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Determination of Cannabinoid and Terpene Profiles in Cannabis Oils by Mid-Infrared Spectroscopy: 1. Cannabinoids

Introduction

Cannabis oils are made by treating parts of the marijuana plant with a solvent that concentrates the cannabinoids, terpenes, and other compounds. Example of the solvents used include butane, ethanol, and supercritical carbon dioxide. After evaporation of the solvent the resulting product is frequently a brown viscous oil. These oils are sold directly to consumers, used in vape pens, and in infused products (edibles).

To insure patients receive the proper dosage of their cannabis medicine, support label claims, and assure product quality cannabis oils should be tested for their cannabinoid and terpene profiles prior to sale. A cannabinoid profile should include not only a traditional measurement of potency such as THCA, THC, CBDA, and CBD but also trace cannabinoids such as CBGA, CBG, CBN, CBC (cannabichromene), and THCV (tetrahydrocannabivarin). Similarly, a terpene profile should contain quantitative information on a number of terpenes including myrcene, beta-caryophyllene, alpha-humulene, limonene, linalool, and alpha-pinene amongst others. These profiles not only give potency and label claims information but are detailed enough to give a chemical fingerprint of a product, sometimes called a chemotype.

The cannabinoid content of cannabis oils is typically tested after manufacture by a cannabis analysis lab using high pressure liquid chromatography (HPLC). While HPLC can be accurate, to obtain results involves significant sample preparation, copious amounts of solvent, sacrifices substantial amounts of valuable sample, requires skilled personnel, and necessitates use of expensive equipment housed in a lab. This prevents most extractors from performing in-house testing, making it difficult for them to optimize their processes, control product quality, and maximize profits by having a complete understanding of their product and how it is made. Additionally, by only testing one aliquot of each batch of oil by HPLC, the results obtained are not representative and do not give a true picture of the potency and chemical composition of a cannabis oil. It has been recently discovered that cannabis oil potency degrades with a half-life of 7.9 months [1]. This means cannabis oils need to be tested frequently throughout their lifetime to insure patients are getting the correct dosage of their medicine. Doing the needed amount of testing with an HPLC would be slow and expensive.

We have invented a novel mid-infrared spectrometer for general quantitative chemical analyses. The instrument is small and lightweight and can be used anywhere, features push button operation so anyone can use it, requires no sample preparation so it is fast and easy, and sacrifices little sample. This instrument was used to discover that cannabis oil potency has a half-life [1]. This article focuses on the use of this instrument to determine cannabinoid profiles in cannabis oils and how that information may be applied in the cannabis industry. A future article will discuss the instruments use to determine terpene profiles in cannabis oils.

Experimental

Samples of cannabis oils of varying compositions, manufactured by POP Naturals of Oregon, were purchased from Kind Peoples Dispensary, Soquel CA. Cannabinoid profiles were measured using HPLC by CW Analytical of Oakland CA. Mid-infrared spectra of each sample were measured in triplicate using the BSS 2000 Cannabis Analyzer from Big Sur Scientific, Capitola CA (www.bigsurscientific.com). The BSS 2000 is a small, lightweight, mid-infrared spectrometer capable of accurately quantifying cannabinoids in cannabis buds, oils, and solids such as shatter and wax. To analyze a cannabis oil a few drops of sample are placed on the BSS 2000's sampling window as seen in Figure 1.

Figure 1 A photo of the BSS 2000 Cannabis Analyzer with a sample of cannabis oil resting on its sampling window.

Spectra were measured in the mid-infrared (MIR) from 1250 to 952 cm^{-1} at an instrumental resolution of 12 cm^{-1}. Analysis time is about 2 minutes per sample. The mid-infrared was chosen as opposed to the near-infrared (NIR) because MIR spectra are 10x to 100x more sensitive than NIR spectra, and because many more chemical bonds can be seen in the MIR as opposed to the NIR [2].

Mid-infrared spectra and cannabinoid weight percent values of the same samples were used to construct a predictive multivariate mathematical model using the Partial Least Squares (PLS) algorithm [2]. The model was built using Big Sur Scientific's Model Builder software. Methods were validated by challenging the model with a validation set of samples of known cannabinoid composition that it had not seen before. The difference between the known concentrations as measured by HPLC and as predicted by the BSS 2000 were used to calculate the correlation coefficients and accuracies (standard errors of prediction) listed below. Models for the cannabinoids THCA, THC, CBDA, CBD, CBGA, CBG, CBN, CBC, and THCV were built. A validation set of 7 samples was used.

Results and Discussion

A measure of the quality of a spectroscopic model is the linearity of a plot of the known values versus the predicted values, in this case weight percent cannabinoid as measured by HPLC versus the predicted values from the BSS 2000 Cannabis Analyzer. In a perfect world the two techniques would give the same values for the same samples and the resultant line would have what is called a correlation coefficient, R^2, of 1. R^2 is a measure of model quality and the amount of variance spanned by a model [3], and the closer to 1 the better the model. For spectroscopic calibrations, R^2 values greater than 0.99 are considered excellent [3]. Figure 2 shows a plot of cannabis oil THCA weight percents as measured by HPLC versus as predicted for the same samples by the BSS 2000.

