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Dissolving Acidic Cannabinoids for a THCA CBDA Solution

CANNABINOID CARBOXYLIC ACIDS THCA AND CBDA: THEIR POTENTIAL FUNCTIONS, APPLICATIONS, AND METHODS OF EXTRACTION

Introduction to a cold extraction method that preserves carboxylic acid form of cannabinoids THC and CBD

By Kate Welch, Pharm. D & CAT Scientific

The cannabinoids THCA and CBDA, short for delta-9 tetrahydrocannabinolic acid and cannabidiolic acid, respectively, are precursors to their more well-known and well-studied metabolites, THC (aka delta-9 tetrahydrocannabinol), the primary psychotropic cannabinoid found in cannabis, and CBD (cannabidiol), its primary non-psychotropic cannabinoid.

Found most abundantly in fresh cannabis plant material (Eichler et al. 2012; Turner et al. 1980), THCA and CBDA de-carboxylate the acidic part of the molecule into the active molecules THC and CBD. This occurs primarily by exposure to heat via smoking, cooking, or heated extraction of the dried or fresh plant, but also can form more slowly over time via extended exposure to light and atmosphere (Hazekamp 2008).

Until recently, THCA and CBDA were not considered to be able to survive metabolism (i.e. inhalation by the lungs or digestion by the stomach and intestines and processing by the liver); nor were they considered to have any pharmacological activity in and of themselves (Jung et al 2007; Takeda et al 2008).

However, recent in vitro and animal research using extracted THCA or CBDA reveals measurable actions on certain enzymes and receptor sites, suggesting some potential therapeutic effects for these cannabinoids and necessitating the elucidation and refinement of specific extraction techniques that preserve these particular acidic forms of these cannabinoids in order to provide material for further experimentation and research.

CBDA was the earliest discovered cannabinoid acid, in 1955 (Brenneisen 2002). As for THCA, there are actually two forms: THCA-A was isolated in 1965; THCA-B, an analogue, was isolated in 1975. Some plants express more of one or the other for unknown reasons (ElSohly and Gul 2014), but THCA-A is usually the most prominent, and the most studied (Brenneisen 2002). For the purposes of this article, THCA-THCA-A as found in the fresh or dried cannabis plant.

First, it is important to distinguish between the carboxylic acids that are precursors to THC and CBD in the fresh or dried plant material, and those that are the acid metabolites of smoked or ingested THC and CBD, formed in the liver or tissues and found in the bloodstream and filtered through the urine for excretion.

The primary non-psychoactive metabolite of THC is also an acid, 11-nor-9-carboxy-delta-9-tetrahydrocannabinol (Foltz 2007). This metabolite forms via the enzyme alcohol dehydrogenase from the primary liver-produced metabolite of THC, the equally psychoactive 11-hydroxy-THC.

Removal of pure THC occurs rapidly from the bloodstream; 11-nor-9-carboxy-delta-9-THC accumulates and continues to form and be excreted into the urine as the THC in the bloodstream or from tissues that secrete stored THC into the bloodstream. As a result, urine drug assays intended for detection of human cannabis consumption primarily screen for the presence of this particular form of THCA (Chesher and Longo 2002).

Animal research confirms that biological enzymes do not themselves convert THCA to THC: pure THCA given to rats led to acid metabolites of THCA only, not THC or acid metabolites of THC (Jung 2007).

THCA and CBDA lack psychoactive effects (Kwong 2002) even when administered in pure form by IV to animals or humans (Grunfeld et al 1969). There is no evidence at this time that the acidic metabolites produced in vivo share the potential biological effects of it acidic precursors present in the fresh or dried plant.

Quantitative detection of THCA in raw plant material heretofore has primarily been intended to help predict the THC potency of a specific weight or volume of dried plant when it is eventually smoked or heated; liquid chromatography (HPLC) is preferred since it is important that the method of detection must not heat the sample which will immediately convert THCA to THC (Ambach et al 2014).

