Analysis of Heavy Metal Contaminants in Hemp and Cannabis Flower using ICP- Mass Spectrometry

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Overview

The recent evolution of legislation in the European Community and other European 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 [1]. 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.

Figure 1: Cannabis plants can bioaccumulate metals

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 pharmaceutical products are defined by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) [2] and the in the European Pharmacopoeia. The limits of the permissible daily exposure (oral intake) are presented in Table 1.

Element	PDE (oral intake)	PDE (parenteral)
Arsenic	15 µg/day	15 µg/day
Cadmium	5.0 µg/day	1.7 µg/day
Lead	5 µg/day	5 µg/day
Mercury	30 µg/day	3 µg/day

Table 1: Permissible daily exposure for heavy metals impurities in pharmaceutical products for human use

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 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% HNO3. 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 are provided in Table 2. Prior to quantitation, various parameters such as torch position and focusing lens voltages were automatically optimized as part of a routine tuning procedure.

Torch	Mini Torch
Nebulizer	Coaxial
Spray chamber	Cooled cyclonic
Spray chamber T.	5° C
RF Power	1.20 kW
Sampling Depth	5mm
Plasma Gas flow	8.0 L/min
Aux Gas flow	1.1 L/min
Carrier Gas flow	0.7 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

Internal standards, Y and Tl, were added automatically using the internal standard addition kit. 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 is presented in Table 3 and representative curves are provided in Figure 2.

Element	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}Hg	^{205}Tl	0	1	5	10
^{207}Hg	^{205}Tl	0	1	5	10
^{208}Hg	^{205}Tl	0	1	5	10

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

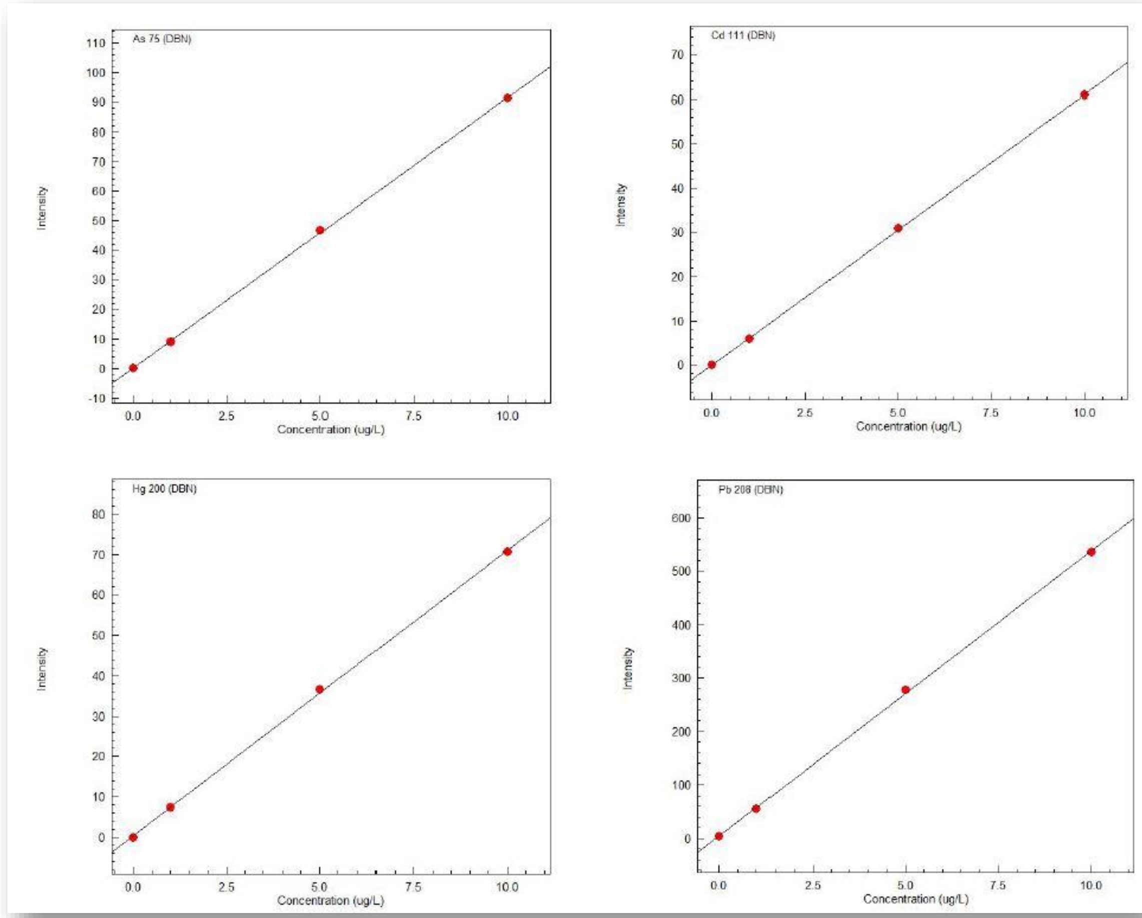

Figure 2: Calibration curves for As, Cd, Hg, and Pb [µg/L]

In order to reconfirm the appropriate dynamic range of the instrument up to the ppm levels at which regulatory limits are set, a second set of calibrations were produced, showing linearity at higher concentrations (5000 µg/L).

Element	Blank	Fortified Blank	Recovery Rate
^{75}As	0.0091	1.91	95.0%
^{111}Cd	0.0053	1.968	98.1%
^{112}Cd	0.0075	1.92	95.6%
^{114}Cd	0.0063	1.976	98.5%
^{200}Hg	0.062	2.53	95.5%
^{202}Hg	0.59	2.62	101.5%
^{206}Hg	0.102	2.14	101.9%
^{207}Hg	0.099	2.16	103.1%
^{208}Hg	0.101	2.17	103.5%

Table 4: Results in [µg/L] of ICPMS-2030 analyses of blank and fortified blank samples as well as recovery rates in percent. Recoveries of 2 ppb are to be expected according to the sample preparation

Discussion

The results presented in Table 4 demonstrate 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.

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 drinking water by DIN EN ISO 17294-2:2005-02 method.

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.

References

[1] Cannabis Legislation in Europe, European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2018

[2] ICH guideline Q3D on elemental impurities EMA/CHMP/ICH/353369/2013

Disclaimer

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