Sawbones 583: Kratom

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["Medicines" by The Taxpayers plays]

Justin: Hello, everybody, and welcome to Sawbones! A marital tour of misguided medicine. I'm your co-host, Justin McElroy.

Sydnee: And I'm Sydnee McElroy.

Justin: I'm feeling pretty excited, babe.

Sydnee: Are you feeling excited about this episode?

Justin: Hm, sort of.

Sydnee: Or about the Capri Sun you're opening.

Justin: Yeah, it's the Capri Sun.

Sydnee: Yeah.

Justin: I was—I looked in there, and I saw a Capri Sun Moon Punch, and I was so overwhelmed with thirst, and so—I mean, all I could think about was how refreshing it was about to be. I got a second one.

Sydnee: You got two.

Justin: Because I saw—because I knew that this episode was going to be about Kratom, and I knew that I was going to ask if I could have it and you were going to say no so many times—

Sydnee: Yeah, you can't have it.

Justin: That you wouldn't be able to tell me no about the two Moon Punches.

Sydnee: Are you—

Justin: So you would be like—you'd feel bad about the—how you told me no so many times about Kratom, that I'd be like, I might crack open a second Capri Sun Moon Punch, I knew you wouldn't be like "No."

Sydnee: Mm-mm. Did you tell Cooper we had more of the Moon Punch? Because she loves the Moon Punch. And I told her we were out. So—

Justin: I moved it downstairs.

Sydnee: [gasps] You have a secret supply.

Justin: I won't drink the second Moon Punch though.

Sydnee: She settled for Tropical Punch, but she wanted Moon Punch.

Justin: I will swap that Moon Punch out mid sho—mid episode, at like the commercial break. I'll make this first Moon Punch last until the act break, then I'll refresh my Capri Sun for the second half.

Sydnee: Do you think this is—do you think this is some sort of a like trademark violation for us, Moon Punch?

Justin: Oh my god, it hitted even harder—it hit even harder—

Sydnee: Didn't Charlie—

Justin: Than I thought it would.

Sydnee: Charlie started with the punching the moon.

Justin: Yeah.

Sydnee: And this is Moon Punch.

Justin: Oh, it is Moon Punch. I didn't even realize that. What the heck?

Sydnee: I feel like we got a lawsuit on our hands right here, Justin.

Justin: A lawsuit on our hands.

Sydnee: First—

Justin: Here they come, probably. Probably Unilever. [chuckles]

Sydnee: Speaking of—speaking of legal gray areas, let's talk about Kratom. What do you know about Kratom, Justin? It's very popular.

Justin: Yeah. I don't actually know anything about Kratom. I—

Sydnee: You don't know anything about Kratom?

Justin: No, I remember when we were at ha—we had some people over recently and everyone was like, "Syd, can we do Kratom?" And you were very much like—

Sydnee: No.

Justin: "Listen, y'all, no Kratom."

Sydnee: No, I said don't do Kratom. Well, there were—there were also—we had our—it was like a big friend and family gathering, so there were kids around. So I was like, "Listen, kids, don't do Kratom." So, I first became aware of Kratom—it's been a while. It's been around for a while. And it's not new, it's just all of a sudden become super popular, and there's a good reason for that. But it's been around for a while, and it was first brought to my attention by some patients of mine.

Justin: Oh, really?

Sydnee: Who would talk about it as—because of—we live in the middle of where the opioid crisis has I think hit the hardest.

Justin: Mm-hm.

Sydnee: Here in West Virginia. And so I have a lot of patients who have struggled with trying to use less pain medication or trying to find alternatives for their substance use disorder. Or just because they haven't been diagnosed with substance use disorder, but they have had pain meds in the past. They're not on them now, but they're looking for something that works similar. You know? So, I had a lot of patients ask me about Kratom. And I had read about it, and at the time I thought, well, this is like an herbal thing that works a little bit like opioids, but it doesn't seem like it works a lot like it.

Justin: Mm-hm.

Sydnee: Probably not a good idea, because if it if it works like an opioid, it could be addictive. But at the time when I was being asked these questions, we really didn't have a lot of data.

Justin: It's always wild when you start to see these things pop up like, it feels like it's always at like… truck stops first.

Sydnee: Mm-hm.

Justin: You start seeing it and you're like, wait, is that like a real drug? Or is that like, you know, poppers or something?

Sydnee: [titters]

Justin: And then you start seeing 'em pa—then all of a sudden it's in a dr—in a drink and you're like, hold on a second! Is this—like, what am I drinking here? Is this sugar speed? What's happening?!

