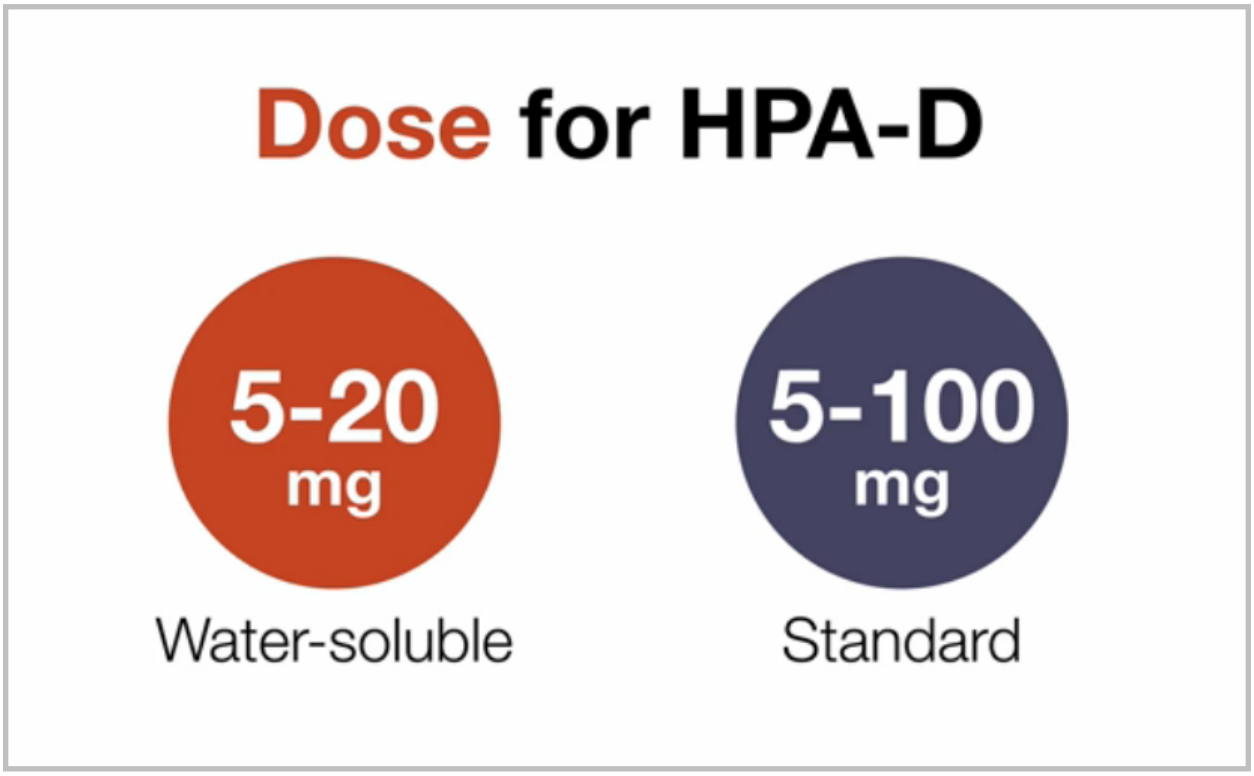
HPA-D 3-5 – Part 11

Because pure CBD is not psychoactive, it is not a Schedule I regulated substance, and it can be sold over the counter and shipped to all 50 states.

It is often sold in liquid form, occasionally in a capsule form. The delivery format of CBD does play a big role in how bioavailable it is. Water-soluble forms tend to be more bioavailable. When it is not water soluble, 90 percent of the cannabinoids can be destroyed by the liver. Water-soluble forms are also faster acting. As an important note, if any of your patients work in an environment where they are drug tested, it is possible for CBD use to result in a positive THC test, just like eating a poppy seed bagel can cause a positive for opiates depending on the type of the test. Many of the more pure products contain 0.03 percent THC or less, which is well below the federal limit of 0.3 percent, but patients should use discretion if they do get tested in their work environment.



The dosage for CBD varies tremendously in studies and depends a lot on the condition. It can range from as little as 2 mg per day for mild pain relief to 1,280 mg per day that was used in one study for schizophrenia. As mentioned, it also depends on the delivery format. If using a high-potency, water-soluble form, I suggest that most patients with HPA-D start with approximately 5 to 20 mg per day. You can increase that to 50 mg of water-soluble form at a maximum. If using fat-soluble standard preparations, start at 50 to 100 mg per day, and you can go up to as high as 400 to 600 mg per day.

