

Quick and Real-Time Potency Determination of Cannabinoids Using FTIR Spectroscopy

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Introduction

Cannabis products that are currently on the market consist of either dry material such as flower buds, concentrates such as shatter, budder, waxes, oils, extracts, and distillates, or infused products such as food and candies. The main active ingredients in these products are chemical compounds called cannabinoids, which provide either a medicinal or recreational effect to consumers. Of the many different cannabinoids that have been isolated from cannabis plants, tetrahydrocannabinol (THC), tetrahydrocannabinolic acid (THCA), cannabidiol (CBD), and cannabidiolic acid (CBDA) compounds are generally those of greatest interest and the most prevalent found in commercial cannabis plants.

The cannabinoid profile of most commercial cannabis cultivars is either enriched with THCA content or CBDA content. THCA is the acidic form of THC. THCA gets decarboxylated as the samples gets dried or exposed to heat, converting THCA to THC (the psychoactive component). Therefore, to measure the real potency, both THCA and THC should be considered. The total THC content refers to the addition of THCA and THC potency value, with the correction factor of 0.877 for THCA value before adding to the THC value. The correction factor is due to the molecular weight difference between THC and THCA.

Because different product forms of cannabis have different potency levels, potency determination is one of the more important analytical requirements, so that the proper dosage in products can be achieved, and the proper dose can be recommended to the consumer. The Agilent Cary 630 FTIR (Fourier transform infrared spectroscopy) provides a fast, easy, accurate, and economical system to measure laboratory-grade potency measurements of cannabis products. Some of the products that have been tested using the Cary 630 FTIR for potency consist of concentrates (shatter, budder, waxes) and distillates with THC potency values as high as 93 %.

FTIR spectroscopy has been used to analyze complex spectra and matrices, a good definition of cannabinoids, using chemometric methodology. Unique chemical signatures from each compound are then used to develop the multivariate calibration model to calculate the potency value.

Major Benefits of FTIR Analysis

- Real-time potency value (for example, total THC, THC, THCA) measurements in seconds
- More sample measurement in less time
- Nondestructive sample analysis
- No consumables required
- Portable and easy-to-use
- Small laboratory footprint
- Method-driven software that guides the user in every step of the analysis

Instrumentation

The Agilent Cary 630 (Figure 1), a multipurpose high-performance compact FTIR spectrometer, was used for the cannabis concentrate and distillate samples measurement. The Cary 630 provides major advantages for routine measurements due to its ease-of-use, small footprint, unique dedicated sampling accessories, rugged design, and the implementation of intuitive software. Since different sampling accessories fit the Cary 630 spectrometer body easily, and can readily be interchanged without any alignment necessary for its use, different cannabis sample types (solids, liquids, and gels) can be measured in time-efficient protocols.

The attenuated total reflectance (ATR) sampling technique with diamond as the internal reflection element is well suited for the analysis of cannabis samples such as extracts, concentrates, and distillates, as it requires no sample preparation. Simply by placing the sample on the diamond



Figure 1. Agilent Cary 630 with a 1-bounce diamond ATR accessory.

crystal sensor and ensuring good contact, a good quality spectrum is obtained. A diamond ATR sensor requires a very small amount of sample (on the order of microliters) for analysis, and is nondestructive, saving sample for future use.

Materials and Methods

Extracted samples such as concentrates and distillates obtained from either hydrocarbon or carbon dioxide extraction of cannabis plants were measured using a Cary 630 FTIR and a 1-bounce diamond ATR sampling accessory. The concentrate samples were products such as oils, waxes, budder, shatter, and sugars that were chemically or physically extracted from a cannabis plant, and had a higher concentration of cannabinoids than the starting material. The distillates are high value concentrate samples that have gone through further refining and purification through distillation equipment that removes terpenes, lipids, impurities, and solvents.

Spectra of concentrates and distillates were recorded without any sample preparation, using a Cary 630 spectrometer in the spectral range of 4,000 to 650 cm^{-1} . The diamond ATR sensor was cleaned with acetone or ethyl alcohol before each sample measurement. Each spectrum was the co-addition of 128 scans at 8 cm^{-1} resolution, yielding a total measurement time of 30 seconds.

