SHIMADZU
Excellence in Science

Application News

No. ICP-006

Inductively Coupled Plasma Mass Spectrometry

Analysis of Heavy Metal Contaminants in Cannabis Flower using the Shimadzu ICPMS-2030

■ Introduction

The recent evolution of legislation in the United States of America and other countries has opened up the cultivation and sale of cannabis and related products for medical and recreation use in a variety of states and municipalities. With the availability of cannabis as a commercial product comes the need for analysis and regulation of potency, pesticides, biological contaminants, and heavy metals, among others.

The concentration of heavy metals in plants that are intended for consumption is of concern due to the potentially hazardous effects of these metals related to their toxicity. As they grow, plants can bioaccumulate metals in their tissues that originate from the soil and water in which they are grown. These metals may originate naturally in soils and water as a result of the mineral content of the soil or source of the water, or they may be artificially introduced in the form of fertilizers, pesticides, herbicides, and fungicides commonly applied to increase crop yields.

Some of these metals contained in plants have beneficial metabolic uses, such as iron in beans and leafy greens, whereas others, such as lead, can have deleterious effects including toxicity and carcinogenicity. Here, we explore and discuss the applicability of the Shimadzu ICPMS-2030 to the detection of the "Big Four" heavy metals (i.e., As, Cd, Hg, and Pb) in digested cannabis flower samples for compliance with local and state regulations.

■ Limits of Exposure

Limits of permissible daily exposure (PDE) for heavy metals in cannabis flower are loosely defined; however, many states are adopting regulations as presented in the American Herbal Pharmacopoeia's 2004 manuscript *Cannabis Inflorescence*. These limits are presented in Table 1.

Element	µg / 5 g daily dose	µg / g (ppm)
Inorganic Arsenic	10.0	2
Cadmium	4.1	0.82
Lead	6.0	1.2
Methyl Mercury	2.0	0.4

Table 1: Permissible daily exposure for heavy metals impurities in cannabis per 5 g daily consumption and the equivalent concentration in raw material in µg/g (ppm).

Neither ICP-OES nor ICP-MS analytical methods can provide information on the speciation of an element. That is to say the total concentration of an element is reported with no regard for the initial oxidation state nor complexation of that element (e.g., there is no difference in the instrument response generated by methyl mercury versus mobilized mercuric ions). Since speciation information is not available using ICP-OES or ICP-MS, the analyst operates under the assumption that, to be within the acceptable limits, the total concentration of that element must be below the PDE for the more toxic inorganic forms of these elements.

It is worth noting, however, that speciation concentrations can be quantitated by coupling an inert Shimadzu HPLC system to the ICPMS-2030. Using HPLC allows the analyst to separate metals based on their oxidation state and/or associated complexes and elute them into the ICPMS-2030 for concentration analysis. Shimadzu offers both the hardware and software to enable such analyses.

Shimadzu ICPMS-2030

■ Equipment, Reagents, and Labware

A Shimadzu ICPMS-2030 was used for all analysis in conjunction with a Shimadzu AS-10 Autosampler. In-line addition of internal standards to calibration and unknown samples was accomplished using the Shimadzu Internal Standard Addition Kit. Based on the internal diameter of peristaltic tubing used for sample and internal standard injection, the approximate dilution of the internal standard solution was 90%.

High-purity reagents were used during sample preparation and dilution to ensure minimal contamination. Ultra-pure water (≥ 18.1 MΩ·cm; Millipore) along with trace metal grade nitric acid was used for all dilutions and acidifications. For the sake of brevity, we refer to these simply as "water (or H_2O)" and "nitric acid (or HNO_3)" herein.

All labware was cleaned in a solution of 20% nitric acid, triple rinsed with water, and allowed to dry. All standards and unknown samples were prepared in cleaned, single-use containers so as to minimize any cross-contamination between analytical runs.