As far as when to use it, I typically start with other interventions that we've talked about earlier such as adaptogens and supplemental nutrients first, and then if not successful, add CBD. However, given CBD's impact on all four drivers of HPA-D, it can be a good initial choice and particularly good for patients who have a lot of inflammation and anxiety. Those are two of the major areas where I would consider using it right off the bat. If they don't tend to respond well to a lot of other medications, CBD is generally fairly well tolerated. That said, CBD is quite expensive, especially the water-soluble brands, and it can be somewhat difficult to obtain. A lot of the manufacturers run out of stock, at least at the time of this recording, so it can be a little challenging to work with from that perspective.

Another case where I'll use CBD in the first line of treatment for HPA-D is when a patient has other conditions that warrant CBD use, such as inflammatory bowel disease, rheumatoid arthritis, MS, or if their anxiety is severe.

Summary of botanicals for HPA-D

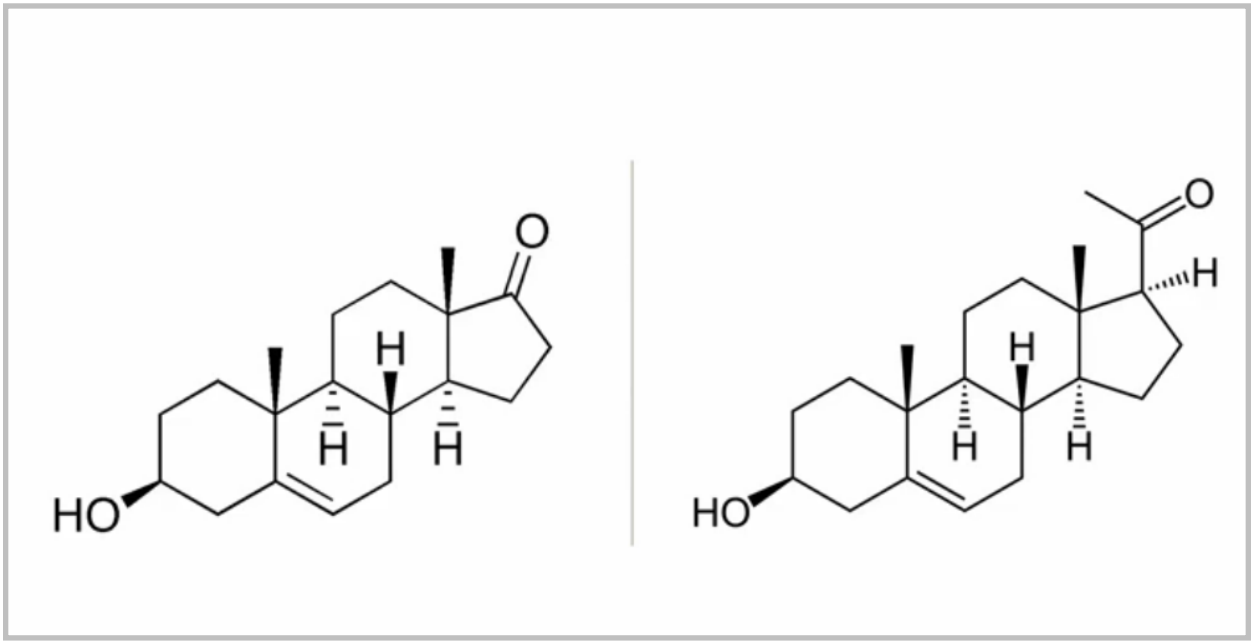
Botanical	Dosage/Comments
Eleuthero	Whole herb/powder:1-6 grams per day; as tincture, 20-40 drops BID/TID; look for 2:1 or 1:1 extract
Pregnenolone	Whole herb/powder: 1-3g daily; as tincture, 20-40 drops BID/TID
Rhodiola	Whole herb/powder: 300–700 mg/d; as tincture, 20-40 drops BID/TID
Ashwagandha (Sensoril)	Whole herb/powder: lowest effective dose 300-500 mg/d, up to 6g/d has been used; Sensoril preferred (standardized to 10% withanolides)
Cordyceps	Whole herb/powder: 1,000-3,000 mg/d; as tincture, 20-40 drops BID/TID; dose depends on quality of preparation
Ginseng	5-20 drops BID/TID; use with caution, only in hypocortisolism
Licorice	1 drop = approx 0.75 mg of glycyrrhizin; 10-20 drops in 2 oz. of water BID/TID; only in hypocortisolism
Magnolia & Phellodendron (Relora)	500 mg daily; can be taken on its own or as part of a formula
CBD	5-50 mg daily (water-soluble); 50-100 mg daily (standard)

I've listed the botanicals that we've discussed on this slide with recommended doses for each. We will discuss specific protocols in the protocol section that is coming right up, and we'll provide this slide to you in a handout format so you can refer to it.

