

Multi-Element Analysis of Cannabis and Hemp using ICP-MS

Agilent 7800 used to analyze 25 elements in a range of cannabis, hemp, and related products



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Introduction

In the U.S., marijuana remains a Schedule I controlled substance. Worldwide, marijuana use is permitted for medicinal purposes in countries including Australia, Canada, Croatia, Czech Republic, Macedonia, and Poland. Currently, 29 US states, the District of Columbia, Guam, and Puerto Rico allow for comprehensive public medical marijuana and cannabis programs.¹ This is also the case in some countries including the Netherlands, Spain, South Africa, and Uruguay.

Countries and U.S. states that permit use of medicinal and recreational marijuana require rigorous testing of cannabis and associated products to ensure safety from contaminants, including inorganic impurities such as the toxic elements As, Cd, Pb, and Hg. The analysis of mineral and additional trace elements provides labeling information that is required when these products are used as nutritional supplements. Since contamination can occur during the manufacturing process, analysis is necessary at all stages of production.

Additionally, the U.S. Agriculture Improvement Act, also known as the Farm Bill, was signed into law in December 2018. A major provision in the law legalizes hemp as an industrial commodity. The DEA, USDA, and FDA have published a combined Statement of Principles in the Federal Register (FR 53365). This statement defines industrial hemp as any part or derivative (including seeds) of the plant *Cannabis sativa* L. with a dry weight concentration of tetrahydrocannabinols not greater than 0.3% (wt/wt).

Trace element analysis of plant and nutritional supplement materials is well established.² Following acidic digestion to break down the primary components of the plant-based samples, ICP-MS is often used for quantitative analysis because of its multi-element capability, high sensitivity, speed, robustness, and wide dynamic range.

In this study, the Agilent 7800 ICP-MS was used to analyze 25 elements in a range of cannabis and hemp-related products.

Experimental

Instrumentation

A standard Agilent 7800 ICP-MS, which includes Agilent's proprietary High Matrix Introduction (HMI) system, was used for the analysis. Sampling was performed using an Agilent SPS 4 autosampler. The 7800 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. The settings for HMI are autotuned as appropriate for the matrix levels of the target sample types. In this case, the HMI dilution factor was 4x. All analytes were acquired in helium (He) collision mode. Using the simple methodology, He mode reliably reduces or eliminates all common polyatomic interferences using kinetic energy discrimination (KED).

Table 1. ICP-MS operating conditions (shaded parameters were automatically optimized during start up for the HMI conditions).

Parameter	Value
RF Power	1,600 W
Sampling Depth	10 mm
Carrier Gas	0.80 L/min
Dilution (HMI) Gas	0.15 L/min
Helium Cell Gas	4.3 mL/min
Energy Discrimination	3.0 V

For comparison purposes, As and Se were also acquired using half-mass tuning, which corrects for overlaps due to doubly charged rare earth elements (REEs). The instrument was automatically tuned for half mass correction in the ICP-MS MassHunter software. The software also collects semiquantitative or screening data across the entire mass region, referred to as Quick Scan. Quick Scan provides data for elements that may not be present in the calibration standards.

Standard Reference Materials (SRMs)

Various SRMs bought from National Institute of Standards and Technology (NIST) were analyzed in this study to verify the sample preparation digestion process. The SRMs used were NIST 1547 Peach Leaves, NIST 1573a Tomato Leaves, and NIST 1575 Pine Needles. NIST 1640a Natural Water was used to verify the calibration procedure.

Samples

A range of cannabis and hemp based products were analyzed in this study including cannabis, cannabis tablets, a cannabidiol tincture, chewable sweets, and a hemp-based body cream.

Standard and sample preparation

Calibration standards were prepared using a mix of 1% HNO₃ and 0.5% HCl. Na, Mg, K, Ca, and Fe were calibrated from 0.5 to 10 ppm. Hg was calibrated from 0.05 to 2 ppb. All remaining elements were calibrated from 0.5 to 100 ppb.

