

1 Introduction

In this poster we present how a single method workflow has been developed and validated per AOAC SMPR® and USP <233> requirements. Recognizing cannabis & hemp is challenging matrix to characterize, data will be presented to show that a single source workflow solution, from digestion to generation of the Certificate of Analysis (COA) is the most ideal.

Developing and validating a standardized microwave digestion and ICP-MS method for the determination of an expanded list of metals in flower and oil products down to ppb levels has special considerations associated with it that are discussed in this

The list of metals expands on the "Big 4" (As, Cd, Pb, and Hg) and the added elements encompass target elements of legalized States (California, Colorado, Connecticut, Massachusetts, Michigan, Maryland, and New York) as well as AOAC, NIST, and ASTM lists of target elements.

This work presents the quantitation limits, repeatability, and accuracy of this method. In addition, the influences of rare earth elements in cannabis are investigated and discussed.

The goal = Validation of metals beyond As, Cd, Pb, and Hg

2 Target Elements by Jurisdiction/Reference

Element	CA/CO/CT/MA	MI	MD	NY	NIST	AOAC	ASTM
As	x	x	x	x	x	x	x
Cd	x	x	x	x	x	x	x
Hg	x	x	x	x	x	x	x
Pb	x	x	x	x	x	x	x
Cr			x	x	x	x	x
Ni		x		x	x	x	x
Ba			x		x	x	x
Cu		x		x	x	x	x
Sb				x	x	x	x
Se			x		x	x	
Co					x	x	x
Mo					x	x	x
V					x	x	x
Zn				x		x	
Ag						x	
Be					x		
Li							x
Mn					x		
Sn							x
U					x		

Table 1. Element Summary by Jurisdiction/Reference

3 Sample Preparation

All samples were prepared using a PerkinElmer Titan Microwave Preparation System (MPS). All digestions resulted in a clear digestate.

Procedure:

1. Weigh 0.5 g of each sample and add to digestion vessel
2. Add a mixture of HNO₃ and H₂O₂ and allow to digest in the fumehood for 15-30 minutes
3. Add 10 µg of Au to the digestion tube to stabilize Hg (200 ppb in final digestate)
4. After digestion, the sample solutions were diluted with deionized water to a final volume of 50 mL.



Figures 1-3. Workflow for sample preparation, from weighing to digestion, and final clear digestate.

4 Inductively Coupled Plasma Mass Spectrometer Parameters

ICP-MS is used for this analytical work since it has the sensitivity to achieve those detection limits required for the Big 4, which can be particularly challenging for ICP-OES or other analytical techniques.

The PerkinElmer NexION 1000 ICP-MS was used in this work however any model of NexION can perform this analysis as it was operated in a single mode of operation: Kinetic Energy Discrimination (KED) or collision mode.

NexION Parameter	Value
Power	1600 W
Plasma Gas	15 L/min
Auxiliary Gas	1.2 L/min
Nebulizer Gas	0.905 L/min
AMS Dilution Gas	0.11 L/min
AMS Dilution	Approx 2.5-3x
Helium KED Gas Flow	4.3 mL/min
Sample Flow	250 µL/min
IS Flow	40 µL/min

Table 2. NexION 10000 ICP-MS Parameters



Figure 4. NexION 10000 ICP-MS

5 Matrix Considerations

Digestions result in heavy matrix

- High acid concentration: >10%
- TDS from the sample in the digestate: 0.5 g → 50 mL

