CONSIDERATIONS WHEN HANDLING DEA-EXEMPT CANNABINOID STANDARD PREPARATIONS USED FOR REFERENCE DETERMINATION

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INTRODUCTION

Several studies have been published regarding inaccuracies observed for potency labeling of infused cannabinoid products. True cannabinoid assessment of these products is highly dependent upon numerous factors such as batch sampling, product chemical stability, and the quality of the analytical methodology used for potency determination. Cannabis derived extracts are classified by the Controlled Substance Act (CSA) as Schedule I substances, and the distribution and monitored by the Drug Enforcement Administration (DEA). Consequently, product testing laboratories rely heavily upon certified DEA-exempt ampuled cannabinoid reference standard formulations prepared by manufacturers with DEA sanctioned exemptions to eliminate the regulatory burden. Since many cannabinoids are not soluble in water, cannabinoid reference standard formulations are typically solvent based, which poses a unique set of handling considerations compared to aqueous solutions.

This poster will investigate three potential sources of error when handling cannabinoid (CBD) and Δ9-THC-isolate cannabidiol (Δ9 THC) (1.0 mg/mL) reference standard formulations and consider how these solutions can be used safely.

METHODS

A Waters ACQUITY UPLC-RHD Class System (Milford, MA USA) was used to perform the study. It was equipped with a Quadrupole Servant Manager (QSM), temperature controlled Sample Manager (FTN), MS Detector (QDa) and UV array detector (PDA). Data was acquired and processed via Waters Empower 3TM Chromatography Data Software (Build 3471, FR2).

Certified DEA-exempt ampuled reference standard formulations of CBD and Δ9 THC in methanol (1.0 mg/mL) were purchased from three certified reference standard manufacturers. CBD and Δ9 THC isolate starting materials were purchased via a registered DEA controlled substance license and dissolved in methanol upon receipt. All sample solutions quantified using this standard after 10 hours would be approximately 10 mg/mL with account for the purity reported in the CoA. Serial dilutions prepared 1.0, 0.4 mg/mL and a linear curve prepared by injecting each solution.

RESULTS AND DISCUSSION

Chromatographic purity determination is dependent upon the ability of a validated method to resolve the analyte from close eluting impurities at a specific wavelength. When the chromatographic profiles of the CBD and Δ9 THC isolate starting materials and the ampuled reference standards were compared, respective impurities were not identified. Although the chromatographic selectivity, it is possible that the reference standard concentration value determined by the cannabinoid testing laboratory may not match the concentration value reported in the respective standard reference CoA.

OBJECTIVE 2: Compare the CoA concentration of the ampuled cannabinoid reference standards to the concentration obtained in the cannabis testing lab.

CBD and Δ9 THC-isolate starting materials were dissolved in methanol at approximately 10 mg/mL, with account for the purity reported in the CoA. Serial dilutions prepared 1.0, 0.4 mg/mL and a linear curve prepared by injecting each solution.

The concentrations (mg/mL) of three manufacturer prepared, certified DEA-exempt, ampuled formulations of CBD and Δ9 THC reference standards were calculated using the linear regression (y=m*x+b) of the curve generated by the respective isolate starting material. The corresponding standard reference solutions were overlaid to compare the chromatographic impurity profile.

OBJECTIVE 3: Determine the stability of the solvent based reference standard solutions after injection.

Ampuled CBD reference standard solution was aliquoted into two, LCMS certified, ACQUITY 12x32 mm autosampler vials and sealed with screw cap septa. The vials were then secured in an indigenous, general laboratories, and the vetivel vial concentration for the same concentration standard formulation for both vials was calculated. The CBD-concentration observed in the first vial was approximately 10% lower than the previously reported concentration standard. The respective vials were then kept in an environment with a temperature of 20°C under the same humidity for 10 hours and the concentration standard concentration was determined. The concentration standard concentration was stable.

In contrast, a hole was observed in the inexpensive, basic silicone septum after one injection. The hole exposed the CBD reference standard solution inside the the air displacement pipette. Rapid evaporation of liquid solvent would result in an increased in the CBD concentration in the vial. Ten hours after the injection, the CBD concentration in the vial by approximately 15% in the vial. Additionally, the exposed air displacement pipette was not protected from the exposure to the air.

RESULTS AND DISCUSSION

The vial with the self-sealing PTFE/silicone septum appeared to be tightly sealed by visual inspection, and the CBD concentration inside the vial, remained stable after repeated injections over several days. Therefore, the vial is not harmful to the inside the vial, remained stable after repeated injections over several days. Therefore, the vial is not harmful to the inside the vial, remained stable after repeated injections over several days.

Additionally, it is important to note that many cannabis testing laboratories do not have an isotope labeled internal standard to confirm the potency of any cannabinoids in the vial with the self-sealing PTFE/silicone septum. As an alternative, an evaluation of incoming reference standards could potentially be made in the future with the self-sealing PTFE/silicone septum.

CONCLUSIONS

The most commonly employed laboratory pipette, the air displacement pipette, is not recommended for pipetting solvent based cannabinoid formulations. Positive displacement and glass pipettes should be used for accurate pipetting of these formulations.

To ensure accuracy, cannabis testing laboratories should verify the contamination of incoming reference standard solutions using the same chromatographic method employed for potency testing of samples.

Cannaboid solvent based formulations should be kept in tightly sealed containers with minimal exposure to the atmosphere. Care must be taken to limit exposure of these solutions to air when performing pipetting, as well as during storage.

REFERENCES