Sydnee: Well, and then Joe Rogan just takes a handful on his podcast—

Justin: Crunches 'em!

Sydnee: And is like—

Justin: Yeah, crunches—

Sydnee: "Here I go!"

Justin: 'Em up. puts 'em on a pita.

Sydnee: "What was that dose?"
"I don't know. Some." So, it—the big appeal that people will tell you about kratom, and we're going to get into where is it from, what is it, what does it do, and should you do it? Which my answer will be no. It is derived from a tree, so it's from a plant, and everybody's really big on that. They're always like, "It's from a plant, it's safe." Which is especially weird when we're talking about the opioid space.

Justin: Mm-hm.

Sydnee: Because Justin, when I say opioid, you might think of the word "opium."

Justin: Which comes from poppies.

Sydnee: A plant.

Justin: A plant.

Sydnee: And there's nobody out here saying we should all do more opioids because they're from plants. [chuckles]

Justin: Somebody's probably saying that.

Sydnee: Probably somebody. So like, the argument that wherever kratom started was a plant, although what you're getting today may well not be a plant. But whatever it started out was a plant, and so therefore it's safe, is a—we know that's not a good argument.

Justin: Mm-hm.

Sydnee: There are plenty of things in plants that when you synthesize them and purify them and concentrate them, and then put them in your human body, can hurt you, or have some sort of effect that could be bad, good, toxic, dependent on the dose. We know this.

Justin: Plants are *wild*.

Sydnee: Plants are wild.

Justin: Good, bad, poison, not poison? They got a whole poison garden over there near the… what is it? It's near…

Sydnee: Barney Castle.

Justin: Barney Castle! Right?

Sydnee: Yeah.

Justin: There's probably others.

Sydnee: Yeah, I think there's lots of 'em.

Justin: You know. Because there's that many plants that are bad—

Sydnee: There's a lot of poison plan—

Justin: For you.

Sydnee: Yes. And so plants certainly can be active, and that can be positive or negative. But the argument "you should eat it because it's from a plant" is not a good argument. So, it—this is—kratom is derived from a type of tree that's related to the—to the coffee tree, so that people are like, "Ah, it's a coffee related substance."

Justin: You know. [chuckles]

Sydnee: It's like coffee. It's not.

Justin: You know, like a cup of joe. [chuckles]

Sydnee: Metragona speciosa—

Justin: Wait, is a…

Sydnee: Metragina.

Justin: Speciosa?

Sydnee: Mitragyna speciosa, not metragona. I don't want to say "mitragyna," that feels weird. It sounds like gynecology, and it has nothing to do with that.

Justin: Yeah.

Sydnee: Mitragyna speciosa. That's the plant.

Justin: Yeah.

Sydnee: It's native to southeast Asia.

Justin: It sounds like a spell you learned at Hogwarts and then the teacher's like—

Sydnee: Mitragyna speciosa!

Justin: "If anybody casts this as a joke, you will be removed from the school. It's a serious spell! Don't do it as a joke."

Sydnee: It contains—this plant contains a lot of alkaloids, 40. And what are alkaloids? First of all. Because that's what everybody says, "Well, I mean, the—it contains 40 alkaloids." And then if you don't know what an alkaloid is, that could sound bad, good, scary, wonderful, you don't know.

Justin: We like alkaline water, right?

Sydnee: [titters]

Justin: Like good—that has a lot of the same letters. [chuckles]

Sydnee: It's an organic compound that has at least one nitrogen, that's all an alkaloid is.

Justin: Yeah.

Sydnee: That can mean a lot of different things. Sometimes we also will call, if we can take whatever the substance was naturally occurring in the plant and then synthesize it in the lab, we might call that an alkaloid too.

Justin: Is "oid," does that mean… like as—is that artificially created or like a derivative?

Sydnee: No. This is the original—

Justin: Like the oi—

Sydnee: This is the OG. The "oid."

Justin: The "oid" ending.

Sydnee: The "oid" means this is the naturally occurring—

Justin: Oh, this is the—got you, okay.

Sydnee: Yeah, this is the thing.

Justin: I'm with you.

Sydnee: Yeah. So… so, but we could make a synthetic thing that we might also call an alkaloid, if it essentially is the same thing. We just didn't get it out of a plant leaf, we made it in a lab, but it's the same thing.

Justin: Gotcha.

Sydnee: Got—okay.

Justin: Chemically it's indistinguishable.