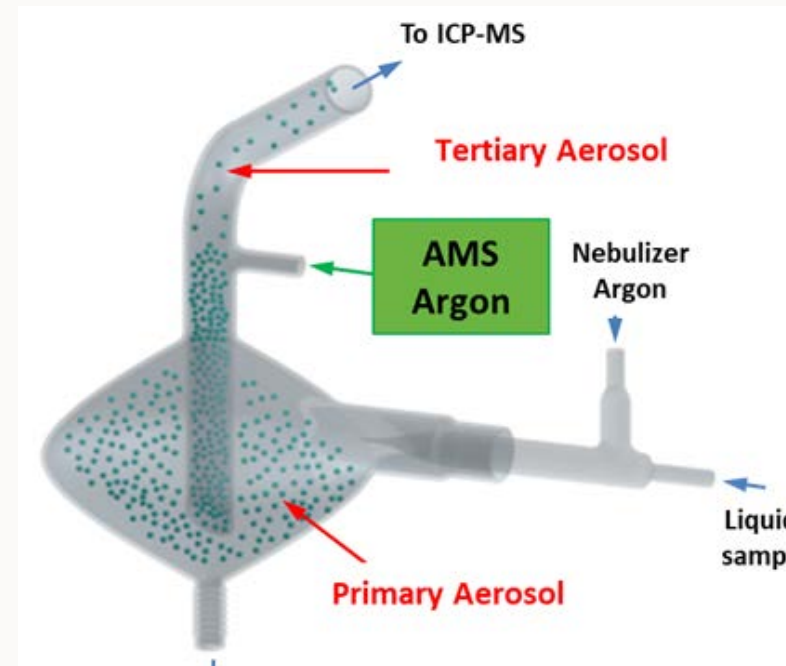


Figure 5. NexION AMS

Mitigate Matrix Effects using All Matrix Solution (AMS)

- Aerosol dilution to reduce plasma loading
- Dilutes up to 200-fold
- Avoids bench dilutions
- More efficient operation and ionization
- Fewer matrix effects
- Less deposition on the interface cones

AMS Benefits = simplified sample preparation, higher quality data, less system maintenance

6 Doubly Charged Interference Investigation

Possible Doubly Charged Interferences:

- $^{66}\text{Zn}^+ = ^{132}\text{Ba}^{2+}$
- $^{75}\text{As}^+ = ^{150}\text{Nd}^{2+}, ^{150}\text{Sm}^{2+}$
- $^{78}\text{Se}^+ = ^{156}\text{Gd}^{2+}, ^{156}\text{Dy}^{2+}$

Isotopes Monitored:

- $^{132}\text{Ba}^{2+}$ @ mass 67.5
- $^{145}\text{Nd}^{2+}$ @ mass 72.5
- $^{147}\text{Sm}^{2+}$ @ mass 73.5
- $^{155}\text{Gd}^{2+}$ @ mass 77.5
- $^{163}\text{Dy}^{2+}$ @ mass 81.5

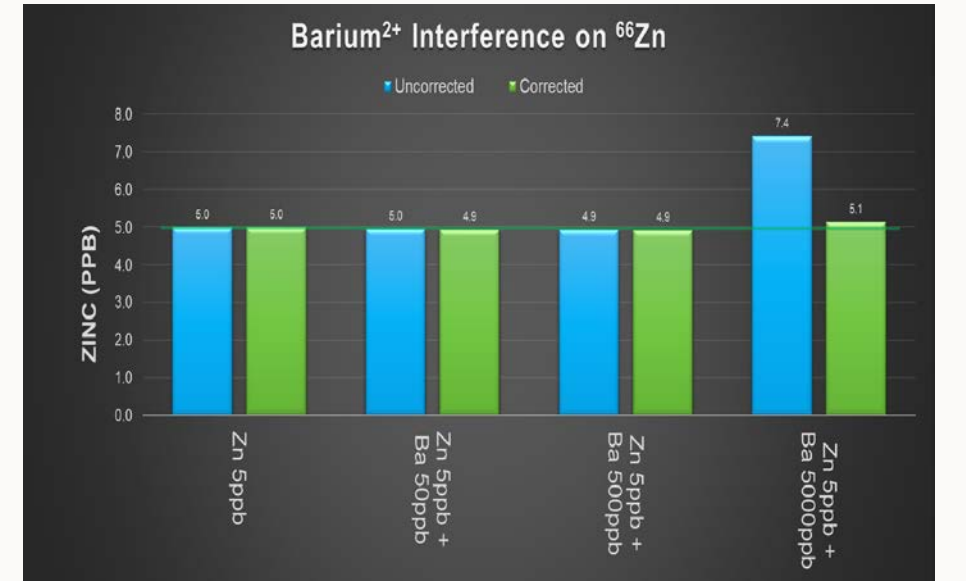
Dynamic Half Mass Correction Equations Used

- Conceptually like an isobaric correction
- Equation is based on relative abundance of interfering element isotopes
- Automatically corrects for the interfering element by monitoring an **alternative half mass of that element during the analysis.**