■ Sample Preparation

Because samples are introduced into the ICPMS-2030 as a liquid, a closed-vessel microwave digestion procedure is required to dissolve cannabis flower samples such that the metals therein are mobilized. To ensure appropriate recoveries of analytes as well as the efficacy of the microwave digestion procedure, we prepared four samples:

1. *Blank* – Consisting only of the reagents used for digestion and dilution.
2. *Fortified Blank* – Identical to the blank sample, but spiked with 5 ppb As, Cd, Hg, and Pb.
3. *Matrix* – Reagents used for digestion and dilution, along with ~0.5 g cannabis flower
4. *Fortified Matrix* – Identical to the matrix sample, but spiked with 5 ppb As, Cd, Hg, and Pb.

Each of the above samples were prepared in digestion vessels that contained 10 mL of 20% HNO_3. The matrix samples also contained ~0.5 g of cannabis flower. Fortified samples were spiked with 5 ppb As, Cd, Hg, and Pb. The digestion vessels were tightly sealed and placed into a rotor within the microwave.

The digestion procedure involved a step-wise increase of microwave power (and therefore sample temperature and vessel pressure) over a period of 40 minutes, followed by time for the samples to cool to ambient temperature.

The 10 mL of digested material was poured from the digestion vessels into clean centrifuge tubes. The digestion vessels were rinsed with water to ensure complete recovery of material from them, and this rinse water was added to the samples in the centrifuge tubes. The 10 mL samples were brought to a final volume of 25 mL by diluting with water. No further dilution of the samples is required prior to analysis using the ICPMS-2030.

■ Analytical Methodology

Sample solutions were analyzed using the Shimadzu ICPMS-2030. Operating conditions for the instrument and analyte elements, masses, and calibration concentrations are provided in Tables 2 and 3, respectively. Prior to quantitation, various parameters such as torch position and focusing lens voltages were automatically optimized as part of a routine tuning procedure.

Internal standards, Y and Tl, were added automatically using the internal standard addition kit along with the peristaltic pump included with the instrument. As such, internal standards were added at a constant rate and concentration to all calibration standards and unknown samples. The final concentration of the internal standards was 10 ppb.

Calibration curves were generated immediately prior to analysis to ensure the most accurate quantitation. The calibration scheme for the instrument is presented in Table 3 and representative curves are provided in Figure 1.

To demonstrate an appropriate dynamic range of the instrument up to the ppm levels at which regulatory limits are set, a second set of calibrations were produced (Figure 2A-D), showing linearity at higher concentrations than the calibration curves used for quantitation in this application note.

Torch	Shimadzu Mini Torch
Nebulizer	Coaxial
Spray Chamber	Cooled Cyclonic
Spray Chamber Temp.	5° C
RF Power	1.20 kW
Sampling Depth	5 mm
Plasma Gas Flow	8.0 L/min
Auxiliary Gas Flow	1.1 L/min
Carrier Gas Flow	0.70 L/min
Total Ar Flow	9.8 L/min
Collision Cell He Flow	6 mL/min
Number of Scans	10
Scan Time	0.2 sec
Total Integration Time	2 sec

Table 2: Operating conditions for the Shimadzu ICPMS-2030.

Element / Mass	Int. Std.	Cal 1	Cal 2	Cal 3	Cal 4
^{75}As	^{89}Y	0	1	5	10
^{111}Cd	^{89}Y	0	1	5	10
^{112}Cd	^{89}Y	0	1	5	10
^{114}Cd	^{89}Y	0	1	5	10
^{200}Hg	^{205}Tl	0	1	5	10
^{202}Hg	^{205}Tl	0	1	5	10
^{206}Pb	^{205}Tl	0	1	5	10
^{207}Pb	^{205}Tl	0	1	5	10
^{208}Pb	^{205}Tl	0	1	5	10

Table 3: Analytical elements and masses, internal standards, and calibration concentrations.

