Welcome to the Huberman Lab Podcast, where we discuss science and science-based tools for everyday life.

I'm Andrew Huberman, and I'm a professor of neurobiology and ophthalmology at Stanford School of Medicine.

Today is an Ask Me Anything episode, or AMA.

This is part of our premium subscriber channel.

Our premium subscriber channel was started in order to provide support for the standard Huberman Lab Podcast, which comes out every Monday and is available at zero cost to everybody on all standard feeds, YouTube, Apple, Spotify, and elsewhere.

We also started the premium channel as a way to generate support for exciting research being done at Stanford and elsewhere, research on human beings that leads to important discoveries that assist mental health, physical health, and performance.

I'm also pleased to inform you that for every dollar the Huberman Lab premium channel generates for research studies, the tiny foundation has agreed to match that amount, so now we are able to double the total amount of funding given to studies of mental health, physical health, and human performance.

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And for those of you that are not Huberman Lab Podcast premium subscribers, you can still hear the first 20 minutes of today's episode and determine whether or not becoming a premium subscriber is for you.

So without further ado, let's get to answering your questions.

The first question is about cratum, and the question is, what are the short and long-term effects of taking cratum?

For those of you that haven't heard of cratum, cratum is a substance that comes from a tree that grows naturally in Indonesia.

The tree itself is called mitrigina speciosa, and it's been known for hundreds of years or more.

We don't really know how long, but at least for a couple of hundred years, that when people chew the leaves of this tree, they experience a mild stimulant effect.

And there's also a process of extraction whereby you can take the leaves and get high concentrations of cratum that nowadays is packaged into various supplements, most often consumed in capsule form, although sometimes it's sold in raw powder form.

Here's the key thing to understand about cratum.

Indeed, at low dosages, cratum has a mild stimulant effect.

However, at higher dosages, it has what's called an analgesic effect, that is a pain-killing

effect, and it acts as a sedative.

And cratum itself acts as an opioid in the body.

This is what's making cratum a very controversial topic these days, in particular because most people have heard of the so-called opioid crisis.

The opioid crisis has been a term coined to largely center around issues that have taken place in the United States, although these issues definitely extend beyond the borders of the United States.

But the opioid crisis is essentially the overconsumption and widespread addiction to opioids. Opioids include things like morphine, oxycodone, also called oxycontin, and there are other opioids similar to those compounds, all of which have the general effect of being painkillers and sedatives.

And in some people, again, some people eliciting a sense of euphoria, in particular at low to moderate dosages.

However, people quickly develop a tolerance to those drugs and need to consume more and more of them in order to get the effect that they initially got from a lower dosage.

And they are not just highly habit-forming, they are highly addictive.

And we can distinguish between habit-forming and addictive by simply saying that addictive means people will continue to take something or do something despite negative consequences. There are other relevant definitions of addiction as well.

I define addiction more broadly as the progressive narrowing of the things that give you pleasure. And indeed, when people get addicted to opioids, it is a very bad picture.

It often hampers many, many areas of their lives and seriously so.

So the opioid crisis refers to the overprescription of opioid drugs.

That's sort of what it's generally taken to mean, but it also includes accessing opioids such as morphine, oxycodone, et cetera, through gray market sources, through black market sources, and on and on.

And of course, the acquisition of the drugs is just one piece.

It's also the overconsumption of those drugs and of course, the addiction to those drugs, which has proved to be so pernicious.

So what does this have to do with cratum?

Cratum is also an opioid and we'll talk about how it differs in its opioid properties from the drugs I just talked about because it is different from morphine and hydrocodone, but it also has some similar properties as well.

But the deal with cratum is that a good number of people out there have managed to wean themselves

off opioids such as morphine and hydrocodone through the use of cratum.

And that has been used as justification for keeping cratum on the market and keeping it legal.

However, and this is a very important however, cratum itself has also proved to be not only habit forming, but addictive, especially when taken at dosages that exceed that lower dose that just generally creates a bit of stimulant, a little bit of euphoric effect.

When people start taking higher dosages of cratum, it is very clear that it does become addictive and itself is very hard to come off of so much so that people experience so

called cratum withdrawal.

Now the reason I mentioned that cratum has been used by a good number of people to wean themselves off of the more potent forms of prescription opioids is that when I solicited for questions about cratum on social media, it was a very binary response.

