HORIBA Scientific

Application Note

Particle Size Matters When it Comes to CBD Stability and Bioavailability

AN229

PARTICLE SIZE MATTERS WHEN IT COMES TO CBD STABILITY AND BIOAVAILABILITY

Background

The hemp industry has grown over the past several years, with a huge surge in popularity after the 2018 US Farm Bill legalized the cultivation, transport, possession and sale of Hemp and CBD derived products.

For legislative purposes, hemp is defined as the Cannabis Sativa species, the same species that produces the psychoactive version, marijuana - with one key difference: hemp products must contain less than 0.3 percent THC (the psychoactive compound). Different **strains** of cannabis are associated with more or less THC and CBD levels. Growers must also control harvest time, plant health, light levels, and harvest curing processes to keep their THC within legal limit.

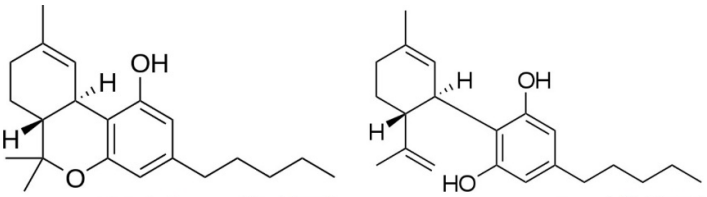

Figure 1. THC and CBD have similar chemical structures but differ in terms of its effect.

Cannabidiol (CBD), the main cannabinoid present in hemp, has made its way into everything from food and beverages, skincare to pharmaceutical products.

A major hurdle with phytochemicals like CBD is that they have extremely low solubility in water, making it very difficult for the CBD to get absorbed into the bloodstream. The oral bioavailability of CBD can be as low as 6%[i] with comparable low efficacy associated with topical or transdermal application methods[ii]. For that reason, the industry has begun to utilize emulsion droplet size reduction methods commonly used in pharmaceutical and nutraceutical[iii] industries to maximize CBD's benefits and maintaining product stability.

This has led to a mass flood of products on the market claiming to have "Nano Particle Water Soluble CBD" or "Nano-emulsion" which are supposedly much more stable and effective. Some companies claim to be up to 90% bioavailable, but unfortunately these are mostly marketing claims that lack any true scientific backing. In this Application Note, we will focus on the importance of monitoring particle size and distribution range throughout two different processing technologies used to improve shelf-life and efficacy of CBD products.

Processing Technologies

After raw CBD rich oil is extracted from hemp, it typically undergoes purification and mixing of the aqueous phase and surfactant(s) to create a coarse emulsion. At this stage, the emulsion is unstable and is unusable. The droplet size may range up to a few hundreds of microns. Two mainstream processing technologies our lab often sees are the Microfluidizer® Processor High Shear Homogenizers[iv] and ultrasonic cavitation. Both technologies are designed to reduce size and size distribution to below 1 micron, otherwise known as Nano-emulsions.

Regardless of the processing methodology, it is important to monitor the change of size as a function of energy applied against time or passes to gain control over final product. For this reason, we believe that laser diffraction is the best analytical approach for handling non-uniform, polydisperse droplets. Laser diffraction such as the HORIBA Partica LA-960 Laser Diffraction Particle Size Analyzer has a wide dynamic size detection range spanning from 10 nanometers to 5,000 microns. It is based on first principle physics where particles scatter light at all directions with an intensity value that is proportional to its size and inversely proportional to its scattering angle. It is also an ensemble technique that provides greater statistical significance and greater sensitivity towards larger particulates. For this reason, laser diffraction is preferable over other techniques such as scanning electron microscopy (SEM) or dynamic light scattering (DLS).

Materials and Method

Two sets of CBD suspensions were submitted and analyzed using the LA-960 laser diffraction analyzer. Each set of samples individually contained an unprocessed emulsion and processed emulsion(s) suppliers aimed to achieve as the final product. In the first case study, a set of three samples treated with Microfluidizer high shear homogenization were measured: unprocessed, two passes, and five passes. The second case study was a set of two samples containing unprocessed and processed emulsions prepared using ultrasonic cavitation. Each sample was added to the analyzer drop-by-drop until an appropriate light obscuration was reached. The LA-960 software then collects data accordingly to the analytical test method below:

Refractive Index: 1.50 | Imaginary (absorption): 0.00i

Dispersant fluid – Deionized water

Pump speed – Gentle pump speed at 3 and stir speed at 2 to avoid disruption of emulsions

Data acquisition time – 5000 (= 5 seconds)

Results and Discussion

As shown below in Figure 2 and Figure 3, the LA-960 successfully tracked and confirmed the effective size reduction using the Microfluidizer and ultrasonic cavitation. In the first case study (Figure 2), the coarse CBD emulsion has a mean size of 82.283 microns. After two passes, the mean size was reduced to 1.546 microns but the size distribution remained wide. After five passes, the sample was effectively reduced to a single narrow peak distribution with a mean of 91 nanometers. A droplet size around 100 nanometers is generally regarded as desirable as it translates to improved CBD absorption, greater stability, and higher transparency.