After weighing the samples (approximately 0.15 g of cannabis plant and between 0.3 to 0.5 g of cannabis product) into quartz vessels, 4 mL HNO₃ and 1 mL HCl were added and the samples were microwave digested using the program given in Table 2. HCl was included to ensure the stability of Ag and Hg in solution. The digested samples were diluted using the same acid mix as the 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. Hemp can be analyzed in similar manner.

Four samples (see Table 6) were prepared in triplicate and fortified with an Agilent Environmental Mix Spike solution (part number 5183-4686) before analysis. The samples, spikes, and SRMs were diluted 5x before analysis to reduce the acid concentration.

Table 2. Parameters for microwave digestion.

Step	Ramp time (Min)	Temp (°C)	Hold time (Min)	Nitrogen gas starting pressure (bar)
1	20	240	15	35

Calibration and calibration verification

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

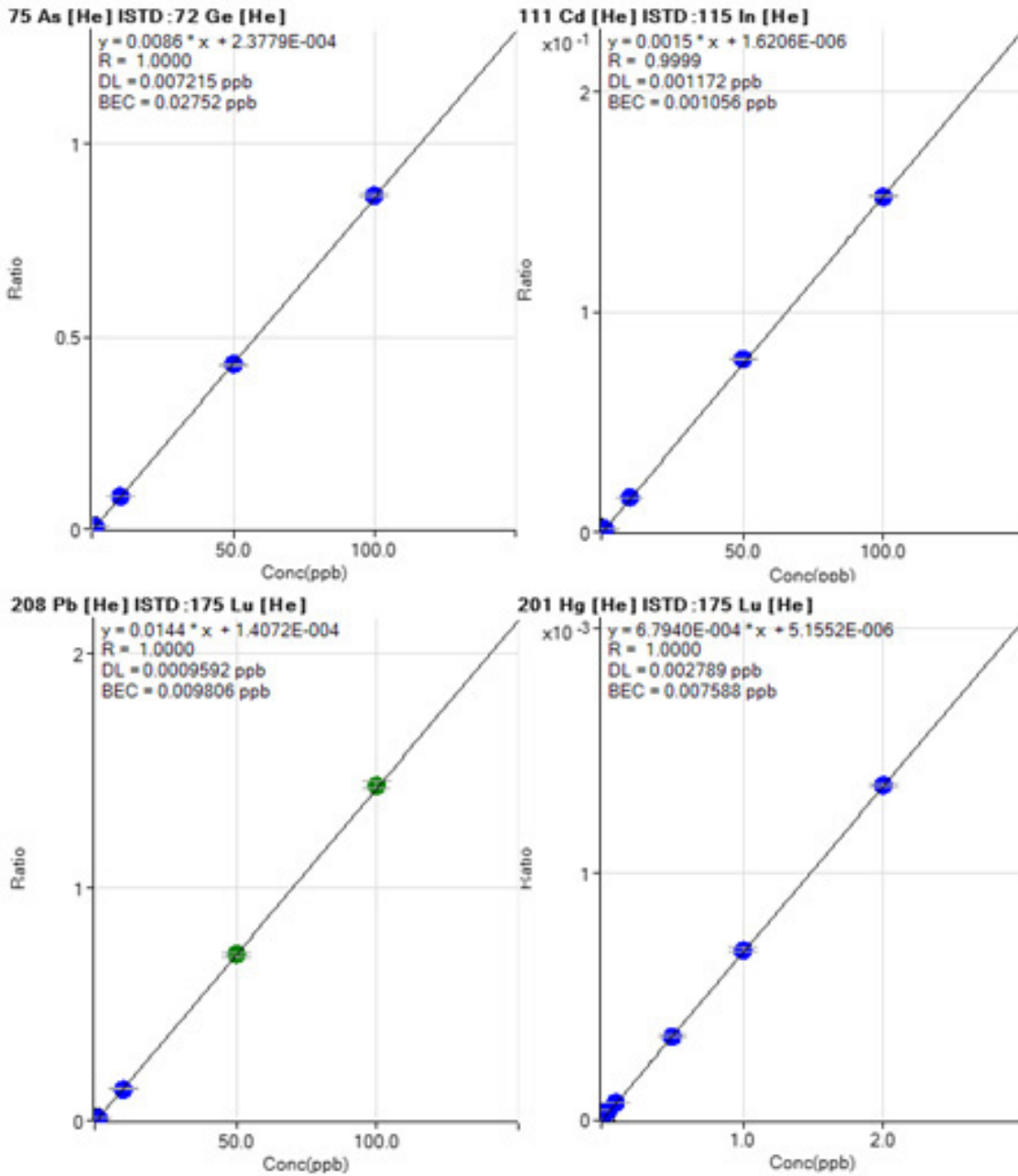


Figure 1. Calibration curves for As, Cd, Pb, and Hg.

A summary of the calibration data, including detection limits (DLs) and background equivalent concentrations (BECs) is given in Table 3.

Table 3. Calibration summary data acquired in He mode. Data for As and Se in shaded cells was obtained using half mass correction tuning.

Mass	Element	ISTD	R	DL (ppb)	BEC (ppb)	
9	Be	⁶ Li	1.0000	0.0130	0.0055	
23	Na	⁴⁵ Sc	1.0000	2.2898	63.9621	
24	Mg		1.0000	0.2617	0.4355	
27	Al	⁶ Li	1.0000	0.2685	0.5958	
