

CPC 250: Purification of Cannabidiol from *Cannabis sativa*

TECHNICAL NOTE TN206

GILSON APPLICATIONS LABORATORY

INTRODUCTION

Cannabidiol (CBD, refer to Figure 1) is a major component of the *Cannabis sativa* plant. CBD is of special interest because it is non-psychoactive and studies suggest that it has therapeutic medicinal properties for the treatment of conditions including pain, inflammation, epilepsy, and cancer.^{1,2} Recent changes in the legal status of *Cannabis* compounds for medicinal use, as well as the decriminalization of marijuana in some locations, has led to increased interest in purification, formulation, and detection of CBD. Although CBD is still classified as a Schedule I drug in the United States, the U.S. Food and Drug Administration has authorized clinical trials to evaluate the use of CBD to treat children with rare forms of epilepsy.³

Cannabinoids are concentrated in a sticky resin found within the glandular trichomes, hairlike structures on the surface of the plant (Figure 2). Although most cannabinoids are nearly insoluble in water, they can typically be dissolved in oils, alcohols, and other non-polar solvents. To ensure consumer safety it is critical to develop standardized CBD products that are free of tetrahydrocannabinol (THC) and other contaminants. Gilson has developed a rapid and reproducible method for large-scale purification of CBD using centrifugal partition chromatography (CPC) (Figure 3). The method can be adapted from milligram to multi-kilogram scale, requires little solvent, and recovers close to 100% of the CBD from a complex crude extract.

MATERIALS AND METHODS

Purification of CBD

A Gilson CPC 250 column was run with an elution rate of 70 mL/min, an extrusion flow rate of 70 mL/min, and a rotation speed of 3000 rpm. The CPC column was controlled by a PLC 2250 Purification System (for preparative liquid chromatography) equipped with a 250 mL/min quaternary gradient pump, UV/VIS detector, fraction collector, and Gilson Glider control software. Analytical HPLC was performed on a Hitachi LaChrom Elite® HPLC System (VWR) equipped with a photodiode array detector (PDA) (200–800 nm). Crude extract was prepared from dried *Cannabis sativa* L. plant material and was filtered before being subjected to CPC. All organic solvents were analytical or high performance liquid chromatography (HPLC) reagent grade.

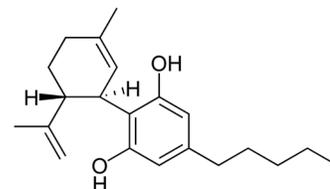


Figure 1
Chemical Structure of CBD



Figure 2
Closeup View of Glandular Trichomes on the Surface of a *Cannabis* Plant



Figure 3
CPC 250 with PLC 2250 Purification System

RESULTS AND DISCUSSION

In this study, 5 g of crude extract of *C. sativa* flowers were subjected to CPC. Using this one-step method resulted in clean separation of CBD from THC and other compounds (Figure 4). 205 mg of CBD was purified from 5 g of crude extract, and the final product had a purity of over 99% as shown by HPLC analysis. For each 5 g sample, 1 L of solvent was consumed for every 10 min of separation.

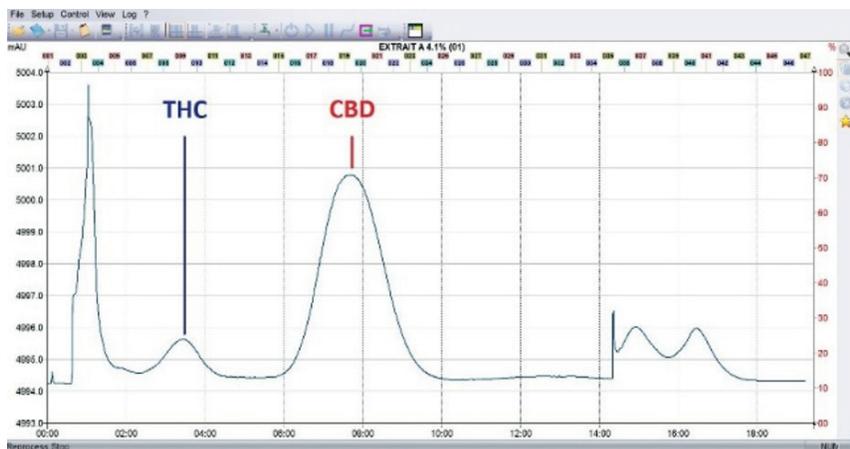


Figure 4
Chromatograph of CBD and THC purified using CPC.

CONCLUSIONS

CPC technology employs a silica-free liquid-liquid chromatography (LLC) column and can be carried out in batch or continuous mode. CPC can be used to purify CBD from crude extracts of *Cannabis* in just one step. Purification parameters can be adjusted according to which cannabinoids are targeted or the desired purity level to achieve THC-free extracts, pure cannabinoids, pharmaceutical-grade products, or standard molecules for use as reference materials or for clinical evaluation. The methodology is adaptable from laboratory to industrial scale. Because the method does not use silica resin there is no irreversible adsorption of the sample to the matrix and therefore no sample loss.

REFERENCES

1. Russo, E.B. (2017) Cannabidiol claims and misconceptions. *Trends Pharm. Sci.* <http://dx.doi.org/10.1016/j.tips.2016.12.004>.
2. Zhornitsky, S. and Potvin, S. (2012) Cannabidiol in humans: the quest for therapeutic targets. *Pharmaceuticals*. 5(5): 529 – 552. <http://dx.doi.org/10.3390/ph5050529>.
3. Throckmorton, D.C., Deputy Director for Regulatory Programs, Food and Drug Administration. Department of Health and Human Services. “Researching the Potential Medical Benefits and Risks of Marijuana” July 13, 2016. Statement to United States Cong. Senate, Committee on the Judiciary, Subcommittee on Crime and Terrorism. <http://www.fda.gov/NewsEvents/Testimony/ucm511057.htm>.

Trademarks

All product and company names are trademarks™ or registered® trademarks of their respective holders. Use of the trademark(s) in this document does not imply any affiliation with or endorsements by the trademark holder(s).

Notice

This application note has been produced and edited using information that was available at the time of publication. This application note is subject to revision without prior notice.