



UNDERSTANDING CBD OIL BIOAVAILABILITY, METABOLISM, AND WATER SOLUBILITY

Introduction

Understanding the bioavailability of CBD oil and all the Phytocannabinoids contained in full spectrum oil is like navigating an uncharted river. Terms like “bioavailability,” “absorption,” and “water solubility” are tossed around and used interchangeably. Not only does this muddy up this uncharted river, but it leaves the consumers left to rely upon clever marketing gimmicks or questionable graphs and tables. By relying upon scientific benchmarks, definitions, previous work, and recent discoveries, we can all get an understanding that will help us avoid getting stranded on an unseen sandbar or swept down this muddy current without a paddle. We will focus on cannabis sativa since this is the most common strain of cannabis in products today. The same principles and data should translate to other cannabis species and other lipophilic compounds.

CBD and THC

Cannabis sativa is a species of herb which has been grown and cultivated over thousands of years. Uses range from clothing, textiles, and paper from its fibers to medicinal and recreational uses with its oils and resins. These oils and resins are lipophilic, or fat soluble. There are well over 100 chemical compounds found in the cannabis sativa, or hemp plant. These chemical compounds are known as cannabinoids. Because they are derived from a plant source, they are also called “Phytocannabinoids.” The most notable and well-studied cannabinoids are THC (tetrahydrocannabinol) and Cannabidiol (CBD). THC, specifically $\text{THC}\Delta 9$, is responsible for the euphoric, mind-altering effects of cannabis and is the primary composition of marijuana due to its high $\text{THC}\Delta 9$. CBD, on the other hand, is a non-psychoactive component of the cannabis sativa plant.

Please see [Hemp vs. Marijuana PDF on BioAbsorb™ website page.](#)

Cannabidiol is a pleiotropic drug in that it produces many effects through multiple molecular pathways. The cannabis plant is also composed of a chemical mixture that includes other phytocannabinoids, terpenes, flavonoids, steroids, and enzymes. While the exact mechanism of action is not fully known, all of these other components have a synergistic effect combined with cannabinoids (Gallily, 2015). This has become known as the entourage effect. The cannabis plant has been consumed by humans for thousands of years in medicine for its sedative, antidepressant, analgesic, anticonvulsant, antiemetic, and anti-inflammatory properties.

Please see [Entourage Effect PDF on BioAbsorb™ website page.](#)

CBD is an antagonist at the cannabinoid receptors, and modulators of the endogenous cannabinoid system are also promising candidates for clinical research and therapeutic uses. Cannabinoid receptors including C1 and C2 are distributed in the central nervous system and many peripheral tissues (spleen, leukocytes; reproductive, urinary, and gastrointestinal tracts; endocrine glands, arteries and heart, etc.) (Pertwee, 2008). Additionally, there is now evidence for non-receptordependent mechanisms of cannabinoids.





Five endogenous cannabinoids, anandamide, 2-arachidonylglycerol, noladine ether, virodhamine, and NADA, have been detected and studied. There is also evidence that besides the two cannabinoid receptor subtypes cloned so far, additional cannabinoid receptor subtypes and vanilloid receptors are involved in the complex physiological functions of endocannabinoids that include, for example, motor coordination, memory processing, pain modulation, and neuroprotection (Grotenhermen, 2004).

Pharmacokinetics

Pharmacokinetics refers to what happens to a substance from entering into the body until the exit of all traces. The absorption of a drug or a supplement into the blood stream and utilization by body systems is also called its bioavailability.

The purpose of this study is to identify and define full spectrum hemp oil and specifically the cannabidiol (CBD) bioavailability when a special absorption product is added. Understanding the pharmacokinetics of a drug is essential to understanding the onset, magnitude, and duration of its pharmacodynamic effects, maximizing therapeutic and minimizing negative side effects.

The Physical Properties of CBD Oil

As mentioned above, both THC and CBD are highly lipophilic and have poor oral bioavailability. The oral bioavailability of CBD and THC has been well documented at 6%. Oral THC formulations have shown variable absorption and undergo extensive hepatic first-pass metabolism, resulting in lower peak plasma THC concentration relative to inhalation and a longer delay (~120 minutes) to reach peak concentration. While the metabolic pathways differ slightly, CBD exhibits similar pharmacokinetics: Following oral administration of CBD, a similar plasma concentration-time profile to oral THC has been observed and documented (Lucas, 2017; Huestis, 2007).