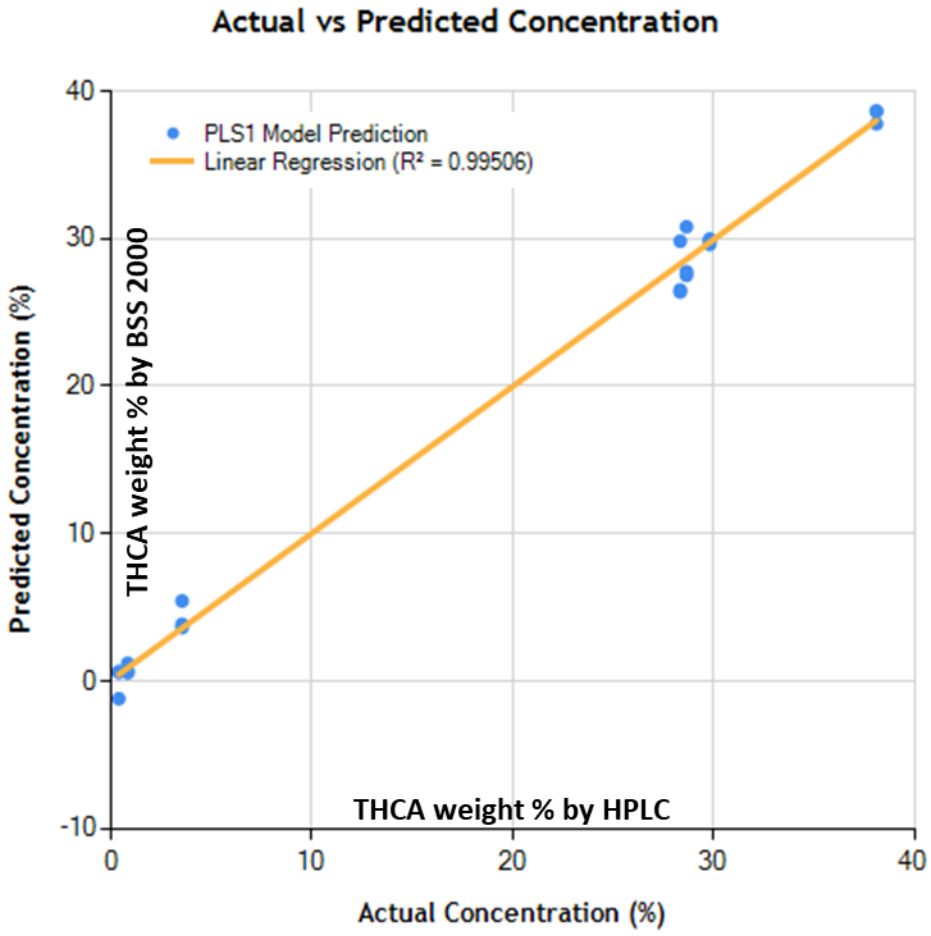

Figure 2 Plot of weight percent total THCA in cannabis oils as determined by HPLC versus as predicted for the same samples by the BSS 2000 Cannabis Analyzer. Note the correlation coefficient of 0.995.

Note that the correlation coefficient for the plot is 0.995, indicating excellent agreement between the HPLC and BSS 2000 results.

The best way to validate a spectroscopic model [3] is to calculate what is called the Standard Error of Prediction (SEP). This metric is determined by taking a set of validation samples, which have a known concentration but were not used in the model, measuring the spectra of these samples using the BSS 2000, predicting their cannabinoid weight percents using the predictive chemometric models previously generated, and then comparing the actual and predicted results. Essentially, the SEP is the standard deviation between the HPLC and MIR results for the validation set. The SEP is the best metric of calibration quality because it calculates how well a calibration does on samples it has never seen before, exactly what a calibration does in actual use.

Calibrations for 9 different cannabinoids were constructed using HPLC results and spectra measured with the BSS 2000. These model's R^2 values and accuracies measured as an SEP are seen in Table 1.

Table 1 Correlation Coefficients and Accuracies Measured as Standard Error of Predictions for 9 Cannabinoids in Cannabis Oils Determined with the BSS 2000 Cannabis Analyzer.

Analyte	R^2	Accuracy, Wt. %
THCA	0.99	±1.1
THC	0.99	±1.6
CBDA	0.99	±0.9
CBD	0.99	±0.9
CBGA	0.94	±0.2
CBG	0.93	±0.1
CBN	0.98	±0.1
CBC	0.99	±0.1
THCV	0.99	±0.1

Note that almost all the correlation coefficients are equal to or close to 0.99, and that all the accuracies are equal to or better than ±1.6 weight percent. These results indicate that the BSS 2000 Cannabis Analyzer can quantitate 9 cannabinoids in cannabis oils accurately, representing not only a potency test but a true cannabinoid profile.

Given the speed, ease of use, and portability of the BSS 2000, this means extractors can now place this device next to their extractors and test product while it is being made and immediately after manufacture to understand their processes better, optimize extraction conditions and potency, reduce operating costs, and thus increase profitability. Dispensaries could use this instrument to test incoming product for the accuracy of label

claims, monitor stock to make sure it has not degraded since we now know cannabis oil potency has a half-life [1], and perform point of sale testing for customers to insure they are getting the correct dosage of their cannabis medicine. Lastly, the detailed cannabinoid profile available gives a true chemotype of cannabis oils, allowing fingerprinting, tracking, and a more fundamental understanding of the chemical composition of these important materials.

Conclusions

We have shown that the BSS 2000 Cannabis analyzer from Big Sur Scientific, which uses mid-infrared spectroscopy, can accurately quantitate THCA, THC, CBDA, CBD, CBGA, CBG, CBN, CBC, and THCV in cannabis oils. Applications of this discovery in the cannabis industry were discussed.

References

[1] Brian C. Smith, *Determination of Cannabis Oil Potency Degradation Rate and Mechanism by Infrared Spectroscopy*, Terpenes and Testing Magazine, Nov.-Dec. 2017, pg. 48.
[2] Brian C. Smith, *Fundamentals of Fourier Transform Infrared Spectroscopy*, CRC Press, Boca Raton, 2011.
[3] Brian C. Smith, *Quantitative Spectroscopy: Theory and Practice*, Elsevier, New York, 2002.