Sydnee: Yes. And this—and this is going to become relevant when we talk about modern kratom preparations. So, alkaloids are made by a lot of different things, bacteria, fungus, plants, animals. And they can do a lot of different things. We know that alkaloids have a wide range of activities within human bodies, probably animal bodies too, we know.

And so, eating plants can have an impact on you from a pharmacological perspective. This is not groundbreaking, but this is where something like kratom comes into the conversation. Does it do stuff? *Yeah*. So, should we just eat all plants that do stuff? No. [titters] And will eating a plant that does stuff have the same effect on you as if you take the substance in the plant that does stuff, and concentrate it and put it in a gummy?

Justin: No.

Sydnee: No. And that's really key to understand, it's the reason why we don't tell people who we want to put on digoxin, "Go eat that foxglove." While yes, the substance that is the, you know, that we made digoxin out of is in foxglove, I have no way of knowing how much would be in the foxglove plant you chose to eat today.

Justin: Right! We have to refine these things we have to process them and we have to—

Sydnee: Yes.

Justin: Right?

Sydnee: Now, kratom has been used in traditional medicine for centuries. And good reason, it has stuff in it that does stuff. And so, you know, it's—we talk about on the show, like one of the most prominent things when you get

to like sort of full-traditional medicine, the stuff that tends to actually work is usually like a laxative. [chuckles]

Justin: Sure, a laxative or a—

Sydnee: A diuretic.

Justin: Or what's the word…

Sydnee: In a medic.

Justin: A medic.

Sydnee: Yeah. Something that you can see the outco—you know if it worked or not. [titters]

Justin: Yeah.

Sydnee: There's no question. You don't—you might not always know—

Justin: The proof is in the proverbial pudding.

Sydnee: Prior to us measuring blood pressure, you would never know if a medicine was lowering your blood pressure. You know if it made you poop or not.

Justin: Yeah.

Sydnee: Right? So, it's probably been popular and used for a long time because it does something, particularly in Thailand, Malaysia, Indonesia, parts of Papua New Guinea. This plant has been—it grows wild. It's also been cultivated because it is used for several different things. So, small doses of kratom, it is usually thought of as something to give you energy. And this is part of what you'll see advertised in gas stations. People would chew the leaves while they were out working or fishing to try to like keep 'em awake.

Justin: Okay.

Sydnee: You see the coffee relationship here, where you could promote this as like, "Oh, it's just like, you know, you drink some coffee, you chew a kratom leaf."

Justin: Yeah.

Sydnee: No big deal. And they also found that it was good for pain relief, so it would be used for pain relief for stomach issues, again, fatigue. And there were a lot of different preparations, you could use it for—or you could just chew the leaves. So you just pick them right off and chew 'em. You could turn it into some sort of tea, that's a very traditional preparation of it, br—stew—brew it into a tea. Which there are a lot of things like that, like we—I have gotten into foraging recently and we collect nettle and brew it into a tea.

Justin: Sure.

Sydnee: Not really because I think it's doing something, but because Cooper likes the taste of it.

Justin: Mm-hm.

Sydnee: And it's out in the yard and that's fun. But there also were some historical accounts where people who were addicted to opium started touting the benefits of kratom as a way to alleviate withdrawal symptoms.

Justin: Same way we would use like methadone or something like that?

Sydnee: Similar, but not exactly. And I want to make sure to make that clear, kratom as we know it at this moment would not be a replacement for methadone or buprenorphine, commonly known as suboxone. It would not work in that same way. Because a key—a key factor with those other medications is that they are not—the goal is not to produce euphoria. You're not trying to get high.

Justin: You can't do that anymore, that—it's actually the series finale just aired, so you can't produce any more Euphoria.

Sydnee: Thank goodness. [titters]

Justin: Legally speaking.

Sydnee: I can't say I'm sad about that one. [chuckles] So, the—so, it is—I—yes, that is the way people would sort of say like, "Hey, you can use it." But they're not really saying use it to help yourself stop using opium, as much as like if you can't get opium and you're going through withdrawal—

Justin: Here's another drug?

Sydnee: Here's some kratom.

Justin: Okay.

Sydnee: So like—and again, I just want to make that distinction, because this isn't the same as like, "Let me put you on a standardized medication that will help reduce your substance use." That's not what this is.

Justin: Not this.

Sydnee: Okay? And again you can—you can chew it, you can make all kinds of different products that would—that would cause these kinds of results, and has been used for a very long time. We first figured out the chemical that probably was doing stuff, the alkaloid that was most responsible for the effects, back in 1921, mitragynine. So, this is the active substance.