THC levels from smoking are much higher. Human clinical studies have shown bioavailability levels as high as 30% with peak plasma concentrations occurring 10 minutes after inhalation (McGilveray, 2005). Recently, cannabis extractors have been producing crystalized CBD and other cannabinoids through supercritical CO₂ or by stripping the cannabinoids out through chemical extraction methods such as ethanol. Further processing has led to reducing these crystalized cannabinoids into nano sized particles. Regardless the size or the form (crystal or liquid) cannabinoids are lipophilic or oil based. The physical properties remain the same regardless of the size. Any alteration of the form or structure of these cannabinoids would be subject to an FDA application for a new dietary ingredient (NDI) or novel food ingredient.

Increasing bioavailability of poorly absorbed compounds is an ongoing challenge in the both pharmaceutical and nutritional science. BioAbsorb™ is a proprietary micellization process which micellizes a decarboxylated full spectrum hemp oil (including CBD and trace amounts of THC) mixture suitable for oral ingestion. According to the manufacturer each particle size is approximately 22 nm making it highly permeable in water. Models with BioAbsorb™ have demonstrated a rapid and almost complete absorption (85%) in the intestinal lining using Franz diffusion apparatus.

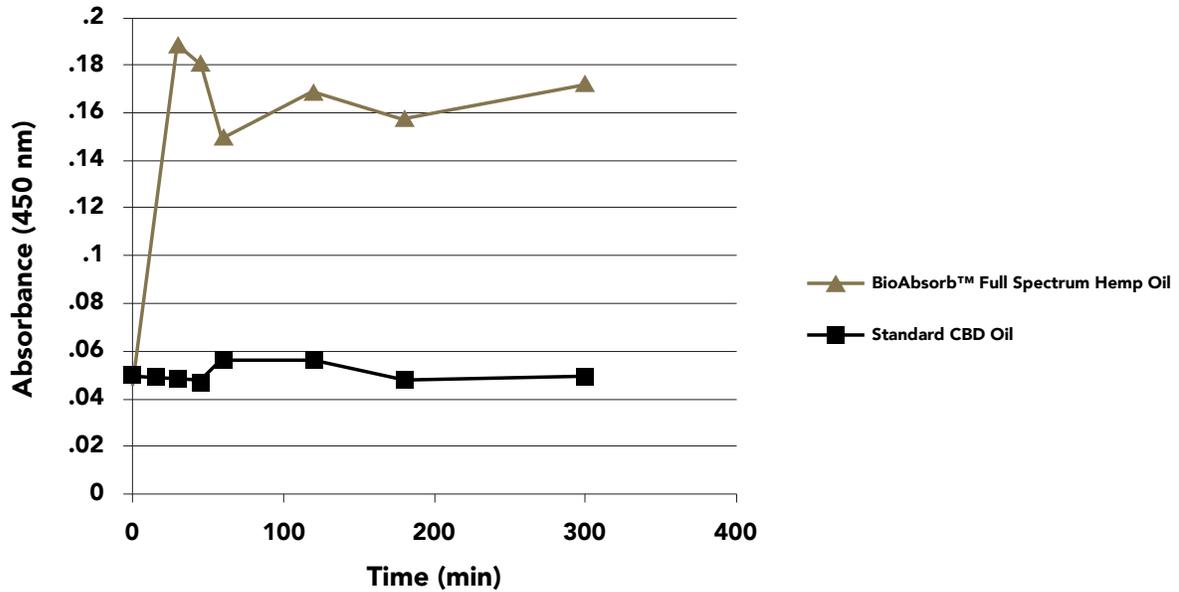


Figure 1. BioAbsorb™ CBD oil and standard CBD oil (formulated in MCT) absorption in intestinal model.

Absorption

Absorption is a term that can have multiple meanings depending on the context it is used: 1) Absorption of a compound through a cell wall layer simply means the quantity or measurement of a compound to pass through that layer. 2) Absorption can also be measured through the skin or other mucosal layers in the body. These studies are generally done ex-vivo (outside the body) or in a lab model. Although absorption models will provide a good indication of how well compounds will pass through cell layers in ideal conditions, these models do not take into account the stability of a compound outside the body, in the mouth, stomach acid, or how it is broken down in the digestive system. It only tells us that in ideal conditions, a compound can pass through from point A to point B. Figure 1 is an illustration of CBD oil in a simple absorption model.