Doubly Charged Investigation Summary:

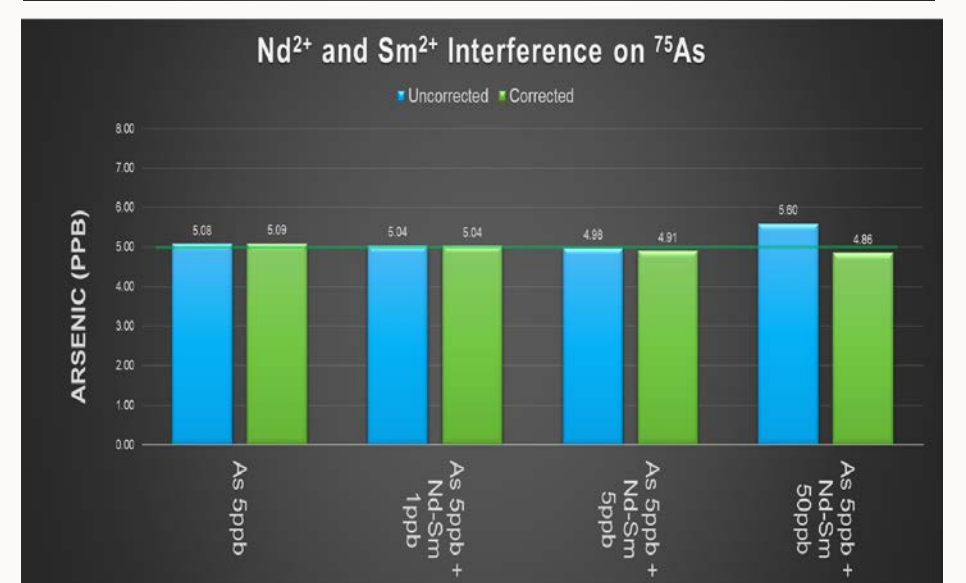
$^{132}\text{Ba}^{2+}$ on $^{66}\text{Zn}^+$

- No significant interference until Ba is in the ppm level in the digestate
- All samples tested the Zn concentrations were MUCH higher than Ba, therefore this wasn't an issue



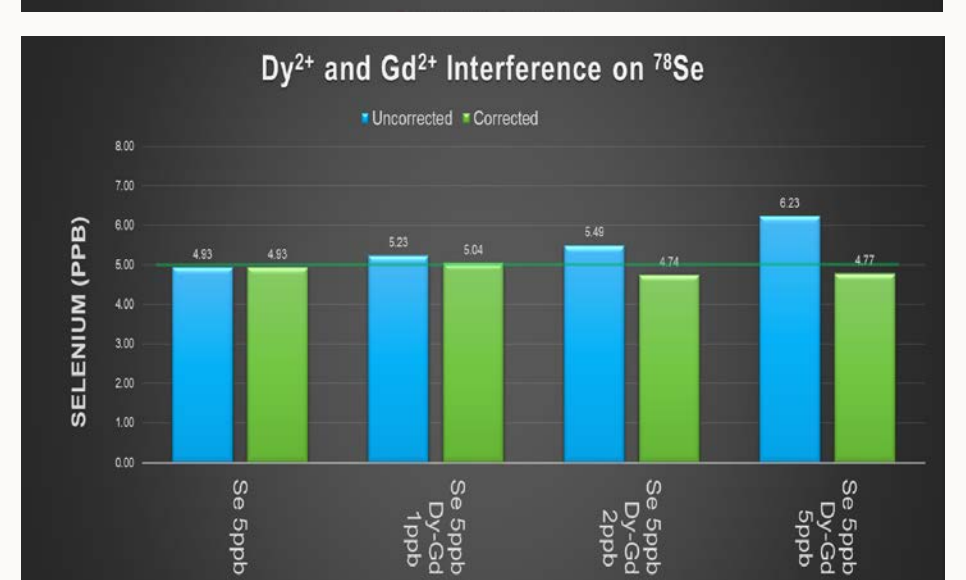
$^{150}\text{Nd}^{2+}$ & $^{150}\text{Sm}^{2+}$ on $^{75}\text{As}^+$

- No significant interference until both Nd and/or Sm are in the high ppb in the digestate
- Interfere at relatively similar levels and with
- 100 ppb total of the two REEs resulted only in a 10% bias on As
- Only samples with elevated levels of REEs were NIST peach and tomato leaves and a tobacco sample



$^{156}\text{Gd}^{2+}$ & $^{156}\text{Dy}^{2+}$ on $^{78}\text{Se}^+$

- Slightly more influence on Se than with As or Zn interferences
- All cannabis samples tested the Se concentrations were lower than 5ppb in the digestate.
- Gd has a relatively larger interference than the other doubly charged interferences have with a factor of about 1.4



Figures 6-8. Effects REE Doubly Charged corrections.