In fact, there was one camp, a very rabid camp that said cratum is terrible.

I took this stuff.

I got addicted.

It was extremely hard to come off of.

There were additional comments in there, such as I know somebody who literally had to go to rehab because of cratum, who developed a bunch of other addictions because of cratum. Essentially many, many responses of people who had only bad experiences with cratum, meaning they liked it enough at first that they continue to take it and it became addictive for them or somebody that they know.

However, there was another camp that was equally vocal, which kept saying no. If one really adheres to the lower dosages of cratum, cratum itself can be a useful tool for getting off other opioids.

And there were even a few bona fide medical professionals, medical doctors, that is, and I happen to know them and their reputations is quite good, who chimed in and sort of reconciled the two camps by saying, indeed, if one can avoid taking cratum at all, you should. There is no reason to take this thing thinking that it's quote unquote good for you. You would be wise to avoid taking it because there is a high probability if you take it at a given dosage or at a dosage that is going to get your brain and body into a state of euphoria, analgesia, and that sort of classic opioid effect that it's going to become habit-forming or addicting for you.

That said, these same medical professionals acknowledged that a fair number of people that they knew managed to get off of the more potent forms of opioids, such as morphine, oxycodone, and so forth, using cratum.

And they said, well, if it's a choice between being addicted to morphine and hydrocodone versus taking cratum and addicted to those substances and cratum somehow allowed them to taper off of those substances, that they would look more favorably upon cratum if and only if they would also commit to progressively lowering their dose of cratum and eventually coming off of cratum.

So the general takeaway from all of that is if you can avoid taking cratum, meaning if you haven't taken it already, don't.

And that reminds me of a very important point, which a guest on the Huberman Lab podcast, Dr. Robert Merlanca, who's a MD and PhDs, my colleague at Stanford School of Medicine, is a world expert on the mechanisms underlying addiction and dopamine and drug reinforcement, among many other things.

What he said on the podcast is absolutely true, which is that it is impossible to get addicted to a substance that you've never consumed.

That might seem obvious, but think about that one again.

It is impossible to get addicted to a substance that you've never consumed.

So I think the safest statement to make is if you have not tried cratum, you would be

wise to avoid it because you stand a chance to become addicted to it.

If however you are somebody that's addicted to other forms of opioids, you absolutely should talk to your physician about that and how to get off of those opioids.

But there is evidence that some people have used cratum to successfully wean themselves off the more potent forms of opioids that I talked about, namely morphine and hydrocodone as well as a few others.

Now, if you're somebody who already takes cratum, you need to be very thoughtful about the dosage that you take.

And you also need to be thoughtful about the fact that people differ dramatically in their response to opioids.

This is so important and people do not talk about this enough.

We hear, for instance, that, oh, you know, if people are taking anywhere from one to five grams, maybe one to six grams of cratum per day, that's keeping it in the dosage range for which people don't generally tend to get addicted.

People hear things like that.

And by the way, when I say one to five or one to six grams per day, I'm not talking about the individual compounds that are present in cratum.

There are a couple of different plant alkaloids I'll talk about in a moment that are present in cratum, and these have different effects on the opioid system.

So nowadays, some of the companies that sell cratum, and by the way, this is sold over the counter as a supplement, it does not require a prescription to purchase at least at this point in time in the United States.

Some of these products will have a higher concentration of one or the other alkaloids within them, such that you can't really compare one gram of one brand of cratum to one gram of another brand of cratum, because they can have wildly different levels of these different alkaloids, and these different alkaloids have wildly different impact on different aspects of your brain and body biology, in particular, how much they tend to impact the so-called endogenous opioid system.

Okay, so when we talk about dosages, we have to keep this in the back of our mind, and we have to keep in the back of our mind that there does seem to be a subgroup of people. We don't know how big this subgroup of people is, but we know it's not everyone, but it's somewhere between 10 and 40% of people seem to respond to opioids in a particularly potent way.

They really like them, and perhaps not surprisingly, people outside of that category don't tend to like opioids.

I can certainly say that I am somebody who, when I've been prescribed things like Vicodin or any other opioid post-surgery for pain, I hate taking those drugs.

I absolutely hate it.

I'd rather deal with the pain.

They make me nauseous.

They make me feel terrible.

That said, I know people who love opioids.

It's like a natural fit for their chemistry in the sense that it tends to evoke more euphoria.