Furthermore, lab analysis of this decarboxylation reaction provides estimates that smoking cannabis yields approximately a 30% conversion of THCA to active THC; other methods such as cooking or heated solvent extractions will yield 70-90% conversion (Dussy et al 2005).

However, it is important to note that to date there is poor correlation between the percentage of THCA to THC conversion already present in a cannabis product to be consumed and the resulting pharmacokinetics (measurements in the bloodstream) or pharmacodynamics (measurable psychoactive or psychomotor effects) in humans. For example, a small study compared the levels of THC and THC metabolites (both active and inactive) in men who consumed a fixed amount of either a) a heated cannabis sativa extract; b) and unheated cannabis sativa extract; or c) pure pharmaceutical THC (aka dronabinol or Marinol®).

The unheated extract, surprisingly, turned out to provide both the highest CBD and THC blood levels on average, suggesting that whatever CBD and THC was initially ingested from the cold extract was readily absorbed and persisted in the bloodstream the longest. The heated extract, however, provided the highest total exposure to THC activity because of the sum of THC plus active metabolite 11-hydroxy-THC measured in the bloodstream. Both extracts measured blood levels of THC on average higher than in subjects given the pure pharmaceutical THC, even though both the unheated and heated cannabis extracts were CBDA dominant strain (CBDA/THCA ratio >1) (Eichler et al 2012).

While the above stury provided states interesting existentific about) the fate of CBD and THC after oral consumption from either heated or unheated extracts, it did not examine the pharmacokinetics or pharmacodynamics of CBDA or THCA, though there were more of these acidic forms of the cannabinoids present and ingested in the unheated extract than the heated one (and none present in the dronabinol). Thus, important questions remain about both the unique biological effects of these acidic cannabinoids on the human body as well as their potential entourage effects either kinetically or dynamically with their better-studied de-carboxylated metabolites.

Here is some of the most compelling evidence that shapes what we know about the carboxylic acid forms to date: both THCA and CBDA independently of any other phytocannabinoid, provide significant anti-nausea and anti-vomiting effects. In rats, THCA appears to be a considerable anti-nausea and anti-vomiting compound. In a study conducted in 2013, researchers determined not only that THCA was more potent compound in this regard than THC but also that THCA apparently mediated

this response via 5HT1a (aka serotonin) receptors rather than the CB1 (cannabinoid) receptors whereby THC appears to exert its own anti-nausea effects as shown in other animal models (Rock 2013).

Researchers repeated similar experiments with CBDA as well, demonstrating that CBDA reduced both toxin and motion-induced nausea and vomiting in rats, via an asyet-to-be-determined enhancement of 5HT-1A serotonin receptor activation (Bolognini et al 2013). Unlike the THCA experiment— which showed THCA and THC exerting anti-nausea effects via wholly different receptor mechanisms—CBDA appears in vivo and in vitro to work pharmacologically more similarly to CBD (e.g. both via serotonin-receptor activation), though CBDA was shown to be more potent than CBD in its serotonin-receptor-mediated effects.

Additionally, CBDA and THCA have been shown in vitro to block, in varying degrees, both cyclooxygenase (COX) enzymes 1 and 2, which are each distinct mediators of inflammation and pain secondary to inflammation. Non-steroidal anti-inflammatory (NSAID) drugs such as acetylsalicylic acid (aspirin), ibuprofen, naproxen, indomethacin, and diclofenac all work via COX 1 and 2 inhibition, and, like CBDA and THCA, contain a carboxylic acid group in their structures that suggests this part of the molecule is integral to the way they work.

In one assay, CBDA but not THCA significantly inhibited both COX 1 and 2-mediated oxidation activity, with the CBDA showing a strong preference for inhibiting COX 2 specifically (Takeda et al. 2008).

A second study demonstrated that both THCA and CBDA inhibited COX 1 significantly but only THCA inhibited COX 2, and by only a little over 30% (Ruhaak, L. et al 2011).