Justin: Okay.

Sydnee: That we think primarily makes whatever you feel like kratom is doing for you, it's primarily the mitragynine doing it. And there's some other stuff in there too, but this is the—this is the top alkaloid, okay?

Justin: Mm-hm.

Sydnee: And you will see that sometimes advertised today, and it's often like abbreviated as MG2, you'll see that out there, but mitragynine was advertised separate from kratom.

Justin: Okay.

Sydnee: Like locally it was just known as kratom, or sometimes tom-tom, but it would also be called mitragynine on some packaging, okay? Through later studies they started to isolate like, okay, mitragynine's the thing—and this was back in the '60s—that seems to have an effect on people. And specifically, they started to find a very small amount of 7-hydroxymitragynine, which is a very potent version of that mitragynine.

Justin: Okay.

Sydnee: Is the best way to think about it. I mean, it—when it comes to like chemical compounds, sometimes we can make one little change, add one little thing to a ring, and make it way more potent or way less potent.

Justin: Hm.

Sydnee: And what they found is that through—and this may be naturally occurring in the plant itself, or it may be through our interactions with mitragynine. In our bodies, we create 7-hydroxymitragynine. But one way or another, what we know is that while it only makes up less than 2% of the alkaloids in kratom—

Justin: Mm-hm.

Sydnee: It is the most potent piece in terms of having any effect in the human body.

Justin: Okay.

Sydnee: Does that make sense?

Justin: Yeah.

Sydnee: Okay. So, what we know about mitragynine, and even more so about the 7-hydroxy—which i'm going to go ahead and say, if you've heard of 7-OH, this is what I'm talking about. And that is also now advertised at, you know, drugstores, gas stations, anywhere that they're selling kratom products you'll see—kind of like with with CBD, they did the delta-9, it was like the new—

Justin: Right, yeah.

Sydnee: It's just a spin on it. It's the same idea. 7-OH is the new kratom. It is kratom.

Justin: Is like a refined… in layman's terms, would you—could you describe it as a refined version of kratom?

Sydnee: If kratom is—let's imagine kratom as the leaf.

Justin: Okay.

Sydnee: You're imagining a leaf, just a green leaf.

Justin: Yeah.

Sydnee: We pulled out of it mitragynine, which is the most potent part of it.

Justin: Mm-hm.

Sydnee: And this is just a chemical molecule. And then we purified that into 17-O—or to 7-OH. And then we made a ton of it.

Justin: We just never knew when to leave well off alone, you know?

Sydnee: That's 7-OH.

Justin: Yeah.

Sydnee: Yeah. We took the—we took the thing that did the thing—

Justin: And made it…

Sydnee: Yeah.

Justin: More?

Sydnee: Made it more.

Justin: Yeah.

Sydnee: Yeah. The effects are dose dependent. In low doses of mitragynine or 7-OH, you are going to feel more energy, so it does tend to have some stimulant property when you take a little bit. Which is probably why people working in the fields would chew the leaves and wouldn't be harmed by it, but would feel subjectively more energized.

Justin: Okay.

Sydnee: Right?

Justin: Yeah.

Sydnee: But when you take more of it, what we've noticed is that it can start to have the opposite effect.

Justin: Oh, like a—

Sydnee: Sedative.

Justin: Mm-hm.

Sydnee: Yes.

Justin: Okay.

Sydnee: Like knocks you out, puts you to sleep. It also does, we know, help with pain at higher doses, or we think. When I say "we know," let me be

really clear, there are no great clinical studies on any of this right now, not kratom, not seven—not 7-OH, not mitragynine. There are no large double-blind, placebo-controlled trials where we have exposed individuals for various—you know? We have not done that. A lot of this data is pre-clinical, or small groups of people who are using unregulated products—

Justin: Yeah!

Sydnee: With variable amounts of the substance.

Justin: And you gotta wonder like who's funding it and everything, yeah.

Sydnee: Yeah. So, I do not have good data to tell you for sure. But what we think, based on what we know so far, mainly on pre-clinical data, meaning like in a lab and in animals, we know that at low doses it might make you feel more energized, and then at higher doses it helps with pain and sedates you.

There are a ton—there's a ton of like pre-clinical research that's been done on other things that it was used for historically, like inflammation, antibacterial. You will see stuff out there about weight loss, in addition to pain, depression, anxiety. And what we know so far is that in a lab we see some effects.

Justin: Mm-hm.

Sydnee: But we don't know in humans because we haven't done it.

Justin: Right.