They just immediately like the feeling.

Some of you may remember the episode of the Huberman Lab podcast that I did about alcohol, and there, too, I discussed the fact that about 8% to 10% of people who consume alcohol get an increased dopamine response to alcohol that's not observed in other people.

That particular subgroup of people is very, very at risk for developing alcohol use disorder.

That particular subgroup of people is very, very at risk for developing alcohol use disorder, sometimes called alcoholism, because they can drink in a way and they experience a high from drinking in a way that other people simply do not experience.

Now, like everybody else, if they consume too much alcohol, they get drunk, so it's not about the drunk effect.

It's about the dopamine and other sorts of chemicals that are released in those people in response to alcohol that other people just don't seem to experience at the same level of potency.

So, again, with things like cratum and the other opioids, there's a category of people and it's a much larger category of people.

Again, 10% to 40%, we don't know exactly how many because the studies are not really completed and there aren't enough of those studies yet, unfortunately.

When those people take an opioid, wow, oh, wow, do they like it?

And those people in particular are very much at risk for developing an addiction to opioids.

And so those people especially should never, ever go near cratum if they haven't, or if they are already taking cratum, these are the people that are constantly ratcheting up their dose.

These are the people that tell you, no, I'm not addicted, but if you were to say, hey, all right, well, then let's do an experiment where you don't take cratum for a week. Those are going to be the people that are suddenly going to get anxious about the mere idea of that.

I've also talked about this in reference to cannabis when I did an episode about cannabis. Again, I'm not putting a blanket statement out there about cannabis as being good or bad on that episode.

I talked about the fact that cannabis does indeed have various therapeutic uses, but that there are a good number of people who rely on cannabis for anxiety control and other ways of modulating their brain chemistry and bodily chemistry such that if you were to say, hey, are you addicted to cannabis?

They'd say, no, I don't have to smoke cannabis.

I don't have to take my edibles.

But if you were to push them a little bit and say, all right, well, then let's do an experiment where you don't consume any cannabis in any form for 10 days.

They don't like the idea of that experiment at all.

So much so that were they to run that experiment, they would experience a lot of the withdrawal symptoms associated with addiction.

So I can't in good faith say that cratum is safe for everybody because it is simply not.

Now, is it safer than the other opioids?

And if so, why?

Well, in order to address that, let's take a short glance at the pharmacology of cratum

and how it works in terms of its neurochemistry in the body.

And I'm going to keep this pretty brief because in the future, I'm going to do an extended episode all about opioids and I will include cratum in that conversation.

But just to back up a little bit and discuss what opioids are, opioids are compounds that can activate the so-called endogenous opioid system.

All of us have within our brain and body the capacity to release our own opioids.

That's right.

You have opioids within your body.

They are released from neurons and they bind to so-called opioid receptors.

Perhaps some of you have heard of the so-called runner's high.

The runner's high is a euphoric state.

It's a fairly mild euphoric state in most cases, but it's a euphoric state induced by long duration effort, AKA the runner's high.

The runner's high is just a phrase used to explain that when we engage in long duration, repetitive action effort, the body starts releasing these endogenous opioids.

They bind to receptors and they trigger things like analgesia, relief from pain.

They trigger mild euphoria.

They tend to change our perception of the outside world, make things look more beautiful, shiny.

They give things a little bit of a sheen.

What I just described is a mild version of what people experience when they take something like morphine.

When people take morphine, there's a more of a sedative effect.

There's more of a euphoric effect and there's more of a dreamlike effect.

And again, it will depend on dosage.

Cratum and morphine and hydrocodone all have the property of acting like the endogenous opioids, but at much higher potency.

When you bring them into your system, they cross the blood-brain barrier.

So they go into the brain and they bind to a number of different opioid receptors.

The mu-opioid receptor, by the way, these names all follow Greek alphabet letters.

So the mu-opioid receptor, the kappa-opioid receptor, they're a bunch of different ones.

Cratum binds preferentially to the mu-opioid receptor and somewhat to the kappa-opioid receptor.

There's a big misconception out there.

A lot of people, especially people who are proponents of Cratum, will say no, morphine and hydrocodone bind the mu-opioid receptor, whereas Cratum binds the kappa-opioid receptor.

So it's a different compound, very, very different, not true, not true.