Simple Absorption Model

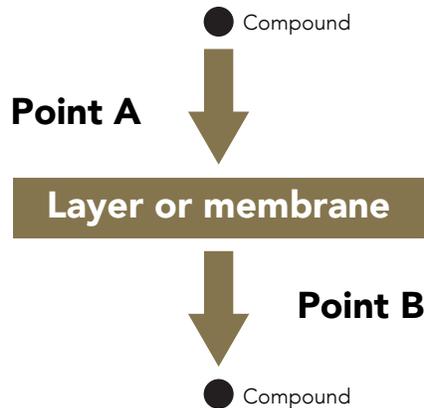


Figure 2. Simple Absorption Model. Getting a compound from Point A to Point B through a layer or membrane.



Bioavailability

The absorption of a drug or a supplement into the bloodstream and utilization by body systems is also called its bioavailability. Bioavailability is a measurement of a compound or substance in the body. For example: The overall bioavailability of cannabis in the body would need to be measured in the bloodstream. The specific bioavailability of cannabis to a specific end organ would require the measurement of the amount of cannabis in the end organ compared to the amount delivered orally, inhaled, rectally, or topically. If cannabis were to be delivered intravenously the bioavailability would be 100% since all of the cannabis is being delivered directly to the bloodstream. These are universal and well-established practices in both pharmaceutical and nutritional/food sciences.

Water Solubility

The term water solubility can be very confusing in the cannabis space. A cannabis product that has been manufactured to dissolve and disperse in water is not necessarily water soluble: In fact, most, if not all, are not; they are water dispersible, not water soluble. This is very apparent in the nano space where cannabis crystals (isolates or distillates) can be reduced into such small particles that they disperse evenly in water making them highly water dispersible.

The methods and practices of solubilizing lipophilic compounds has been and remains the holy grail in pharmaceutical and nutritional delivery. Pharmaceutical companies have spent billions of dollars developing lipophilic delivery methods. Over 20 years ago a process was developed by the pharmaceutical industry called liposomes to mimic the body's way to break down lipophilic compounds. The body itself uses a system called micellization to breakdown lipophilic compounds for the body to utilize. Liposomes, while initially looked very promising, were found to be highly unstable and never materialized as viable products in pharma. In the early period of CBD product development, several companies launched liposomal cannabis products. Shelf life and heat sensitivity (liposomes fall apart above 80° F) became too problematic for these products to be seriously considered therapeutic.

Micellization, however has been the long-established method to mimic the body's natural water solubilization phase. Micellization can work well when working with isolated compounds but when dealing with the complex nature of a botanical oil with many different constituents and properties, it became problematic due to the complex nature of the oil. While many companies can produce a bench top sample of a cannabis micelle, the large-scale production of micelles using full spectrum oil has been limited to one company in the early stages: PurhealthRX. PurhealthRX and its scientists began micellizing commercially in 2011 and entered the cannabis space in 2014 following the 2014 Farms Bill where section 7606 opened the way for industrial hemp compounds to be studied and developed.

Clinical Studies

The only valid way to document bioavailability is through studies. Cell models such as Caco-2 and Franz Diffusion are two models used widely in the pharmaceutical and nutritional sciences world to measure absorption of drugs and nutrients taken orally. PurhealthRX began testing micelles alone, and in comparison, to standard full spectrum oil utilizing the Franz Diffusion method early in the development of micellized full spectrum oil. PurhealthRX completed two separate Human Clinical Trials looking at bioavailability of BioAbsorb™ in human subjects. Late in 2019, a large study was



completed with support from the National Institute of Health (NIH) where safety and several clinical outcomes were measured. In conjunction with this study blood was drawn from 50 patients at the end of the study to assess the level of BioAbsorb™ in the bloodstream following 60 days of daily use.

Human Clinical Studies

HPLC Testing

High-performance liquid chromatography (HPLC; formerly referred to as high-pressure liquid chromatography), is a technique in analytical chemistry used to separate, identify, and quantify each component in a mixture. Each component in the sample interacts slightly differently with the adsorbent material, causing different flow rates for the different components and leading to the separation of the components.

Human Studies

PurhealthRX completed 2 separate human studies that evaluated the blood levels of BioAbsorb™ orally administered to human subjects over a 12-hour period. Each time set had three vials of arterial blood drawn. Each sample was testing using HPLC. The report indicates the average of the three blood vials drawn and tested from each subject at each time point. Samples were drawn at: Baseline and post ingestion of product at 15 minutes, 30 minutes, 45 minutes, 1 hour 45 minutes, 2 hours 45 minutes, 3 hours 45 minutes, 4 hours 45 minutes, 5 hours 45 minutes, 6 hours 45 minutes, 7 hours 45 minutes, 8 hours 45 minutes, 9 hours 45 minutes, 10 hours 45 minutes, and 11 hours 45 minutes. Two consecutive studies were carried out with fourteen subjects participating for a period of twelve hours. At the onset of these studies each subject had arterial blood drawn to set the Baseline of CBD in their bodies, each had a Baseline of 0.0 mg of CBD at Baseline. Each subject was given an oral dose of one vial of Full Spectrum Hemp oil containing 134 mg of BioAbsorb™ Full Spectrum Hemp Oil. Vials were prepared by PurhealthRX and delivered to the researcher for use in this study. Each subject was given a vial and instructed to place the liquid under their tongue and hold it there for 30 seconds before swallowing. The nurse in attendance let each subject know when their 30 seconds was up so they could swallow the remaining liquid.