39	K	⁴⁵ Sc	0.9999	2.8386	60.8172	
44	Ca	⁶ Li	1.0000	1.0935	14.7211	
51	V	⁴⁵ Sc	1.0000	0.0046	0.0978	
52	Cr		1.0000	0.0070	0.0339	
55	Mn		0.9999	0.0123	0.0772	
56	Fe		0.9999	0.0048	0.7538	
59	Co		1.0000	0.0007	0.0042	
60	Ni		0.9999	0.0127	0.0282	
63	Cu		⁷² Ge	0.9999	0.0060	0.1106
66	Zn		⁴⁵ Sc	0.9999	0.0335	0.2284
75	As	⁷² Ge	1.0000	0.0162	0.0509	
75	As		1.0000	0.0107	0.0420	
78	Se		1.0000	0.2533	0.4015	
78	Se		1.0000	0.1102	0.4232	
95	Mo		0.9998	0.0024	0.0091	
107	Ag	¹¹⁵ In	0.9998	0.0048	0.0090	
111	Cd		0.9999	0.0026	0.0064	
137	Ba	¹⁷⁵ Lu	1.0000	0.0075	0.0361	
201	Hg		1.0000	0.0057	0.0182	
205	Tl	²⁰⁹ Bi	1.0000	0.0068	0.0499	
208	Pb	¹⁷⁵ Lu	0.9999	0.0042	0.0300	
232	Th		1.0000	0.0006	0.0037	
238	U		1.0000	0.0010	0.0027	

As part of the instrument quality control (QC), NIST 1645a Natural Water was used as an Initial Calibration Verification (ICV) standard. The results given in Table 4 show that the recoveries for all the certified elements present in 1640a were excellent, ranging from 93 to 104%. A mid-level calibration standard comprising mineral elements at 5 ppm, Hg at 1 ppb and all trace elements at 50 ppb was used as the Continuing Calibration Verification (CCV) solution. The CCV was analyzed six times throughout the run.

The mean recoveries and range are also given in Table 4. All CCV recoveries were within $\pm 10\%$ of the expected value.

Table 4. ICV and CCV recovery tests. Data for As and Se in shaded cells was obtained using half mass correction tuning.

