THC Remediation via Reversed-phase Flash Chromatography

Overview

The hemp-derived CBD market is one of the fastest growing in the world. According to Grandviewresearch.com, the global CBD market size was $4.6 billion in 2018 and projected to grow 22%/year (CAGR) through 2025[1]. With states, provinces, and countries now creating regulations around allowable THC levels (typically <0.3%), CBD producers must efficiently remove THC from their hemp extracts in order to legally market their products for medicinal and therapeutic application.

While there are several methods to remediate THC, for those wanting a "spectrum" product, not just CBD isolate, flash chromatography has become the technique of choice due to its relative simplicity, efficacy, and scalability. What is required is ethanol (or methanol), a column packed with a hydrophobic sorbent (typically C18 bonded silica), a pressure source for the solvent (pump or pressurized solvent reservoir), and a UV detector set to a wavelength between 270 nm and 280 nm.

For THC remediation, a simple step gradient is most common because it exploits the major hydrophobicity (polarity) differences between THC and CBD, Figure 1. While CBD contains two phenolic (-OH) groups, THC contains only one (-OH) plus an ether (-O-) making it less polar (more hydrophobic) than CBD. This polarity difference allows CBD to elute from the column faster than THC. With THC retained on the column longer, when CBD elutes it is typically devoid of THC.

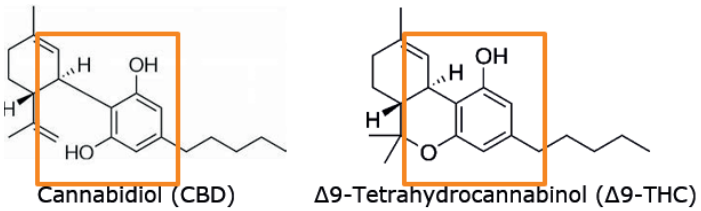

Figure 1. CBD and THC chemical structures. CBD is less hydrophobic due to its two -OH groups. THC has one -OH group and an ether (-O-) making it retain longer on the C18 column and allowing CBD to elute first with minimal THC contamination.

The step gradient most commonly employed is simply...

Step 1: 70% ethanol/30% water or 80% methanol/20% water

Step 2: 100% ethanol

Distillate sample preparation is usually 1-part distillate to 1-part ethanol (or methanol). Using these sample preparation and gradient methods with sample loadings of 3% to 5% (% of the column media mass), maximum THC remediation occurs.

Sample load percentages are strongly influenced by the THC content in the distillate so having an accurate analysis prior to flash chromatography can help guide loading decisions. The higher the THC content, the lower the column loading capacity.

Materials and Methods

Flash System:	Biotage® Selekt
Flash Column:	Biotage® Sfär C18 12 gram
Solvent A:	Water
Solvent B:	Methanol
Flow Rate:	30 mL/min.
Equilibration:	80% B for 2 CV @ 100 mL/min.
Step 1:	80% methanol/20% water for 4 column volumes (CV)
Step 2:	100% ethanol for 4 CV
Detection:	Black - PDA-UV 200–400 nm Red – 207 nm Blue – 274 nm



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Results and Discussion

As an example, a hemp extract distillate with 12% THC was purified using the methanol/water method with a 3% load (35 mg), Figure 2.

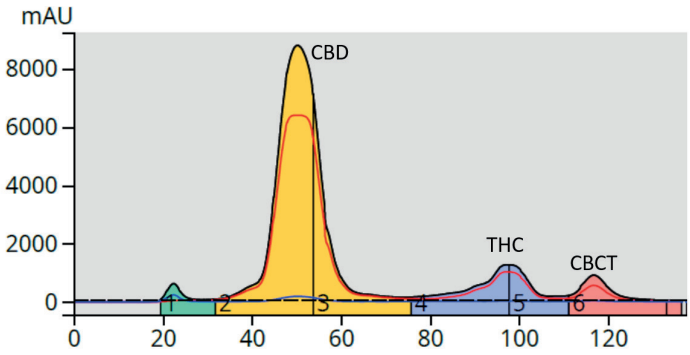

Figure 2. Hemp distillate (12% THC) purification using a 3% load (35 mg) on a 12-gram Biotage® Sfär C18 column and an 80% to 100% methanol step gradient. CBD (yellow peak) is fully resolved from both THC (blue peak), the injection solvent peak (green), and the minor cannabinoid cannabicitran (CBCT).

Using this methodology all THC was remediated and the CBD purified, Figure 3.

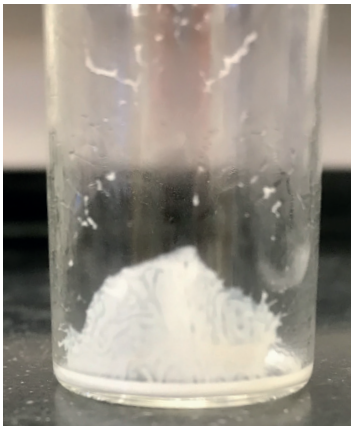

Figure 3.
Purified CBD crystals from Fraction 2.

Conclusion

While a milligram-scale purification is small, these simple methods are robust and lend themselves to scale-up techniques to columns as much as 4000 times larger (for example Biotage® Flash 400L cartridges). Distillates with lower THC content (<3%) have been successfully purified using these flash chromatography methods with sample loadings of as much as 10% in some cases.

References

1. Grandviewresearch.com

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