Both studies showed that the carboxylic acid forms CBDA and THCA had stronger overall COX-inhibiting activity than their de-carboxylated forms CBD and THC, however. More research is needed to clarify the role the acidic cannabinoids play in moderating inflammation and determine whether or not they may be safer alternatives for this than NSAIDs, which have well-known dose-dependent or long-term use detrimental effects on the gastrointestinal and cardiovascular systems due to their COX inhibition.

Lastly, both CBDA and THCA show in vitro activity at some of the various cation channel receptors collectively known as transient receptor potentials that play important roles in pain and inflammation signal transduction such as TRPV1 and TRPV4(the "vanilloid" type); TRPA1(the "ankyrin" type) and TRPM8 (the "melastatin" type). They can block, activate, or de-sensitize these to activation by another activator (Cascio and Pertwee 2014). These are likely additional mechanisms by which the carboxylic acid forms of the cannabinoids work independently of their decarboxylated forms to moderate pain and inflammation both centrally and peripherally.

The carboxylic acid cannabinoids CBDA and THCA are likely to be important contributors to the relief of nausea, inflammation, and pain that humans have attributed to the cannabis plant for millennia. What makes them worth studying individually today are not only their individual roles within the entourage of effects that cannabis is so well known for, but also in their ability to relieve nausea or pain alone while bypassing the sometimes debilitating or unwanted psychoactive effects produced by cannabinoids like THC that activate the CB1 receptor.

The recent popularity of websites and electronically-published books extolling the benefits of juicing of fresh cannabis leaf or whole plants to treat a variety of ailments are likely attributable to the role that CBDA and THCA play on various biological targets as enumerated above.

CBDA and THCA can also be extracted and purified out of most any other cannabis extract (Wohlfarth et al 2011) but, short of the capabilities of sophisticated chemical separation of CBDA and THCA from all other cannabinoids in a lab, one will most easily obtain an extract with a much higher percentage of the carboxylic acid cannabinoids via cold-process extracts of the fresh plant. The resulting extract must continue to be stored in a cool, dark place (Taschwer 2015) in order to preserve its unique characteristics, and should be ingested rather than smoked if the goal of therapy includes reducing the psychoactive effects produced by THC.

References for CANNABINOID CARBOXYLIC ACIDS THCA AND CBDA: THEIR POTENTIAL FUNCTIONS, APPLICATIONS, AND METHODS OF EXTRACTION (http://www.catscientific.com/wp-content/uploads/CBDAandHCA_Kate-Welch-referencest.pdf)



Dissolving Acidic Cannabinoids for a THCA Tincture

By Bob Wilcox, CAT Scientific; August 18, 2015

Producing an Acidic Cannabinoid Solution has its challenges, primarily decarboxylation. Starting with fresh material is paramount; it's mainly in Carboxylic acid form.

Choosing an extraction method should be given careful consideration. Using a solvent like Ethanol as a carrier, some decarboxylation is possible if evaporated with heat.

For ease and wanting to steer clear of activation we performed a dry ice extraction; eight ounces of fresh material with a 200 Micron Bag yielded 45 grams of glandular trichome's-Keif.

Liquid Coconut Oil is used as the carrier for the cannabinoids. It has a high fat content, is stable, pleasing to the palate and doesn't solidify when refrigerated.

A CAT X1000D Homogenizer Drive with a G-20 Knife Generator Shaft Assembly is used to dissolve the cannabinoids in Liquid Coconut Oil. The X1000D Homogenizer Drive is needed to provide the torque to process the high viscosity of the media; Liquid Coconut Oil & Keif.

G-20 Knife Generator shafts are sealed to prevent abrasive material, like Keif from being processed through the shaft tube, thereby possibly damaging its O-rings, ball bearings, springs, and other components.

The Knife Generator is engineered so that as powders are added into liquids they won't congeal, it cuts while processing; splitting open the trichomes so the cannabinoids readily dissolve and diffuse in the carrier.