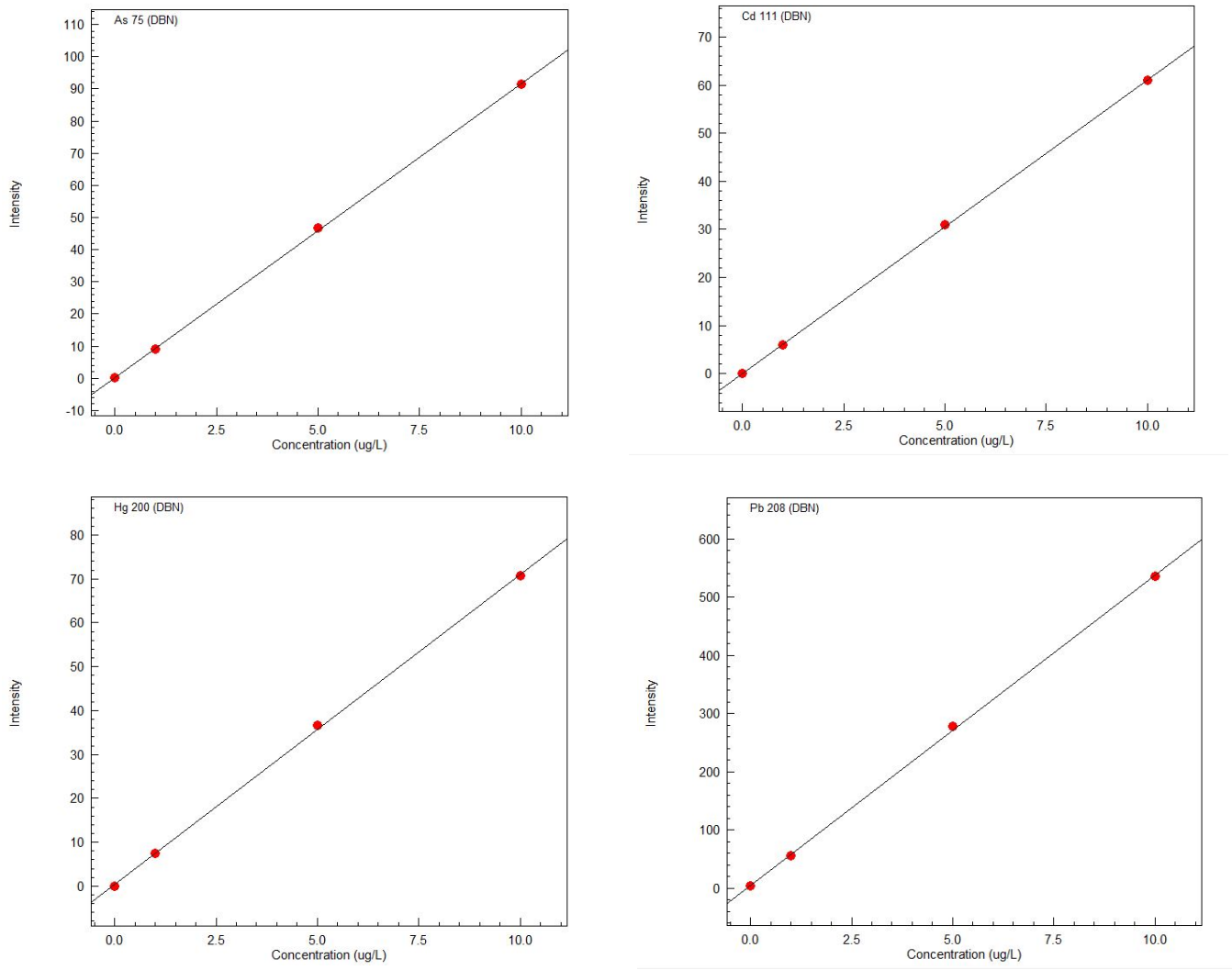


Figure 1A-D: Calibration curves constructed at 0, 1, 5, and 10 ppb for As, Cd, Hg, and Pb.

■ Results

Results of sample analyses are presented in Tables 4 and 5.

