Ratio CBD:THC Implications / Characteristic Effects (Cannabidiol:Tetrahydrocannabinol) Oct 31, 2018

The CBD modulates the high of THC and reduces its adverse/side effects linked with psychosis. CBD is basically the antidote/balancing agent to THC in the original source (the cannabis plant).

I do not recommend adding THC unless you have an appropriate cancer (not worsened by CBD/THC-see below), or fibromyalgia or severe pain, and only in a balanced regimen of no more than 1:1 CBD:THC, or closer to 3:1 or 4:1. THC only (0:1 CBD:THC) is recreational use marijuana that will not help and I do not support.

0:1 (**THC only**) Strong "high" psychotropic effect (especially over 30mg if ingested) Euphoria, confused thought. Strong side Effects: Tachycardia, anxiety, paranoia, memory impairment, potential addiction. **"Recreational" use only (? Illegal in PA)**

1:1 (**Balanced CBD:THC**) Relaxation with very light "high" effects Little euphoria. Promotes calmness and tranquility.

2:1, 4:1 or higher (**CBD dominant**) Little sedation. Few to no "high" effects: No euphoria, sedation, light-headedness.

1:0 (**CBD only**) No "high" effect, at all. Ease up general mood. High therapeutic potential use: antipsychotic, relaxing, used in epilepsy treatments; few side effects. In reducing inflammation, may also reduce risk of vascular disease

20:1 or 1:0 CBD:THC or just CBD oil

Targets Neurological issues:

Anxiety and Depression
Arthritis, neck pain, back pain
Attention Deficit disorder
Cerebral Palsy
Epilepsy (at high doses)
Parkinson's disease and Restless Leg Syndrome

3:1 or 4:1 CBD to THC

Targets Auto-Immune Conditions:

Auto Immune Diseases
Breast Cancer
Crohn's Disease / Ulcerative Colitis
Extreme Arthritis, Rheumatoid arthritis
Irritable Bowel Syndrome
Multiple Sclerosis
Pain and inflammation
Post-traumatic stress disorder
Psoriasis

1:1 CBD to THC

Targets certain cancers and helps other issues:

Appetite Stimulation
Autism
Certain Cancers (but avoid in melanoma and colon cancer as these can have CB1 and CB2 receptors)
Fibromyalgia
Severe Pain

Recommended Product for Cost Effectiveness

Elixinol 300 mg CBD Tincture for sublingual dosing

1. Most cost-effective $29 per 300 mg
2. Meets all high-quality criteria
3. Sublingual dosing for better bioavailability
4. Also available as liposomal formulation (more potent so use 1-4 sprays per day) $60

Dosing

1. Start with 2.5 mg (1/4 dropper) to 5 mg (1/2 dropper) once daily depending on symptoms
2. Less is more with this therapy: there is a therapeutic window that if you are taking too much it may not work as well as taking less. Therefore, it is important to titrate up slowly
3. If after 3-5 days, if still not having significant relief of symptoms, may increase to 5 mg twice daily. If you need more, you may need a balanced CBD/THC product (medical marijuana)
4. When you are feeling better, try titrating down again. You may end up only needing a small dose once or twice weekly to control your symptoms; we are not looking for complete pain relief but the alleviation of suffering.
5. If using the liposomal version of Elixinol, reduce dose by 50-70% (is much more bioavailable); if using ½ dropper (5 mg) of tincture, you may only need 1-2 sprays of the liposomal version

What you may notice

1. Feeling more relaxed and sleeping better
2. Better focus and improved memory and recall
3. Fewer anger management issues
4. Less neck and back pain

Safety

1. There is no "high" as has zero THC content
2. Urine drug screens will be negative
3. It is a potent anti-inflammatory so could increase effect of immunosuppressant meds and increase risk of infections or Herpes reactivation (fever blisters)
4. Drug interactions if large doses (600 mg) taken orally; not an issue with these small doses sublingually as it has little effect on the liver

What is CBD oil (Cannabidiol)? What are the risks?