For the experiment, we wanted to see what percentage of CBDA- mg/ml is achievable with 5% by weight of Keif to 500ml of Liquid Coconut Oil, which comes to 25 grams.

Heat is easily generated while processing due to the high viscosity of the media. To avoid the possibility of further decarboxylation, we chilled 500ml of Nature's Way Liquid Coconut Oil to 38°F and placed it in a one liter beaker. 500ml is the minimum that can be processed in a one liter beaker with a G-20 Knife Generator, while introducing powders into liquids.

The CAT X1000D is clamped on its drive stand so the Knife Generator is immersed in the Coconut Oil about a 1/16th of inch from the bottom of the vessel. The device is powered on with the speed set at 4000rpm's. About 12 grams of Keif are added into the Coconut Oil. The motor speed is then increased to 8500 rpm's and the vessel is moved around the shaft for about 45 seconds. The motor speed is decreased back to 4000 rpm's and the rest of the Keif is placed into the oil. The motor speed is increased again to 8500 rpm's for about 45 seconds while moving the vessel around the shaft. That completes the processing.

We're not quite sure if additional time processing; say a minute, would increase the CBDA percentage. The temperature of the solution rose from 38°F to 75°F in 90 seconds, so we decided not to do any further processing with the X1000D Homogenizer. Instead, we placed the solution on the MCS78 Magnetic Hotplate Stirrer for an hour with no heat, just stirring. We don't know if the hotplate stirrer is even needed. We thought it couldn't hurt.

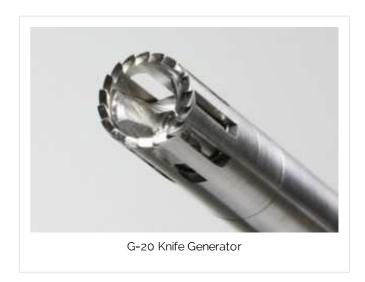
We then vacuumed filtered the solution and sent a sample to the lab for a potency analysis. Here are the results; CBDA Solution Analysis (http://www.catscientific.com/wp-content/uploads/CBDA-Solution-Analysis.pdf), and the Flower Analysis (http://www.catscientific.com/wp-content/uploads/Flower-Analysis.pdf) for the CBDA material we used for the dry ice extraction.

This process is relatively fast, about 1 ½ hours from extraction to completed solution.

Some additional testing will have to be done to discover if more time spent processing, two and a half minutes compared to 90 seconds increases the percentage of CBDA. The additional time will require the vessel to be chilled to prevent further decarboxylation.







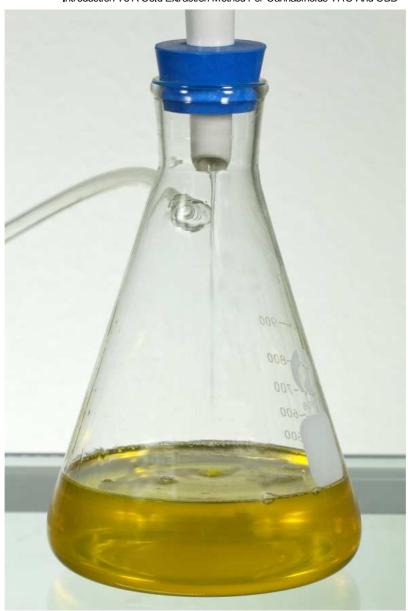












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Kate Welch, Pharm D & CAT Scientific

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15 Comments

Steve Short on November 30, -0001 at 12:00 am

Cannabinoids are only very poorly soluble in glycerin as the latter is far too polar.

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=40582#respond)

arrie on May 16, 2016 at 12:47 pm

Hello Bob,

Great article.

Could you please elaborate on the filtering aspect like the micron size of the filter and the temperature of the solution during filtering.

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=38302#respond)

Kevin Roelofs on May 18, 2016 at 10:57 am

Arrie, they drew a vacuum on the beaker, and ade filtering thru a coffee filter.