7 Method Validation

AOAC SMPR 2020.001 was reference for method validation. This is the Standard Method Performance Requirements for the Determination of Heavy Metals in a Variety of Cannabis and Cannabis-Derived Products.

This

- Refers to USP chapter 233.
- Requires the big 4: As, Cd, Pb, and Hg
- LOQ of less than or equal to 10 ppb for Big 4.
- Other metals are noted as optional as it covers multiple jurisdictions.
- Analyte performance is based on concentration range

Limit of quantitation (LOQ)	≤10 ppb, µg/kg		
	Repeatability (RSD), %	Reproducibility (RSD), %	Recovery, %
Range			
>10 ppb to 100 ppb	15	32	60-115
>100 ppb to 1 ppm	11	16	80-115
>1 ppm to 10 ppm	7.3	8	80-115

Figure 9. AOAC SMPR 2020.001 Method Performance Requirements

Analyte	LOD (3xSD - µg/L)	LOQ (10xSD - µg/L)	Analyte	Mean (µg/g)	Repeatability (% RSD)	Analyte	Spike Level (µg/g)	Mean Spike %Recovery
Arsenic	0.002	0.005	Arsenic	0.051	1.2%	Arsenic*	0.2	102%
Cadmium	0.0003	0.0010	Cadmium	0.015	1.6%	Cadmium	0.2	104%
Lead	0.002	0.008	Lead	0.133	2.8%	Lead	0.2	95%
Mercury	0.002	0.005	Mercury	0.049	3.1%	Mercury	0.2	111%
Cobalt	0.0004	0.0014	Cobalt	0.771	2.7%	Cobalt	0.2	93%
Vanadium	0.001	0.003	Vanadium	0.395	4.6%	Vanadium	0.2	100%
Nickel	0.023	0.076	Nickel	0.636	1.8%	Nickel	0.2	111%
Silver	0.0002	0.0008	Silver	0.005	11.6%	Silver	0.2	100%
Selenium	0.008	0.028	Selenium	0.040	3.1%	Selenium*	0.2	96%
Lithium	0.002	0.006	Lithium	0.101	2.8%	Lithium	0.2	95%
Antimony	0.0006	0.002	Antimony	0.011	3.4%	Antimony	0.2	97%
Chromium	0.040	0.132	Chromium	0.249	2.0%	Chromium	0.2	88%
Barium	0.013	0.044	Barium	12.7	2.0%	Barium**	0.2	NA
Molybdenum	0.0004	0.0013	Molybdenum	0.403	1.2%	Molybdenum	0.2	101%
Copper	0.043	0.142	Copper	17.9	1.7%	Copper**	2	83%
Tin	0.0004	0.001	Tin	0.002	1.4%	Tin	0.2	99%
Beryllium	0.0003	0.001	Beryllium	0.004	0.5%	Beryllium	0.2	99%
Manganese	0.024	0.080	Manganese	91.5	1.3%	Manganese	20	92%
Uranium	0.00007	0.0002	Uranium	0.007	1.6%	Uranium	0.2	101%
Zinc	0.316	1.05	Zinc	56.4	1.6%	Zinc**	20	89%

Tables 3-5. Method Validation Data: LOQ, Repeatability, and Spike Recoveries

* = half mass corrected
** = spike concentration too low

8 Summary

- ▶ Robust digestion system is able to digest any cannabis and related matrix we have tested to date.
- ▶ Digestates have a heavy matrix and NexION's AMS mitigates these matrix effects
- ▶ Cannabis samples analyzed had negligible levels of elements that would cause doubly charged interferences → however correction is possible and simple to use
- ▶ Method was successfully validated based on AOAC SMPR/USP <233>