MicroLab software was used to collect the data and create a method for future unknown sample analysis. The partial least squares (PLS) chemometric algorithm was used to build the calibration model that correlates the reference HPLC or GC measured potency value with the FTIR-measured

spectral data. During PLS model building, the spectral data were preprocessed using mean-center and Savitzky-Golay 1st derivative with nine-point smoothing. Separate models for each cannabinoid (THC, THCA) and total THC were built separately for concentrate and distillate samples obtained from hydrocarbon and carbon dioxide extraction processes.

Results and Discussion

Table 1 shows the PLS calibration results for concentrates and distillates. Table 1 also shows the potency range and the calibration model performance criteria for THC, THCA, and total THC prediction. The root mean square error of prediction (RMSEP) value was calculated from the predicted results of validation samples (the samples that were not used in building the calibration model). An RMSEP is a statistical metric that gives an estimation of the error in an unknown sample analysis. An RMSEP of 1 % indicates that the error is ~ 1 % of the predicted potency value (for example, for 75 % total THC prediction, the value can be approximately 75 ± 0.75 %).

Table 1. PLS-1 Calibration model statistics of potency value determination by FTIR.

| Sample type after extraction | Cannabinoid | R ² | Potency range (wt.%) | RMSEP % | Solvent used for extraction |
|------------------------------|-------------|----------------|----------------------|---------|-----------------------------|
| Distillates | Total THC | 0.99 | 74–94 % | 1 | Hydrocarbon (HC) |
| Concentrates | Total THC | 0.95 | 68–87 % | 6 | HC |
| Concentrates | THCA | 0.95 | 63–83 % | 6 | HC |
| Concentrates | THC | 0.99 | 1–6 % | 0.8 | HC |
| Concentrates | Total THC | 0.94 | 36–66 % | 5 | CO ₂ |

The concentrates calibration models included the spectra of different concentrate types such as waxes, budder, shatter, and sugars. The training (calibration) set samples were chosen so that possible variations in the extraction processes, spectral data measurement, and the expected concentration range in the future unknown samples were covered.

Figures 2, 3, and 4 highlight typical steps that were followed to create the calibration model and the MicroLab method for cannabinoid potency determination using FTIR spectroscopy, after designing the training set.

The calibration samples spectra were first measured with a Cary 630, then the potency values of those samples were measured using an HPLC or GC reference technique. Figure 2 shows the ATR spectra of distillate samples that cover a total THC value range of 74–94 %.

The multivariate calibration model was then created using the spectral region of the calibration spectra related to the THC and THCA absorption bands. For complex samples such as concentrates and distillates, multivariate chemometric algorithms such as PLS-1 are needed to extract the information from the spectra related to the cannabinoids of interest. Figure 3 shows the PLS-1 calibration model plot for the total THC content (wt.%) in distillate and concentrate samples. Similar plots were obtained for THC and THCA calibration (figure not shown).

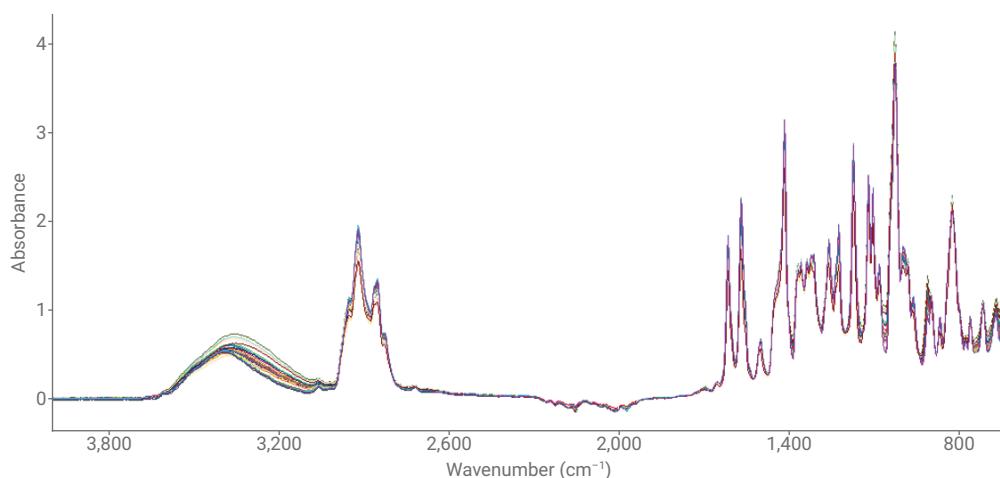


Figure 2. ATR spectra of distillate samples with different total THC content.