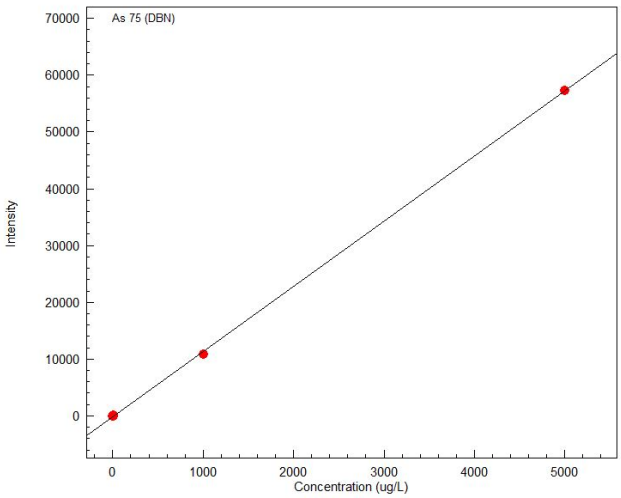
	^{75}As	^{111}Cd	^{112}Cd	^{114}Cd	^{200}Hg	^{202}Hg	^{206}Pb	^{207}Pb	^{208}Pb
Blank	0.0091	0.0053	0.0075	0.0063	0.62	0.59	0.102	0.099	0.101
Fortified Blank	1.91	1.968	1.92	1.976	2.53	2.62	2.14	2.16	2.17
Yield	*95.0%*	*98.1%*	*95.6%*	*98.5%*	*95.5%*	*101.5%*	*101.9%*	*103.1%*	*103.5%*

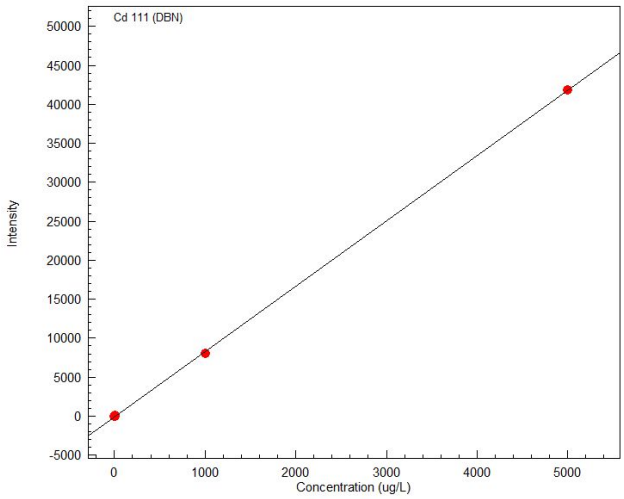
	^{75}As	^{111}Cd	^{112}Cd	^{114}Cd	^{200}Hg	^{202}Hg	^{206}Pb	^{207}Pb	^{208}Pb
Matrix	0.0016	0.43	0.39	0.41	0.46	0.84	0.262	0.258	0.248
Fortified Matrix	1.97	2.51	2.44	2.39	2.493	2.791	2.2	2.18	2.17
Yield	*98.4%*	*104.0%*	*102.5%*	*99.0%*	*101.7%*	*97.6%*	*96.9%*	*96.1%*	*96.1%*

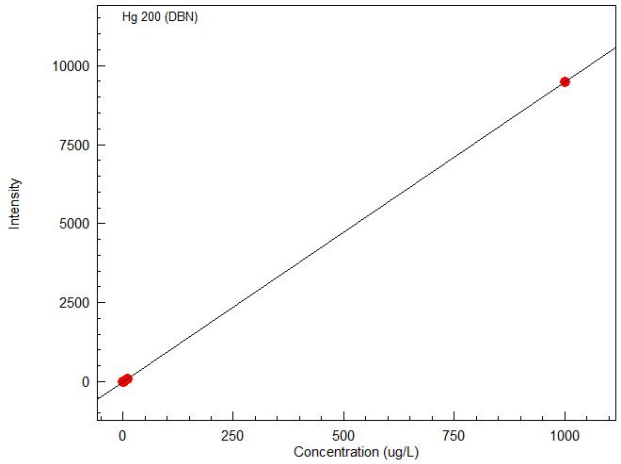
Table 4*:* Results, in ppb, of ICPMS-2030 analyses of blank, fortified blank, matrix, and fortified matrix samples as well as recovery yields, in percent. Note that recoveries of 2 ppb are to be expected as a result of diluting the samples during preparation by 2.5 times from their initial 5 ppb concentration.

