>	<b>0.039<sup>R</sup></b>	<b>(121)</b>	<b>0.029</b>	<b>0.009</b>		
<b>111 Cd</b>	<b>0.210</b>	<b>0.006</b>	<b>0.233</b>	<b>90</b>	<b>0.014</b>	<b>0.003</b>	<b>0.013</b>	<b>108</b>
<b>201 Hg</b>	<b>0.0380</b>	<b>0.0010</b>	<b>0.0399</b>	<b>96</b>	<b>0.0420</b>	<b>0</b>	<b>0.0432</b>	<b>98</b>
<b>Pb**</b>	<b>0.144</b>	<b>0.002</b>	<b>0.167<sup>R</sup></b>	<b>(86)</b>	<b>0.41</b>	<b>0.01</b>	<b>0.47</b>	<b>86</b>
52 Cr	3.4	0.9	3 <sup>R</sup>	(113)	0.46	0.23	0.3 <sup>R</sup>	(153)
55 Mn	434	12	488 <sup>R</sup>	(89)	49.2	1.1	54.1	91
59 Co	0.060	0.005	0.061 <sup>R</sup>	(98)	0.086	0.005	0.09 <sup>R</sup>	(96)
60 Ni	1.43	0.10	1.47 <sup>R</sup>	(97)	0.787	0.024	0.936	84
63 Cu	3.22	0.30	2.8	115	4.79	0.13	5.69	84
66 Zn	32.01	0.77	30.9	104	10.14	0.29	12.45	81
78 Se	0.110	0.007	0.099 <sup>R</sup>	(111)	0.118	0.024		
107 Ag	0.0167	0.004			0.006	0.001		
137 Ba	4.99	0.08	6	83	45.06	1.52	48.8	92

\*n=9, replicate sample digestion, each in triplicate. R: noncertified reference value. \*\*Pb results were based on the sum of the signals measured at mass 206, 207, and 208.

### Spike recoveries

A spike recovery test was carried out to check the accuracy of the 7850 ICP-MS method. Table 6 shows the results for all SMPR elements spiked at three concentration levels (low, medium, and high) in the FMB. Table 7 shows the spike recoveries for As, Cd, Hg, and Pb at three concentration levels in four cannabis samples (one from each sample type in Table 2).

The recoveries for As, Cd, Hg, Pb in all the cannabis samples were within the AOAC SMPR recovery requirements of 60–115% for low spikes, and 80–115% for medium and high spikes (Table 7).

**Table 6.** Mean recovery results of all SMPR elements in the FMB. Mean calculated from three separate digests of the FMB, each measured in triplicate.

Mass	Element	Fortified Method Blank (FMB) Recovery, %		
		Low Spike $\geq 10$ to 100 ppb	Medium Spike >100 ppb to 1 ppm	High Spike >1 to 10 ppm
75	As	107	105	101
111	Cd	102	101	98
201	Hg	102	106	104
206, 207, 208	Pb	114	105	102
52	Cr	109	117	111
60	Ni	105	118	110
63	Cu	98	115	110
66	Zn	117	112	103
78	Se	102	108	100
107	Ag	108	116	110
121	Sb	102	107	99
137	Ba	108	111	105

Data for As was obtained using the half-mass correction routine in ICP-MS MassHunter.

**Table 7.** Mean recovery results of As, Cd, Hg, and Pb in cannabis sample digests. Mean calculated from three separate digests, each measured in triplicate.

Mass	Element	Native Level in Matrix ppb, µg/kg	Spiked Sample Recovery, %		
			Low Spike ≥10 to 100 ppb	Medium Spike >100 ppb to 1 ppm	High Spike >1 to 10 ppm
<b>Flower (Inhaled)</b>					
75	As	91.2	87	95	107
111	Cd	209	99	101	100
201	Hg	16.9	95	94	102
206, 207, 208	Pb	306	66	109	100
<b>Hemp Butter (Oral)</b>					
75	As	0.48	108	103	102
111	Cd	0.16	98	100	95
201	Hg	<LOQ	103	104	101
206, 207, 208	Pb	3.73	95	102	98
<b>Pain Relief Cream (Topical)</b>					
75	As	11.8	64	97	100
111	Cd	2.26	93	99	98
201	Hg	6.86	78	89	103
206, 207, 208	Pb	12.4	69	100	102
<b>CBD Crude Extract (Manufacturing)</b>					
75	As	3.15	88	99	100
111	Cd	1.11	98	97	98
201	Hg	5.76	85	91	94
206, 207, 208	Pb	188	63	89	100

Data for As was obtained using the half-mass correction routine in ICP-MS MassHunter.

## Conclusion

The AOAC First Action method for the ICP-MS determination of As, Cd, Hg, and Pb and additional optional elements in cannabis samples enables manufacturers to routinely test for these metals in ingredients and final products. The method development for the AOAC method was performed on the Agilent 7850 ICP-MS. A range of cannabis samples were prepared using microwave digestion in HNO<sub>3</sub> and HCl to ensure complete digestion of the varied samples, and chemical stability of the analytes.

The accuracy of the method was evaluated by analyzing four plant-based SRMs and conducting a spike recovery test at different concentration levels for As, Cd, Hg, and Pb in four cannabis samples. Excellent recoveries were achieved for all four elements, within the requirements specified in the AOAC method. The 7850 ICP-MS also met the LOQ requirements for As, Cd, Hg, and Pb of  $\leq 10$  ppb in the original samples, as specified in the AOAC method.

## References

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Printed in the USA, October 14, 2021  
5994-4080EN