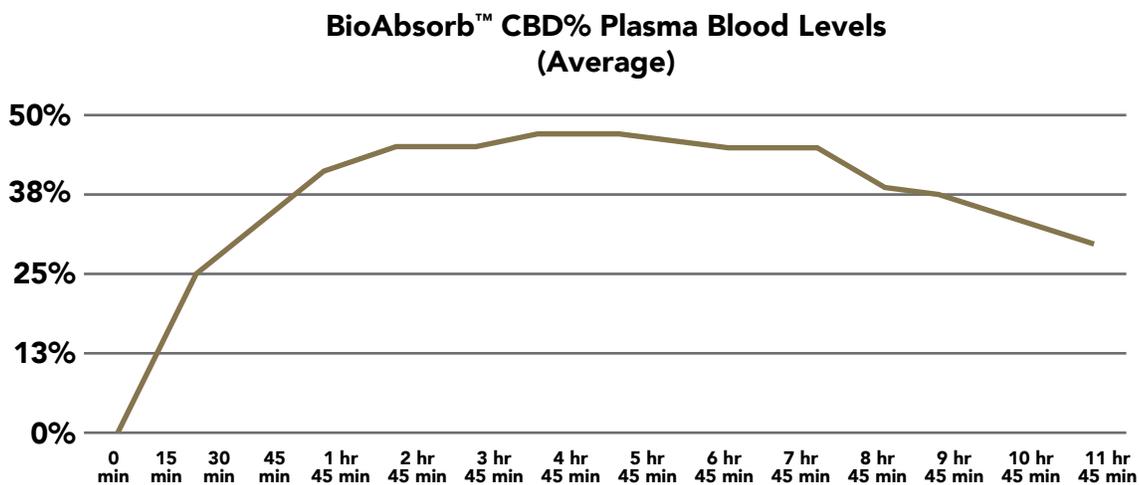


Figure 3. Plasma blood levels prior to adjustment for blood volume.



Human Bioavailability of Full Spectrum Hemp Oil (FSHO)

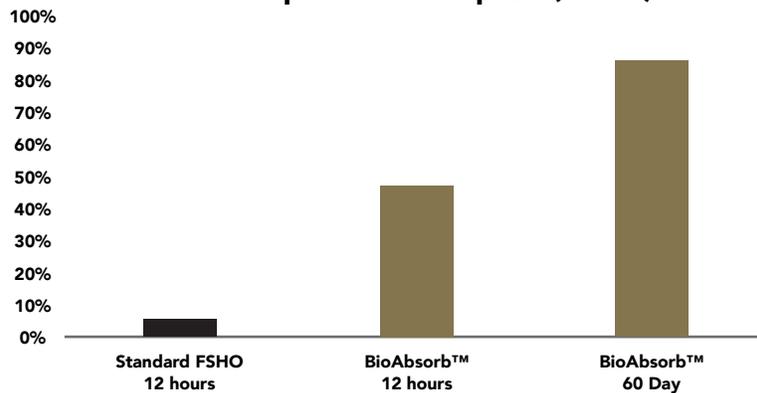


Figure 4. Plasma blood levels of Standard Full Spectrum Hemp Oil (FSHO) and BioAbsorb™ FSHO at different time intervals.

Summary

The onset of BioAbsorb™ is rapid and it has a lasting duration of CBD availability in the bloodstream. All the patients were measured to have over 50% of the available CBD in their bloodstream by the first measurement of 15 minutes. This exceeds what has been shown with CBD or THC that has been inhaled or vaped. It can be summarized that the blood levels of BioAbsorb™ Full Spectrum Hemp Oil measured significantly higher than what has been seen with standard CBD oil and other solubilizing methods. From these studies it is concluded that the uptake of BioAbsorb™ Full Spectrum Hemp Oil far exceeds the average uptake of CBD products available on the market today.

References

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