Cratum, morphine and hydrocodone all bind to the mu-opioid receptor, and that's what's largely responsible for its opioid-like effects, especially when you get the dosage up to a level where you start getting the mild sedation, the analgesia, the pain relief.

And keep in mind, a lot of people are taking Cratum because they want pain relief.

And when that mu-opioid receptor system is activated, it indirectly activates a lot of the reinforcement circuitry in the brain that relates to dopamine and serotonin.

This is another area that we'll go into in more depth in the future, but there's been

a lot of controversy.

People are saying, oh, you know, Cratum doesn't trigger the dopamine system, therefore, it's not addictive.

But that is simply not true.

It indirectly activates the reinforcement circuitry that includes both dopamine and serotonin.

But its primary effect is to hit this mu-opioid receptor system that exists in a bunch of places in the brain, but mainly in the brainstem and a structure called the periaqueductal gray nucleus, which then provides pain relief.

It triggers a number of different shifts in cognition.

It's what creates that mild euphoria, et cetera, et cetera.

Now how can we be so confident that Cratum is acting so similarly to hydrocodone and to morphine, albeit with lower potency?

And the reason is if you give people a drug that blocks the mu-opioid receptor prior to them taking Cratum, they don't experience any of the classic effects of taking Cratum. No euphoria, no analgesia, no sedation, even at the low dosages, no mild stimulant effect.

So we really have to look at Cratum as an opioid.

That's just the honest truth.

And if you're somebody who doesn't like this message because you like Cratum, I'm not telling you that you don't like Cratum.

I'm telling you, you likely like Cratum because it's an opioid.

So again, if you go online and you start asking questions about Cratum, again, you're going to see these two camps.

You're going to see the Cratum is terrible.

It's addictive.

It's everything bad camp.

And then you're going to see the other camp out there, very vocal as well, talking about how Cratum helped them avoid other things that are worse.

And this is an argument that frankly, I don't think we want to lean on.

The idea that substance A is not as bad as substance B and that making substance A unavailable is just going to send everyone running for substance B. That's a weak argument, frankly.

I heard this argument around cannabis.

And by the way, I think pretty balanced about cannabis.

If you listen to the episode I did on cannabis, I think you'll agree that I believe that cannabis has its therapeutic applications.

I also believe that young people, especially young males with a predisposition to psychosis should not be taking high concentration THC cannabis because the data tell us they are already at risk of psychosis and they are at a much greater risk of psychosis if they do.

So I think I'm pretty balanced about the story on cannabis.

But I often hear the argument, oh, cannabis isn't as bad as alcohol and therefore cannabis is good.

That's simply not rational.

What we should be saying is whether or not it's cannabis or alcohol or Cratum or any

substance for that matter, what are the potential benefits?

What are the potential risks?

And again, this is far too much than we can go into in this AMA and we will go into in a future full length episode of the Huberman Lab podcast.

But the other thing to really keep in mind is the lack of regulation over Cratum supplements.

Now as many of you know, I am a fan of many, not all, but many supplements in certain conditions.

I always say behaviors first, then nutrition, then if and only if it's needed, rely on supplementation.

But supplementation is a big category.

But when we're talking about supplements that are opioid compounds, I start to get nervous because of the high abuse potential and the high addiction potential of opioids.

And Cratum is included in that category.

A couple of other key notes about Cratum.

While death directly from Cratum is fairly rare, it has happened.

Now, hydrocodone and morphine suppress respiration, actually suppress breathing by way of a mechanism

that if you're a listener of the Huberman Lab podcast, you know about, which is the so-called physiological sigh.

Many of you heard me talk about the physiological sigh is something that you do voluntarily, the double inhale through the nose and then a long exhale in order to rapidly reduce your level of stress.

As far as we know, that's the fastest way to deliberately lower your level of stress.

But the physiological sigh was discovered in the 1930s as a spontaneous pattern of breathing that occurs involuntarily in sleep in order to reinflate the lungs and offload carbon dioxide and bring oxygen back into the system on the subsequent breath.

When I interviewed Dr. Jack Feldman, who is a professor at University of California, Los Angeles, and really the pioneer of the modern neuroscience understanding of respiration, he talked about some studies in his laboratory that were exploring why people die when taking opioids.

This is a major issue associated with the opioid crisis.

And what he mentioned was that the opioids bind to particular receptors in the brain stem locations that generate physiological sighs.