Mass	Element	ICV (NIST 1640a)	NIST 1640a Certified Value (ppb)	Recovery of ICV (%)	Recovery of CCV Mean $\pm 1\sigma$, (n=6)%	Recovery Range of CCV, %
9	Be	3.048	3.026	101	96 \pm 4	92–102
23	Na	3082	3112	99	97 \pm 3	93–100
24	Mg	1031	1050.2	98	98 \pm 2	95–101
27	Al	52.79	53.00	100	100 \pm 3	93–104
39	K	597.29	575.3	104	100 \pm 3	97–105
44	Ca	5553	5570	100	103 \pm 3	96–106
51	V	14.58	15.05	97	97 \pm 2	95–100
52	Cr	38.56	40.54	95	97 \pm 3	95–103
55	Mn	40.65	40.39	101	99 \pm 2	97–102
56	Fe	36.48	36.80	99	99 \pm 2	97–102
59	Co	19.65	20.24	97	96 \pm 3	93–101
60	Ni	24.50	25.32	97	96 \pm 3	92–99
63	Cu	82.79	85.75	97	96 \pm 2	94–100
66	Zn	54.23	55.64	97	95 \pm 3	92–99
75	As	7.854	8.075	97	95 \pm 3	92–99
75	As	7.780	8.075	96	93 \pm 3	90–97
78	Se	19.67	20.12	98	95 \pm 3	93–99
78	Se	19.74	20.12	98	94 \pm 4	90–99
95	Mo	44.18	45.60	97	96 \pm 3	91–100
107	Ag	7.810	8.081	97	98 \pm 2	96–100
111	Cd	3.884	3.992	97	95 \pm 3	92–99
137	Ba	152.2	151.8	100	97 \pm 2	94–100
201	Hg	0.0304	–	–	95 \pm 4	92–101
205	Tl	1.592	1.619	98	101 \pm 4	98–109
208	Pb	11.89	12.10	98	98 \pm 2	94–100
232	Th	0.0025	–	–	97 \pm 2	94–100
238	U	23.64	25.35	93	96 \pm 2	93–98

Internal standard stability

Figure 2 shows the ISTD signal stability for the sequence of 58 samples analyzed over ~four hours. The ISTD recoveries for all samples were well within $\pm 20\%$ of the value in the initial calibration standard. These ISTD recoveries are comparable to the results obtained routinely using ICP-MS, demonstrating the robustness of the 7800 ICP-MS with HMI.