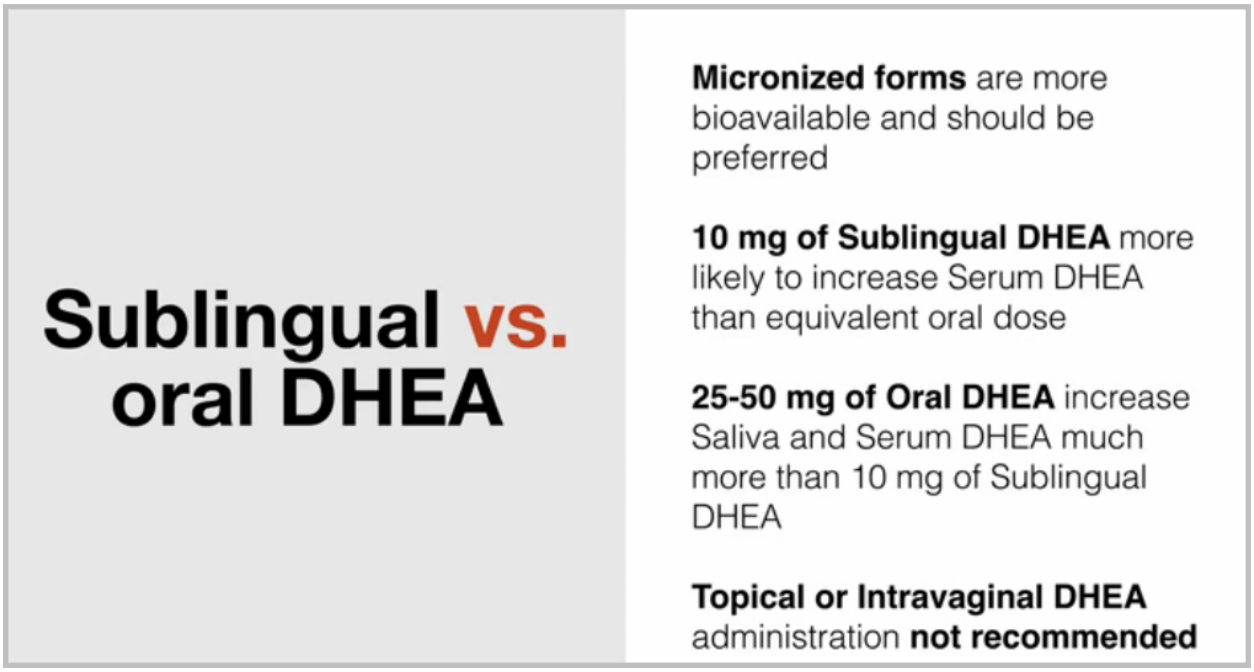
In general, I prefer tinctures for most of these botanicals because they are more potent than capsule preparations and you can more finely tune the dosage, which is often necessary because patients have pretty widely varying sensitivities to these botanicals. In terms of suppliers, I like Herb Pharm tinctures a lot. Many of them are organic and wildcrafted, and they have glycerine versions of a lot of the botanicals above for those patients who are alcohol sensitive.

Next, I want to talk a little about adrenal glandulars. The use of animal organs for therapeutic purposes is common in traditional cultures. Today, dessicated thyroid gland is still the active principle in some thyroid medications such as Armour and Nature-Throid. In the U.S., right up to the late 1940s, different bovine and one porcine adrenal preparations were prescribed for patients with Addison's disease. In most cases, dessicated organ products are not standardized for any peptides or hormones, and none that I know of have been clinically tested for HPA-related function in humans using modern research techniques, so that's the downside. They have been used traditionally for a long time and even up to the 1940s in the U.S., but they haven't been well studied in the modern research. It's really hard to say much about them other than they appear to be safe after many years of clinical use and what we can observe of using them clinically. I have personally found them to be helpful in some patients in both hypercortisol

and hypocortisol states. They seem to have a gentle, stabilizing effect. They are not as stimulating in many cases as some of the adaptogens, and when taken in the morning, they can just have, like I said, a stabilizing, kind of calming but also energizing effect. I like the Dr. Ron's brand of adrenal glandulars because he uses dessicated adrenal glands from pasture-raised animals in New Zealand.