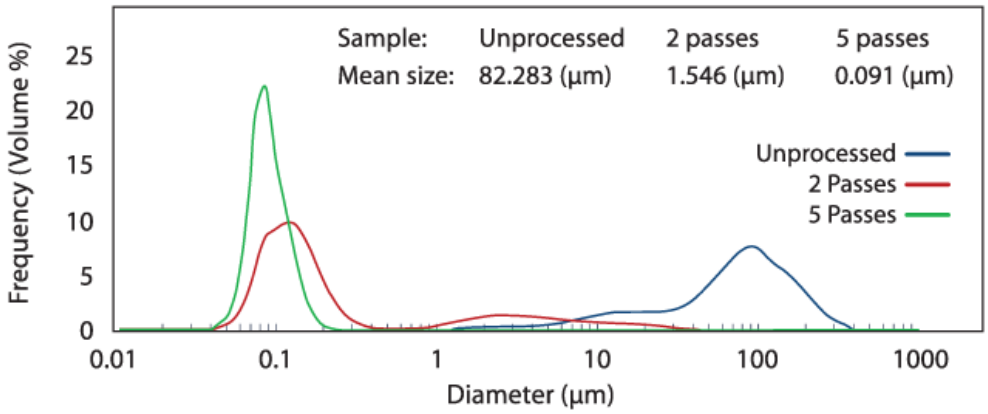

Figure 2. The first case study demonstrates the LA-960's ability to monitor drop size changes as a function of passes using the Microfluidizer high shear homogenization. The final CBD product after processing should display a clean and narrow distribution with a mean size in the nanometer range. CBD emulsion of high polydispersity tends to lead to flocculation over time; homogeneity is preferred and recommended.

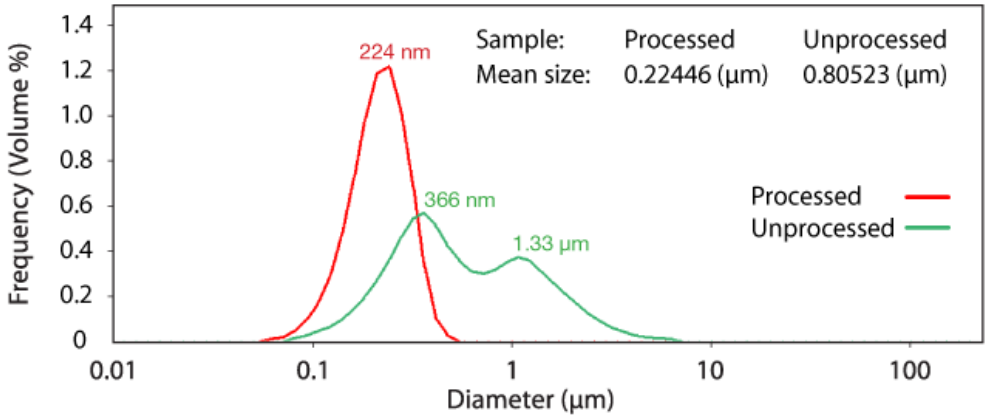

Figure 3. Two CBD emulsions processed in two different ultrasonic amplitudes were measured using the LA-960 laser diffraction analyzer. Green is the graph for unprocessed emulsion. It displays a bimodal distribution ranging roughly from 70 nanometers to 7 microns. Red trace is the distribution after the sample's been treated with sonication. Here we see a much narrower peak with a mean size of 224 nanometers.

The second case study examines the effect of ultrasonic cavitation technology on droplet size reduction. As seen in Figure 3, unprocessed CBD suspension in green exhibits a broad bi-modal size distribution. The LA-960 multi-modal deconvolution software function calculates that the first peak has an average size of 366 nanometers and 1.33 microns for the second peak. After processing, we see further size and size distribution reduction into a single, narrow peak distribution with a mean size of 224 nanometers. Similar to the first case study, homogeneity of CBD droplet size in the nanometer range is an indicator of longer shelf life and greater absorption.

Conclusion

The measurement results and the analytical test methods show that the LA-960 offers an excellent technique for monitoring and characterizing emulsion droplets from nanometers to micrometers. The choice of processing technology rests on formulation and application consideration but neither circumvent the need to understand droplet size and size distribution. To properly enhance CBD bioavailability and stability, it is critical to optimize droplet size and size range by selecting laser diffraction as the analysis technique.

HORIBA Statement

HORIBA products and solutions are intended to be used for quality control and safety testing in facilities where such use is permitted under applicable law.

References

[i] CANNABIDIOL (CBD) Pre-Review Report. Agenda Item 5.2. World Health Organization. Expert Committee on Drug Dependence, Thirty-ninth Meeting, Geneva, November 6-10 2017

[ii] Bruni, Natascia, et al. “Cannabinoid Delivery Systems for Pain and Inflammation Treatment.”

[iii] Particle Characterization of Nutraceutical Products. HORIBA Scientific.

[iv] Microfluidizer® Processors - High Pressure Homogenizers. Microfluidics.

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