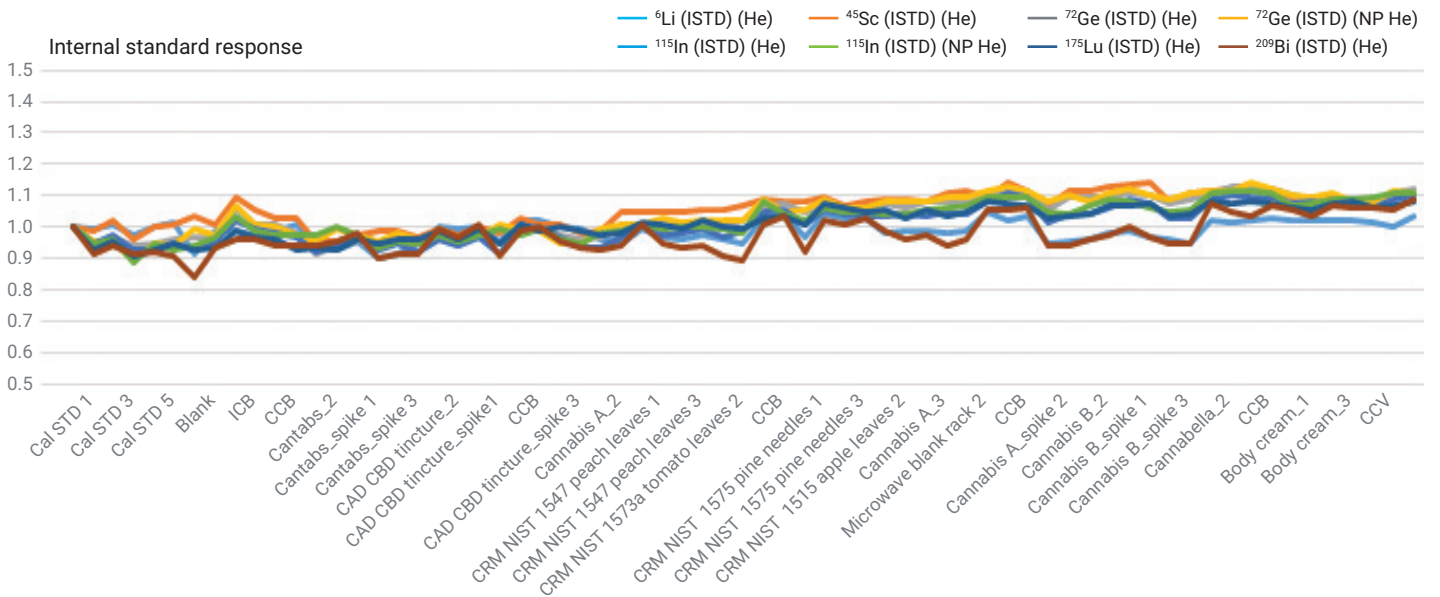


Figure 2. Internal standard signal stability for the sequence of 58 samples analyzed over ~four hours.

Results and discussion

Three SRMs were analyzed to verify the digestion process (Table 5). For most elements, the mean results were in good agreement with the certified concentrations, where certified values are provided. The measured results for As in NIST 1547 and Se in both NIST 1547 and 1573a did not show such good agreement. Some plant materials may contain high levels of rare earth elements (REEs), also known as lanthanides (LA). These elements have low second ionization potentials, so readily form doubly-charged ions (REE⁺⁺). As the quadrupole mass spectrometer separates ions based on their mass-to-charge ratio (*m/z*), these doubly-charged ions appear at half their true mass. Doubly-charged ions of

the REEs ¹⁵⁰Nd, ¹⁵⁰Sm, ¹⁵⁶Gd, ¹⁵⁶Dy, ¹⁶⁰Gd, and ¹⁶⁰Dy therefore appear at *m/z* 75, 78 and 80, potentially causing overlaps that can bias the results for As and Se in samples that contain high levels of the REEs. The 7800 ICP-MS corrects for these interferences using “half mass correction”, which is automatically set up in the ICP-MS MassHunter software. The improvement provided by half-mass correction is illustrated in the corrected results for As and Se shown in the shaded cells in Table 5.

Note that the recoveries for As and Se shown in Table 5 (indicated by ††) are calculated relative to the original certified values (1991 revision). These certified values have subsequently been removed from the certificate (2017 revision) so may not be reliable.

Table 5. Mean concentrations (ppm) of three repeat measurements of three SRMs, including certified element concentrations, where appropriate, and % recovery.

