THE USE OF ORTHOGONAL METHODS TO MONITOR THE MAJOR DEGRADATION PRODUCTS OF CANNABIDIOL (CBD)

Catharine Layton, Jacquelyn Runco and Andrew Aubin, Waters Corporation, Milford, MA USA

INTRODUCTION

The debate surrounding the use of cannabis for medicinal purposes has been a hot topic for several years. Although there are at least 83 active substances identified in cannabis, most people associate the bio-chemical with the psychoactive cannabinoid tetrahydrocannabinol (THC). Recent attention however, is being given to the non-psychoactive cannabinoid cannabidiol (CBD), as it is non-psychoactive and has been shown to be effective in acting as a neuroprotectant.

Some CBD preparations are reported as dietary supplements and are sold as-is, claiming to provide benefits from the cannabinoids and terpenes. However, for these manufacturers of these preparations, it is important to monitor for the presence of contaminants, especially by-products of THC degradation. This is of major importance for ensuring health and safety when using unregulated degradation products (either through degradation products resulting in the delivery of a different CBD dose than expected).

Extracts prepared from cannabis products can pose a significant risk to public health. For manufacturers of these preparations, it is important to monitor for the presence of contaminants, especially by-products of THC degradation. This is of major importance for ensuring health and safety when using unregulated degradation products. As more research becomes available regarding potency of the various THC isomeric forms, as well as the less potent isomeric form, (+) Δ9-THC, critical review of the chemical and structural verification of important degradation products will become essential for the documentation of product purity and stability.

METHODS

Cannabinoid reference standards were fully separated within 3.5 minutes by UPLC normal-phase, as shown in the Figure 1 normalized overlay. Convergence chromatography was used to distinguish the (+) Δ9-THC standard by convergence chromatography. Reversed-phase separation was used to identify degradation products of cannabidiol (CBD) as (±) Δ8-THC and (±) Δ9-THC. High figure shows the convergence separation of cannabinoid reference standards (±) Δ8-THC, Δ9-THC, (±) Δ9-THC and (±) THC. A high figure depicts the mass spectra of the degradation products at 9 and 6 minutes were tentatively identified as (±)Δ8-THC and (±)Δ9-THC.

RESULTS

Convergence chromatography can be applied to monitor the chemical purity of the degradation products identified as (±) Δ8-THC and (±) Δ9-THC. The acid degradation product eluting at approximately 2.4 minutes, was identified as an unknown with a m/z 320.180, different from CBG (m/z 317.124) which shows the same retention time. The masses of the acid degradation products at 9 and 6 minutes (Figure 2) show the same masses at 315 Da and comparable UV spectra. When compared to the reference standards, the degradation products at 9 and 6 minutes were tentatively identified as (±) Δ8-THC and (±) Δ9-THC.

DISCUSSION

Convergence chromatography was used to distinguish the (+) Δ9-THC standard by convergence chromatography. Reversed-phase separation was used to identify degradation products of cannabidiol (CBD) as (±) Δ8-THC and (±) Δ9-THC. High figure shows the convergence separation of cannabinoid reference standards (±) Δ8-THC, Δ9-THC, (±) Δ9-THC and (±) THC. A high figure depicts the mass spectra of the degradation products at 9 and 6 minutes were tentatively identified as (±)Δ8-THC and (±)Δ9-THC.

Information regarding the stereochemistry of the degradation products identified as (±) Δ8-THC and (±) Δ9-THC was not determined by reversed-phase given that the technique does not typically distinguish between stereo-enantiomeric forms. The two degradation products were collected by the Waters Fraction Manager (Figure 3) and analyzed by UPLC. The samples were analyzed for the presence of the stereo-chemical composition by convergence chromatography.

In Figure 6, the UPLC chromatogram shows that the acid degradation peak collected as Fraction 1 eluted the latest at 21.0 min. The UV spectra of the chromatogram were compared to the acid degradation peak collected as Fraction 1 matches the retention time, mass, and UV spectra of the two degradation products identified as (±) Δ8-THC and (±) Δ9-THC. Fraction 2 was confirmed using Waters Fraction Manager (Waters Fraction Manager Waters Technology 2014). Figure 6 shows the chemical purity of the degradation products identified as (±) Δ8-THC and (±) Δ9-THC. As a result, this method could potentially be used as a fast and efficient way of monitoring an unknown (±) Δ8-THC peak. Figure 7 shows the chemical purity of the degradation products identified as (±) Δ8-THC and (±) Δ9-THC. As a result, this method could potentially be used as a fast and efficient way of monitoring an unknown (±) Δ8-THC peak.