So opioids when taken as drugs suppress physiological sighing and do so during sleep and lack of adequate respiration, meaning people stop breathing during sleep is one of the primary reasons why people die when they take opioids.

Now cratum is not known to suppress respiration when taken at low to moderate dosages. But when combined with any other opioids and certainly when combined with alcohol, it can suppress respiration.

And while the data on this are fairly scant, there is some evidence that cratum induced death is caused by suppression of the respiration system.

So again, death due to taking cratum at the dosages that are recommended on most commercial packaging is fairly rare, although it has happened.

It's unclear if it happened because it was taken in combination with other compounds.

That seems likely, but we can't forget that a lot of people are taking cratum at much higher dosages and in fact, progressively higher and higher dosages from these over the counter sources.

And with increased dosage, there is, yes, an increased risk of respiratory failure.

So again, all of this points to the fact that cratum is simply not a benign substance.

So if we're going to be very honest, the addictive potential of cratum is real.

It is exacerbated for some people compared to others, but it is real.

It's very similarities to other more potent forms of opioids are what make it attractive for some people who are trying to come off those more potent form of opioids.

But the goal, of course, is to completely come off all opioids and cratum itself can be a bit of a trap.

It can be a trap in the sense that people who have never taken other opioids can become addicted to cratum itself.

That is absolutely clear.

That can happen.

It has happened in a great number of people.

It's also clear that cratum can potentially be a trap.

Notice I said potentially because if people are trying to come off other more potent forms of opioids and then they use cratum to do that and then they're ratcheting up their dosage of cratum such that they're now matching the endogenous response to cratum in a way that doesn't really distinguish from the effects that they were getting from morphine and hydrocodone.

Well then they're just using a different form of morphine and hydrocodone.

And I'm sure that some of you are out there saying that is ridiculous.

You cannot compare the effects of cratum to the effects of hydrocodone.

But the potency is about one sixth of hydrocodone.

And there are people out there who are just increasing and increasing both the dosage and modifying the type of cratum that they're taking so that they're getting the cratum that has a particularly high concentration of one of the alkaloids that hits that mu-opioid receptor hardest.

And in doing so, sure, they're not getting the pure hydrocodone effect, but they're getting really close.

So my advice would be if you haven't touched cratum, don't touch it at all, ever.

If you are taking cratum, you need to take note of what we just discussed.

Thank you for joining for the beginning of this Ask Me Anything episode, to hear the full episode, and to hear future episodes of these Ask Me Anything sessions, plus to receive transcripts of them and transcripts of the Huberman Lab Podcast Standard Channel and premium tools not released anywhere else, please go to hubermanlab.com slash premium. Just to remind you why we launched the Huberman Lab Podcast Premium Channel, it's really two-fold.

First of all, it's to raise support for the Standard Huberman Lab Podcast Channel, which of course will still be continued to be released every Monday in full length.

We are not going to change the format or anything about the Standard Huberman Lab Podcast,

and to fund research, in particular research done on human beings, so not animal models, but on human beings, which I think we all agree is a species that we are most interested in.

And we are going to specifically fund research that is aimed toward developing further protocols for mental health, physical health, and performance.

And those protocols will be distributed through all channels, not just the premium channel, but through all channels, Huberman Lab Podcast and other media channels.

So the idea here is to give you information to your burning questions in depth and allow you the opportunity to support the kind of research that provides those kinds of answers in the first place.

Now, an especially exciting feature of the premium channel is that the Tiny Foundation has generously offered to do a dollar-for-dollar match on all funds raised for research through the premium channel.

So this is a terrific way that they're going to amplify whatever funds come in through the premium channel to further support research for science and science-related tools for mental health, physical health, and performance.

If you'd like to sign up for the Huberman Lab premium channel, again, there's a cost of \$10 per month, or you can pay \$100 up front for the entire year.

That will give you access to all the AMAs.

You can ask questions and get answers to your questions.

And you'll, of course, get answers to all the questions that other people ask as well.

There will also be some premium content, such as transcripts of the AMAs and various transcripts and protocols of Huberman Lab Podcast episodes and not found elsewhere.

And again, you'll be supporting research for mental health, physical health, and performance.

You can sign up for the premium channel by going to hubermanlab.com slash premium.

Again, that's hubermanlab.com slash premium.

And as always, thank you for your interest in science.