Element	NIST 1547 Peach Leaves				NIST 1573a Tomato Leaves				NIST 1575 Pine Needles			
	Mean Measured Conc.*	Certified Conc.	Recovery % **	QC Criteria (80-120%) [§]	Mean Measured Conc.*	Certified Conc.	Recovery % **	QC Criteria (80-120%) [§]	Mean Measured Conc.*	Certified Conc.	Recovery % **	QC Criteria (80-120%) [§]
9 Be	‡				‡				‡			
23 Na	27.86	23.8	117	Pass	119.2	136	88	Pass	77.241	63 ^R	123	
24 Mg	4264.2	4320	99	Pass	10213.1	12000 ^R	85		952.9	1060	90	Pass
27 Al	251.7	248.9	101	Pass	513.3	598	86	Pass	584.8	580	101	Pass
39 K	24330	24300	100	Pass	25728.4	27,000	95	Pass	4004.2	4170	96	Pass
44 Ca	17371.6	15590	111	Pass	53,983.3	50,500	107	Pass	2467.6	2500	99	Pass
51 V	0.349	0.367	95	Pass	0.698	0.835	84	Pass	‡			
52 Cr	1.118	1 ^R	112		1.988	1.99	100	Pass	2.429	3 ^R	81	
55 Mn	99.6	97.8	102	Pass	238.7	246	97	Pass	473.4	488 ^R	97	
56 Fe	222.8	219.8	101	Pass	331.1	368	90	Pass	53.167	46	116	Pass
59 Co	0.069	0.07 ^R	99		0.510	0.57	89	Pass	0.074	0.061 ^R	121	
60 Ni	0.788	0.689	114	Pass	1.442	1.59	91	Pass	1.462	1.47 ^R	99	
63 Cu	3.649	3.75	97	Pass	4.330	4.7	92	Pass	3.330	2.8	119	Pass
66 Zn	17.378	17.97	97	Pass	25.953	30.9	84	Pass	34.630	30.9	112	Pass
75 As	0.183	0.06	304	Fail	0.128	0.112	114	Pass	0.048	0.039 ^R	123	
75 As	0.059	0.06 ††	98	Pass	0.109	0.112	97	Pass	0.047	0.039 ^R	121	
78 Se	0.448	0.12	373	Fail	0.143	0.054	265	Fail	0.118	0.099 ^R	119	
78 Se	0.108	0.12 ††	90	Pass	0.064	0.054	119	Pass	0.110	0.099 ^R	111	
95 Mo	0.054	0.0603	90	Pass	0.445	0.46 ^R	97		‡			
107 Ag	‡				0.019	0.017 ^R	112		‡			
111 Cd	0.028	0.0261	107	Pass	1.330	1.52	88	Pass	0.225	0.233	97	Pass
137 Ba	124.9	123.7	101	Pass	56.500	63 ^R	90	Pass	5.371	6	90	Pass
201 Hg	0.028	0.0317	88	Pass	0.033	0.034	97	Pass	0.039	0.0399	98	Pass
205 Tl	‡				‡				‡			
208 Pb	0.846	0.869	97	Pass	‡				0.170	0.167 ^R	102	
232 Th	0.050	0.05 ^R	100		0.091	0.12 ^R	76		‡			
238 U	0.014	0.015 ^R	93		0.028	0.035 ^R	80		‡			

*n = 3, replicate sample digestion, each in triplicate. ** FDA Elemental Analysis Manual (section 3.4 special calculations) 3.4 equation 20. [§]QC Criteria FDA EAM 4.7 (80-120%) for NIST certified values. ^{3 R} Noncertified reference value. ‡ Elements have no certified or noncertified value for the associated SRM.

Quantitative results

Quantitative results are given in Table 6 for two cannabis-related products, cannabis tablets and a cannabidiol tincture, and two lots of cannabis samples (A and B).

Although well below existing regulatory or guideline levels, the concentrations of As (160.0 ppb), Cd (11.33 ppb), Pb (24.00 ppb), and Co (162.1 ppb) were relatively high in cannabis sample A. Pb and Co were also high in cannabis sample B, at 55.40 and 143.4 ppb, respectively.

Spike recoveries

To check the accuracy of the method for actual sample analysis, a spike recovery test was carried out. The four samples were spiked with an Agilent Environmental Mix Spike premixed standard containing multiple elements at 200 ppb, Na, Mg, K, Ca, Fe at 2,000 ppb, and Hg at 4 ppb. Using the 7800 ICP-MS direct analysis method, excellent spike recoveries were achieved for most elements in the spiked samples. All recoveries were within $\pm 20\%$ for all elements in the cannabis tablets, a cannabidiol tincture, and two cannabis samples, as shown in Table 6. The spike results for K, Ca, and Mn in the two cannabis samples were invalid as the spike levels were much too low (20 times lower) relative to the levels present in the unspiked samples.

