Analytical Data Confidence is Highest with Commercially Prepared CRM Mixtures

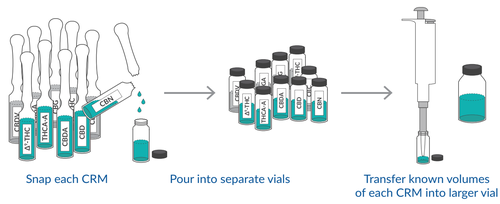
Michael Miller, Samantha Goodwin, and Roxanne Franckowski

Cayman Chemical, Ann Arbor, MI

Introduction

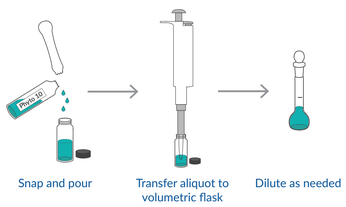
- Standardizing quantitative analysis in the *Cannabis* industry requires laboratories to operate under ISO/IEC 17025 accreditations, necessitating the need for certified reference materials (CRMs).
- Historically, single analyte CRMs have been used for quality control testing due to the lack of multi-component CRM mixtures.
- Cayman designed the Phytocannabinoid Mixture 10 (CRM) to confirm the ten most prevalent phytocannabinoids found in *Cannabis* samples:
  - Cannabidivarin (CBDV)
  - Cannabidiolic Acid (CBDA)
  - Cannabigerolic Acid (CBGA)
  - Cannabigerol (CBG)
  - Cannabidiol (CBD)
  - Cannabinol (CBN)
  - Tetrahydrocannabinolic Acid A (THCA-A)
  - Δ^9-Tetrahydrocannabinol (Δ^9-THC)
  - Δ^8-Tetrahydrocannabinol (Δ^8-THC)
  - (±)-Cannabichromene (CBC)
- A pre-made CRM mixture bypasses all unnecessary steps required in the preparation of a stock mixture from individual CRMs.
- We compared these two methods to generate a standard for the quantitation of ten prevalent phytocannabinoids against a calibration curve.

Method A:
Stock Solution from Individual CRMs



1. Ten individual component CRMs, at a concentration of 1 mg/ml, were used to create a final stock solution to replicate methods practiced in industry.
2. Due to the restrictive size of the ampule opening, the solutions from each were transferred to individual larger vials.
3. 1 ml of each of the ten solutions was pipetted into a single scintillation vial, achieving a concentration of 100 µg/ml.
4. A subsequent dilution was performed for analysis at 1 µg/ml.

Method B:
Stock Solution from CRM Mixture



1. Solution from a single ampule of the pre-made CRM mixture was transferred to a larger vial.
2. A single dilution was made, achieving a concentration of 100 µg/ml.
3. A subsequent dilution was performed for analysis at 1 µg/ml.

Pre-made **CRM mixture** provides **superior reproducibility**, **accuracy**, and **precision** compared to a mixture made from single component CRMs

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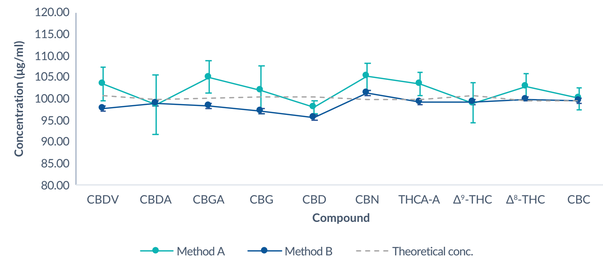
Results

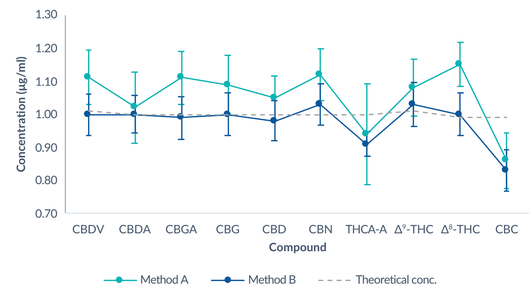
Method Comparison

All solutions were analyzed using the Cannabis Analyzer for Potency HPLC model LC-2030C Plus from Shimadzu Scientific Instruments. A single injection of each solution (n=8) was performed. The experimental concentration for each sample was derived from the generated calibration curve. These concentrations were averaged across all injections for each component, plotted with their respective standard deviations, and compared against their theoretical concentrations.

100 µg/ml Method Comparison



1 µg/ml Method Comparison



Accuracy, Relative Error, and Precision

The deviations observed in Method A (mixture made from individual CRMs) were greater than those observed with Method B (pre-made CRM mixture). Although Method A had acceptable accuracy, a large difference in precision between the two methods is evident (±10% relative error is an acceptable criterion in analytical testing).

100 µg/ml Method Comparison

100 µg/ml	Accuracy (%)		Relative Error (%)		Precision (CV, %)	
Compound	Method A	Method B	Method A	Method B	Method A	Method B
CBDV	102.77	97.14	2.77	-2.86	3.72	0.60
CBDA	98.71	99.10	-1.29	-0.90	7.14	0.63
CBGA	104.94	98.24	4.94	-1.76	3.58	0.66
CBG	101.42	96.55	1.42	-3.45	5.44	0.64
CBD	97.72	95.32	-2.28	-4.68	1.49	0.61
CBN	105.31	101.43	5.31	1.43	2.99	0.62
THCA-A	103.45	99.21	3.45	-0.79	2.53	0.64
Δ^9-THC	98.24	98.40	-1.76	-1.60	4.80	0.61
Δ^8-THC	103.40	100.46	3.40	0.46	2.85	0.58
CBC	100.52	100.02	0.52	0.02	2.64	0.64

1 µg/ml Method Comparison

1 µg/ml	Accuracy (%)		Relative Error (%)		Precision (CV, %)	
Compound	Method A	Method B	Method A	Method B	Method A	Method B
CBDV	1.11	1.00	10.17	-1.04	7.40	6.25
CBDA	1.02	1.00	1.66	0.26	10.72	5.82
CBGA	1.11	0.99	10.94	-0.94	7.09	6.48
CBG	1.09	1.00	8.84	-0.09	8.06	6.54
CBD	1.05	0.98	4.68	-2.24	6.27	6.19
CBN	1.12	1.03	11.80	2.73	7.00	6.18
THCA-A	0.94	0.91	-5.68	-9.33	16.06	4.04
Δ^9-THC	1.08	1.03	7.12	1.61	8.05	6.52
Δ^8-THC	1.15	1.00	16.39	1.46	5.85	6.49
CBC	0.86	0.83	-12.90	-16.04	9.79	7.56

Conclusions

- Although making a mixture from individual components (Method A) generates results within tolerable limits, this data is not as accurate as data generated from a pre-made solution (Method B).
- CRMs provide a metrologically traceable standard that is reliable and accurate but can be compromised when mixing multiple standards together to create a mixture.
- Using a multi-component CRM solution, such as the Phytocannabinoid Mixture 10, will not only save time and cost—it will provide more reliable data than attempting to create a mixture from individual components.