	^{75}As	^{111}Cd	^{112}Cd	^{114}Cd	^{200}Hg	^{202}Hg	^{206}Pb	^{207}Pb	^{208}Pb
Matrix	0.1	21.5	19.5	20.5	23.0	42.0	13.1	12.9	12.4
Fortified Matrix	98.5	125.5	122.0	119.5	124.7	139.6	110.0	109.0	108.5
Limits	*2000*	*820*	*820*	*820*	*400*	*400*	*1200*	*1200*	*1200*

Table 5*:* Results, in ppb, of concentration for raw material, back-calculated for dilution and ~0.5 g initial mass of cannabis flower. The bottom row shows the concentration limits for each element as delineated in Table 1. Note that the results demonstrate sensitivity and adequate recovery far below limits of concentration.







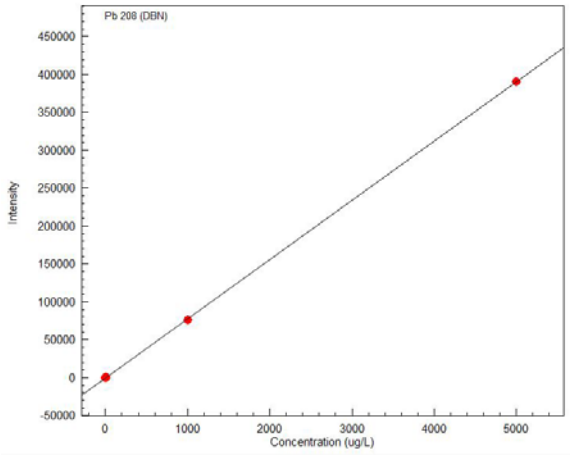


Figure 2A-D: Calibration curves constructed up to 5 ppm (As, Cd, Pb) and 1 ppm (Hg), demonstrating an expanded dynamic range of the ICPMS-2030 up to and including concentrations at which regulatory limits are set.

■ Discussion

The results presented in Table 4 demonstrate that the ability of the ICPMS-2030 to handle an acid-digested cannabis matrix and provide recoveries within the commonly-accepted range of ±10% for analytes in the low parts-per-billion concentration range.

When back-calculating the hypothetical concentrations in cannabis flower in the spiked samples (Table 5), the ICPMS-2030 provides sensitivity well below currently accepted limits for concentration of heavy metals in cannabis. This should allow for future applicability as acceptable concentration limits, if they change, will likely become more stringent over time.

Furthermore, although this application was run at concentrations far below regulatory limits, Figure 2A-D demonstrate that the ICPMS-2030 is capable of producing linearity in calibration curves across a larger dynamic range, in this case, up to ppm levels.

■ Conclusion

The Shimadzu ICPMS-2030 provides the sensitivity and accuracy to meet and exceed compliance with current regulations on heavy metals in cannabis products. With lowest-in-class operating costs, the ICPMS-2030 will help maximize the return on investment of heavy metals testing instrumentation.

As noted in the introduction, this application focuses solely on heavy metals in the cannabis flower material despite the origination of heavy metals from the soil and water in which the plant is grown. The Shimadzu ICPMS-2030 can be used to assess heavy metals in those matrices as well, in particular groundwater by EPA method 200.8.

Shimadzu's ICPMS-2030, along with a wide array of other analytical instrumentation offerings from Shimadzu such as GC, GC/MS, HPLC, and LC/MS, will allow your cannabis laboratory to operate efficiently and be in full compliance with regulations in your state.

Shimadzu does not support or promote the use of its products or services in connection with illegal use, cultivation or trade of cannabis products.
Shimadzu products are intended to be used for research use only purposes or state approved medical research.

First Edition: April 2017

SHIMADZU Corporation
www.shimadzu.com/an/

SHIMADZU SCIENTIFIC INSTRUMENTS
7102 Riverwood Drive, Columbia, MD 21046, USA
Phone: 800-477-1227/410-381-1227, Fax: 410-381-1222
URL: www.ssi.shimadzu.com