Once the calibration models were created, the models were imported into MicroLab PC software to generate a method. The MicroLab PC software, using an unique component reporting feature to set the logic, will include calibration models built for cannabinoids into one single method for future sample analysis. The user can run a single method to get the potency value for different cannabinoids (Figure 4).

At present, there is a lack of standardization in reference methods, making it challenging to have a single method that fits for all. Therefore, the current focus is on developing local methods targeted to specific states, and custom fit them to individual customers. The calibration model and MicroLab method for CBD, CBDA, and other cannabinoids content can be built in a similar manner to the THC calibration model shown here. The extension of this work for potency determination of dry samples such as flowers, trims, and so forth, is ongoing.

Conclusion

FTIR spectroscopy was used to accurately determine the potency value of THC, THCA, and total THC in distillate and concentrate samples. PLS-1 models were combined into a single MicroLab method so that the potency value of THC, THCA and total THC could be directly obtained after measuring the spectra. Since ATR measurements are nondestructive and fast, FTIR analysis saves time in, for example, production workflows, increasing productivity and throughput in sample analysis.

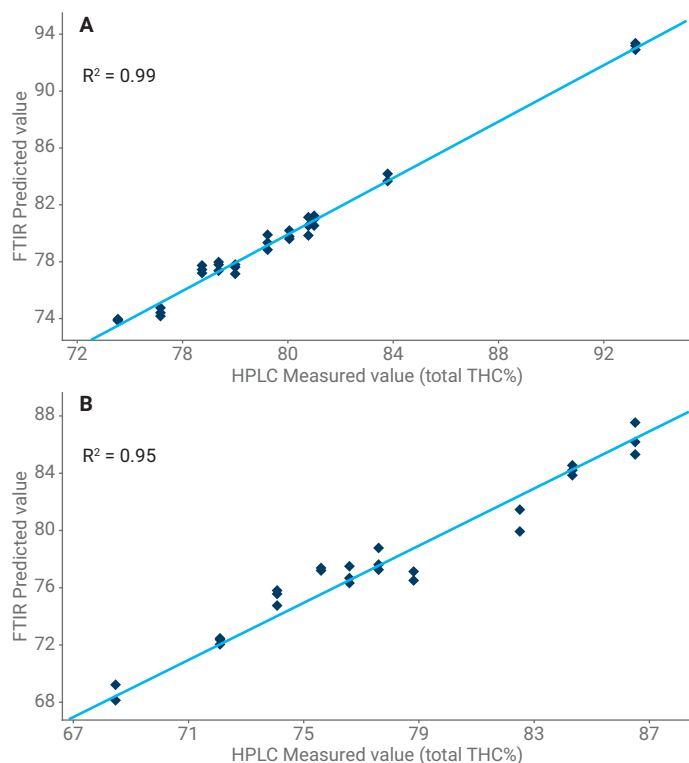


Figure 3. PLS-1 calibration model plot showing the correlation of potency value measured between the reference technique HPLC on the x-axis, and the FTIR-predicted value on the y-axis. A) Distillates sample calibration plot; B) concentrates sample calibration plot.

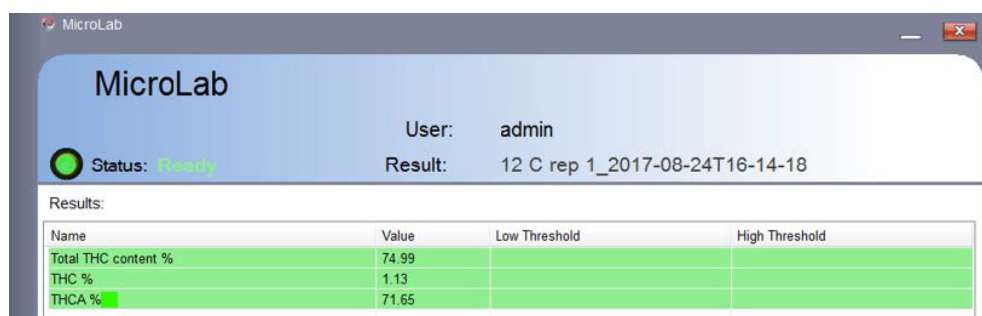


Figure 4. MicroLab method showing the predicted potency value (wt.%) result of unknown concentrate sample analysis.

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