CBD blocks CB1, CB2 receptors (antagonist), with significant analgesic and anti-inflammatory actions without the psychoactive effect (High) of THC.

What is Epidiolex? CBD for rare seizure disorders. A total of 225 patients suffering from Lennox-Gastaut syndrome were divided into three groups. Those taking oral capsules of 20 mg of Epidiolex a day had 42 percent fewer seizures, on average, compared with 37 percent fewer seizures in the group taking 10 mg of the drug, and a 17 percent reduction in the placebo group.

Bigger doses not necessarily better. While the 20-mg dose was slightly more effective than the 10 mg, it was not the first choice of parents, Devinsky said. "When parents were asked to rate how their children did best, **they actually had a slight preference for the 10-mg dose** without knowing what it was," he added.

That's because these kids did not experience as many side effects from the cannabidiol (at 10 mg), which can include tiredness, decreased appetite, diarrhea and signs of possible liver damage, Devinsky explained.

"They got the vast majority of the benefits with fewer of the side effects on the 10 mg dose," he said. The study also showed that Epidiolex is a safe treatment, with only seven patients dropping out of the trial due to side effects -- six from the 20-mg group and one from the 10-mg group.

"Compared to other drugs used to treat epilepsy, I think Epidiolex, which is 99-percent pure cannabidiol, has a better side-effect profile than many of the available drugs," Devinsky said.

The trials for Epidiolex for Lennox-Gastaut and Dravet syndrome) showed increases in aggression and anger compared to placebo but no formal assessment of depression scores or suicidality.

Still, the FDA noted in its approval statement that side effects could occur, such as sleepiness, lethargy, poor appetite and infections, among others. And like other drugs that treat epilepsy, Epidiolex will come with a special warning that use may be tied to higher odds of depression, aggression and suicidal thoughts.

https://consumer.healthday.com/public-health-information-30/marijuana-news-759/low-dose-of-cbd-liquid-eases-epilepsy-seizures-study-733982.html

What is Acomplia? Acomplia (rimonabant) was the first in a new class of therapeutic agents called Cannabinoid-1 Receptor Blockers (CB1). Acomplia was studied for use in the treatment of obesity and related conditions.

How does Acomplia work? Acomplia acts by selectively blocking CB1 receptors found in the brain and in peripheral organs important in glucose and lipid (or fat) metabolism, including adipose tissue, the liver, gastrointestinal tract and muscle. Acomplia switches off the same brain circuits that make people hungry when they smoke cannabis.

CB1 receptor blockade with Acomplia acts to decrease the overactivity of the endocannabinoid system (EC system). The EC system is a recently characterised physiological system that includes receptors such as the CB1 receptor and it has been shown to play an important role in regulating body weight and in controlling energy balance, as well as glucose and lipid (or fat) metabolism.

Sanofi-Aventis has withdrawn rimonabant from the market globally and it is no longer under development. Acomplia was officially withdrawn by the European Medicines Agency (EMEA) in January 2009 due to the risks of dangerous psychological side effects, including suicidality. Previously, the EMEA had suspended Acomplia from the UK market in 2008 because the agency felt the benefits did not outweigh the risks. In June of 2007, the FDA's Endocrine and Metabolic Drugs Advisory Committee recommended against the approval of rimonabant (known in the United States as Zimulti) due to concerns over similar serious side effects. Subsequently, the FDA did not approve rimonabant, and it has never been marketed in the United States.

Rimonobant is an inverse agonist that binds to the same receptor as an agonist but induces a pharmacological response opposite to that agonist. This is more than just blocking CB1, it caused the reverse effect of THC. This was associated with increased risk of suicidal ideation and completed suicides.

CBD is a non-competitive antagonist binds to an allosteric (non-agonist) site on the receptor to prevent activation of the receptor. This blocks THC/ Anandamide effect. Anandamide is the natural THC-like substance in our bodies. CBD does not appear to

induce a response opposite to THC but does block/modulate the effect of THC. But there is still a theoretical risk that some individuals could be at risk. We need to watch for symptoms of worsening mood or negative thoughts.