Finally, I want to talk a little bit about supplementing with bioidentical forms of DHEA and pregnenolone, starting with DHEA. There is a lot more evidence behind DHEA supplementation than pregnenolone. It has been studied quite extensively because, at one point, it was hoped to be the kind of anti-aging panacea when research first showed that DHEA declined with age. Unfortunately, as is often the case, that promise didn't really pan out, but many studies have shown that appropriate supplementation with DHEA can have benefits in several conditions. It has shown effects improving bone mineral density in elderly women; increasing the DHEA-to-cortisol ratio and blunting cortisol's catabolic effects; and improving cardiovascular, sexual, and cerebral functions, especially again in the elderly. There are also several newer studies, though many of them are small, showing that DHEA benefits autoimmune disease, specifically in lupus, rheumatoid arthritis, and IBD, although its use for this purpose tends to be higher and around 200 mg per day. For HPA axis dysfunction, the dose tends to range from 25 to 100 mg a day and, like I said just now, up to 200 mg per day for autoimmune conditions.



It is hard to make sense of the data on sublingual versus oral DHEA, but there are some conclusions that are possible, and this comes from Dr. Williams' book. Number one is that micronized forms of DHEA are more bioavailable and should be preferred. Number two is that 10 mg of sublingual DHEA is more likely to increase serum DHEA than the equivalent oral dose. Number three is that 25 to 50 mg of oral DHEA increases saliva and serum DHEA significantly more than 10 mg of sublingual DHEA, so even though sublingual is more potent, the higher doses that are found in oral preparations are more effective. Number four is that topical or intravaginal DHEA administration is not recommended.

DHEA is considered to be safe for most people, but in a minority of cases, it can increase androgens, particularly in women. I think we covered this elsewhere, but contrary to popular belief, DHEA does not typically do this. It is not normally effective as a way to substantially raise androgen levels, especially in men. Side effects of DHEA include agitation; painful skin breakouts, which is the most common side effect I see; and sleep disturbances. The advantage to sublingual DHEA is that you can dose it more finely, but you have to take a heck of a lot of that to get the 100 to 200 mg dose that is used for autoimmunity, and oral forms might be better. I've also just seen differences in reaction to sublingual and oral DHEA. Some patients are able to tolerate much higher doses of oral DHEA than they are sublingual, and that may just come down to the different routes of administration and the way that it is metabolized as a result.

There is a lot less data on pregnenolone supplementation. The notion of pregnenolone steal, which we now know to be false, was the basis for pregnenolone supplementation for many clinicians. Still, there is some data suggesting that pregnenolone as a supplement may provide benefits for the HPA axis. Most research has focused on pregnenolone's role in mood disorders

and schizophrenia due to its function as a neurosteroid. One study showed that 50 mg per day of oral pregnenolone had modest benefits on depression and mania in bipolar subjects. Much higher doses of pregnenolone have also been studied. Up to 400 mg in healthy males in one study increased serum pregnenolone levels threefold. Interestingly enough, in that study, neither serum cortisol nor serum DHEA levels went up despite the fact that serum pregnenolone increased threefold, so this is another albeit small piece of evidence against the pregnenolone steal, and pregnenolone should not be used as a supplement to raise DHEA or cortisol levels.

Overall, it seems that pregnenolone supplementation increases neurosteroids in the brain and decreases HPA axis activation, and this probably accounts for its purported effect on modulating the stress response.

Published literature suggests that pregnenolone is safe even at doses as high as 400 mg orally. That said, in my clinical experience, it can be quite stimulating and has a tendency to cause anxiety, palpitations, sleep disturbance, and also skin issues. There is no data that compares sublingual versus oral forms or micronized versus non-micronized forms. There is really no data on lower doses, but clinically and anecdotally, patients can benefit from as little as 5 mg a day. Is it placebo? Who knows? We don't have the research to know one way or the other. I don't tend to use pregnenolone or DHEA much except in cases where other interventions are unsuccessful. I've seen a lot higher incidence of side effects. It is much more difficult to dose. There is a lot less research that is supporting them, so for those reasons, I don't tend to use them a lot in my practice.

I am currently exploring DHEA as an adjunctive treatment for autoimmune disease, however, at that higher dose, although I'm finding that many patients simply can't tolerate that high of a dose of DHEA.

Summary of DHEA and Pregnenolone

Hormone	Dosage/Comments
DHEA	Dose ranges from 25-200 mg. Higher dose of 200 mg may be appropriate for autoimmune disease. *For HPA-D, start with lower dose (25 mg/d orally, or 8-9 drops of sublingual) and increase to 50-100 mg/d as necessary. Short-term use recommended.*
Pregnenolone	Dose varies widely, from 5-400 mg/d. *For HPA-D, start with 25 mg/d orally, or 8-9 drops of sublingual) and increase to 50 mg/d as necessary. Short-term use recommended.*

Okay, here is a summary of DHEA and pregnenolone. Again, we'll provide this as part of a handout for you to refer to.