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=38349#respond)

Emmanuela Raquelle on October 2, 2016 at 6:39 pm

If the fresh plant would be soaked in glycerin for a period Of time, would the glycerin then extract the CBDa or THCa from the raw flower into the glycerin to make a tincture sublingual?

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=39089#respond)

David Eldredge on December 1, 2016 at 12:21 pm

How did you come up with a pure sample of trichomes? That had to have been a feat in of itself and rather expensive? This is a very good article. It is exactly what I was hoping to find. I don't believe you can get enough product titer in your blood steam just smoking it to achieve effective results unless you smoke cannabis throughout the day. Charlotte's Web full plant extract from the Stanley Brothers in Colorado Springs has shown much more promise to me and my family than vaping dried flower high in CBD or even smoking it. CW produces no "high" I suffer from an extreme pinched sciatic nerve and my 19 year old daughter is autistic and has show promising results with Charlotte's Web extract. It seems to be more effective than Tylenol, Motrin or even Hydrocodon for my pain. Vaping a whole flower product very high in CBD from a medical dispensary produced a nice high, but did nothing to relieve the pain.

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=39532#respond)

pete on November 30, 2017 at 7:41 pm

awesome

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=41441#respond)

Nancy on December 6, 2016 at 3:21 pm

Do you need to add the coconut oil? Why not just use the powder for those sensitive to the oil (coconut or else) like those with gut issues?

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=39562#respond)

Hiedi Handford (http://www.MyMedicineConsulting.com) on April 30, 2017 at 9:24 pm

I use magnetic spinners in glycerin for my cold extractions. Takes only a couple days. You can also use a grain alcohol/glycerin combination to extract. Glycerin is preferred though, as it doesn't affect the glycemic index the same as sugars do. Filter through your preferred micron and VOILA – you're done. Tastes like the strain too. Terpenes intact.

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=40496#respond)

AManNamed on May 29, 2017 at 9:03 am

Great stuff ty for the shared knowledge.

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=40586#respond)

AManNamed on May 29, 2017 at 9:23 am

I noticed that most promising results for pain and inflammation (your nerve) ingesting not smoking the material. If you can get your hands on an unheated extract, or pure Thca crystalline (non-psychoactive), or a good unheated tincture with multiple derived cannabinoids. You can use these extracts along with your daily anti- inflammatory meda, If you take any anti-inflammatory meds I would recommend to not go over your prescribed dose be light on your organs, stomach and liver. The use of these extracts and meds together will have a substantial improvement in relief. If you want more long term and long lasting results when inflammation has resided I recommend to therapeutically stretch and do controlled positioning movement (yoga), that focuses on you lower back, hips legs, or full body for best results. May you be blessed.

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=40585#respond)

Mr Neil Aspinall (http://ttccgroup%20on%20facebook) on June 23, 2017 at 11:05 am

more research needs to be done with the thca compound as it can directly control GBM brain tomours groth rate, any research in to canabaniods and cancer is good news

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=40583#respond)

Sarah (http://Cannagramma.com) on July 28, 2017 at 4:19 pm

The blood brain barrier prevents THCa from entering the brain to get to the tumors. While THCa may be effective for cancerous tumors in other parts of the body, only THC is effective for cancerous brain tumors. The acid form doesn't get to the brain, decarboxylated form can, thus the high from one and not the other.

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=40691#respond)

Kristin on October 12, 2017 at 12:36 pm

Please clarify about the comment stating that THCa does not cross the blood brain barrier, as I have not seen that point made in any research yet. To my knowledge it does... thank you!

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=41226#respond)

pete on November 30, 2017 at 7:43 pm

wow fascinating

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=41442#respond)

pete on November 30, 2017 at 7:45 pm

is anything left behind in the coffee filter or do all of the cannabinoids and terpenes become part of the solution indefinitely? (with no risk of separating from the oil.)

Reply (https://www.catscientific.com/dissolving-acidic-cannabinoids-for-a-thca-cbda-solution/?replytocom=41443#respond)

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