I have seen a patient with a history of bipolar disorder who felt much better on 5 mg of CBD dosing 2-3 times per day. But after about 2 weeks, he became much worse, with a requirement for urgent treatment with increased medication requirement. This was like what was seen in a rat study, where anxious rats were dosed with CBD and became much calmer, but after about 2 weeks became much worse. This is the time frame to look for. Many clinical trials have a week or less.

Another concern is the mouse study of alcohol and cocaine seeking behavior. There was a reduction in drug seeking behavior with one week of dosing through the skin (percutaneous dosing). The effect was still measurable 5 months later. This is a long time in mouse time. What if adverse effects may last as long?

So less is more. First do no harm. And report any adverse effects to the FDA. This will be critical until more clinical trials are available.

The problem is the suicidality issue was not discovered in large rimonabant clinical trials including 6,300 patients, although there was found to be an increased incidence of depressive symptoms compared to placebo. It was only in post-marketing surveillance that the risks of suicidality and completed suicides were discovered. **Post-marketing data is not being collected and aggregated for the myriad of CBD products.** The larger clinical trials that are available are the ones for balanced CBD:THC for diseases like Multiple Sclerosis, which do not address the questions about CBD alone, without THC and the entourage effect of the balancing of the two effects of agonist/ antagonist.

In a trial in schizophrenia (Leweke 2012) of a total of 42 patients were randomized, 21 subjects on CBD 200 mg 3-4 times per day versus 21 subjects on a standard antipsychotic medication amisulpride 200 mg 3-4 times per day. **One of the 21 CBD patients withdrew from treatment due to persistent suicidal ideation.** Otherwise there is limited data on the effect of CBD on depression scores or suicidality as no studies have addressed this question.

Comparison of amisulpride and cannabidiol revealed no relevant difference between the two treatments (CBD appeared as effective). The confirmatory test of non-inferiority with 80% retention bound yielded a ratio of means 0.94 (CBD/AMI) with 95% confidence interval 0.55–1.59. Thus non-inferiority seems highly plausible, but could not be demonstrated, P=0.27 (one-sided).

Compared with amisulpride, **treatment with cannabidiol was associated with significantly fewer extrapyramidal symptoms (P=0.006; Figure 3a), less weight gain (P=0.010; Figure 3b), and lower prolactin increase—a predictor of galactorrhoea and sexual dysfunction (P=0.001; Figure 3c).** Furthermore, cannabidiol was well-tolerated (Supplementary Table 3) and did not significantly affect hepatic or cardiac functions. (Transl Psychiatry (2012) 2, e94, doi:10.1038/tp.2012.15)

Cancer treatment? There is much discussion about how CBD may induce cancer regression. On the other hand, in the cellular context and dosage dependence, cannabinoids may enhance the proliferation of tumor cells by suppressing the immune system or by activating mitogenic factors.

Also, in many clinical settings, including latent infections caused by HIV-1 or HSV-1, and persistent infection of the liver caused by HCV, cannabinoids lead to worsened disease outcome. **So not yet recommended for cancer.**

How much to take? The averages for CBD bioavailability by method of administration are: **6% – 15% for oral** (swallowed and digested by the GI system) **35% for oromucosal** (absorbed directly through the mouth), 34%-46% for intranasal (applied through the nose), 40% for vaporized (absorbed through the lungs). The low result for the oral is due to the first pass metabolism of the CBD before it gets to the systemic circulation. **So you need 1/3 to 1/6 as much sublingual CBD as the capsules taken by mouth (1-5 mg under the tongue vs. 15-30 mg capsules swallowed whole).**

In summary, what do I do. I take 1 mg (one spray) of the Elixinol liposomal version (similar to 2.5 mg of tincture) under my tongue about once per week, with a rare extra dose but also taking drug holidays (no CBD). It does appear to help my pain tolerance (neck pain) and anger at people tailgating me (but not completely!).

But if you try it and do not feel more relaxed and sleeping better, this approach may not be appropriate for you. Listen to your body. Your body knows.