Table 6. Quantitative data for two cannabis-related products and two cannabis samples plus mean spike recovery results. All units ppb apart from major elements, which are reported as ppm.

Element	Cannabis Tablets	Cannabidiol Tincture	Cannabis A	Cannabis B	Mean Spike Recovery $\pm 1\sigma$ (%)
	Measured Conc. n=3 (ppb)	Measured Conc. n=3 (ppb)	Measured Conc. n=3 (ppb)	Measured Conc. n=3 (ppb)	
9 Be	3.785	2.869	5.323	3.660	109 \pm 6
23 Na (ppm)	20.03	<0.250**	7.372	50.02	110 \pm 4
24 Mg (ppm)	33.19	0.385	5426	5807	113 \pm 10
27 Al (ppm)	2.310	0.240	5.024	4.586	112 \pm 12
39 K (ppm)	46.30	<250.0**	41156	34101	NA
44 Ca (ppm)	18.38	0.119	11394	9681	NA
51 V	16.46	1.102	37.04	25.09	116 \pm 8
52 Cr	104.8	28.52	81.39	272.5	114 \pm 5
55 Mn	183.7	16.34	114103*	229650*	NA
56 Fe	1914	569.4	252188	219811	114 \pm 6
59 Co	5.624	3.177	162.1	143.4	114 \pm 5
60 Ni	38.98	16.06	108.2	185.7	113 \pm 3
63 Cu	121.6	24.87	10865	13467	108 \pm 1
66 Zn	172.2	644.7	72504	126816	96 \pm 9
75 As	7.045	8.855	159.7	24.43	105 \pm 6
75 As	7.840	10.10	160.0	25.94	103 \pm 6
78 Se	29.08	51.20	50.68	83.80	95 \pm 14
78 Se	27.40	38.50	45.78	72.68	94 \pm 13
95 Mo	24.12	34.20	3280	1589	118 \pm 4
107 Ag	0.877	2.847	8.612	10.78	100 \pm 10
111 Cd	4.537	5.579	11.33	7.471	110 \pm 5
137 Ba	99.94	7.978	345.6	888.7	111 \pm 12
201 Hg	<DL	12.72	29.19	27.06	107 \pm 4
205 Tl	<DL	1017	1739	2038	97 \pm 5
208 Pb	17.49	6.892	24.00	55.40	112 \pm 4
232 Th	4.564	2.462	5.548	4.047	113 \pm 6
238 U	5.355	2.142	4.794	3.238	115 \pm 5

Data for As and Se in shaded cells were obtained using half mass correction tuning. * Spike levels were too low (<5%) relative to the unspiked concentration.

** Estimates, based on the DL and BEC data from the calibration summary data.

Conclusions

The analysis of a wide range of trace and minor elements in cannabis, hemp, and associated products is easily performed using the Agilent 7800 ICP-MS. The 7800's HMI capability enables the routine analysis of samples that contain high and variable matrix levels, while minimizing the need for conventional liquid dilution. By automating dilution in the aerosol phase, manual sample handling steps and the potential for contamination during sample preparation can be reduced, producing more accurate results. Agilent's ICP-MS MassHunter Quick Scan function provides a complete picture of the elements present in the sample, as data can be reported for elements not included in the calibration standards.

The automated tuning of the ICP-MS for half mass correction allows As and Se to be determined with good accuracy, reducing the impact of doubly charged interference caused by high levels of REEs.

Validation of the microwave-assisted sample preparation method was demonstrated by the good recovery results obtained for the plant-based SRMs.

The 7800 ICP-MS is suitable for trace metal screening of medicinal and recreational cannabis, hemp, and related products. The analysis can be carried out at all stages of production to ensure product quality control and products that are free of toxic metals.

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