Sydnee: Right? So, it's like a lot of—when we get into some of the herbal realm, it's like a lot of those substances, right?

Justin: Right. The science isn't there.

Sydnee: Yeah. Like in a petri dish, it seemed to do this, we don't know what it'll do in a human body. But the key thing is the mitragynine and the 7-OH, to focus on those. Those probably do have the effects in humans that we're

seeing in the lab. And the reason we know this is because as we began to study specifically these two compounds, what we found is that they interact in the human body with a kind of receptor called a mu-opioid receptor.

Justin: Mm-hm. Mewing. I thought it might lead here.

Sydnee: There are different kinds of opioid receptors.

Justin: Oh, okay.

Sydnee: But the important part is that something that interacts with those receptors in our body will have the same effect as other opioids would when they interact with those receptors in our bodies.

Justin: So it's just an opioid, basically.

Sydnee: It's an opioid. The reason that it would make you feel like you took an opioid is because it could be classified as an opioid. Now, at this exact moment, I don't know that that formal classification has happened, because if you did, could you sell it at the gas station?

Justin: No!

Sydnee: Probably not.

Justin: Probably not.

Sydnee: Right? But it does—it does bind with opioid receptors. Now, there was some initial—and there's been this like flurry of research on mitragynine and 7-OH, just in the last couple of years, as we're trying to figure out, whoa, this stuff seems really popular, a ton of people have started taking it, we have no idea how many people. And then when it enters like popular media and you hear people like Joe Rogan talking about it, you know more people are going to start using it.

So, what the heck does it do? And at first there was some hopefulness like, well, you know what? It does tend to bind with some of the opioid receptors. But the specific ones that are responsible for respiratory depression,

meaning the ones that would make you overdose, it doesn't interact with those as strongly.

So, oh, well maybe it will give you pain relief and help with withdrawal symptoms? Maybe it could be, like you mentioned, like a methadone thing, without causing respiratory depression. But the problem is, a lot of those initial studies were looking at mitragynine and kratom. 7-OH itself, that is going to need to be studied a lot more before we know what it's going to do, right?

Justin: Right?

Sydnee: Okay. So that's exactly what would need to happen before it became super popular, if it was going to be used safely.

Justin: Righht.

Sydnee: Because then if it was a new medication that could be used in the same realm as methadone or buprenorphine, excellent—

Justin: Probably wouldn't be in a can at the truck stop.

Sydnee: Let's do trials, let's figure—let's figure it out, you know. And that's not what happened.

Justin: Mm-hm.

Sydnee: So, what did happen with kratom? I'll tell you after the Billing Department.

Justin: [slurps] That's good timing. Let's go.

[theme music plays]

[ad reads]

Justin: Okay, Syd, so, what did happen with kratom?

Sydnee: Okay. What did happen with kratom is that people started using it, and because it works on the same receptors that opioids do, they liked it. Because in higher doses, and especially when we go to the 7-OH, which is again the most purified form of the active thing that does the thing—

Justin: Mm-hm.

Sydnee: It can create the same symptoms, if you will, of opioid intoxication. It will make you high, you will feel euphoric—

Justin: High from drugs.

Sydnee: You might—yeah. You could hallucinate, it can—it can cause delusional beliefs.

Justin: The drug stuff.

Sydnee: Yes, it can—it—and again, small doses may be stimulant. And those would also make you feel great.

Justin: Yeah.

Sydnee: But then the larger doses, it's an opioid. And so, if something does create euphoria, you are more likely to want to go use it again. And then the other thing that we figured out about kratom pretty quickly, is that because it does bind with opioid receptors, it has addiction potential. So—

Justin: So while we're trying to cure our, you know, replace our methadone, maybe we become addicted to something else?

Sydnee: Exactly.

Justin: Mm-hm.

Sydnee: So, kratom, in commercially available preparations, has been around since the early 2000s. And I think it was pro—it's one of those things where like, you know, people will travel to—Americans go to other parts of the world, they find some sort of traditional folk medicine use, and then we

decide that it must intrinsically be better than anything that's a pill because it's natural.

Justin: Mm-hm. And there probably is a way for us to make it more profitable. [chuckles]

Sydnee: Yes. And we're going to market it.

Justin: And potent.

Sydnee: Yeah. So, it has been sold as a supplement since the early 2000s. I shouldn't say as a supplement. A supplement is a specific designation, it's a food, Justin. It's a food.

Justin: Oh? Delicious.

Sydnee: And it's for anxiety, mood, energy, weight-loss, and to help you quit opioids.

Justin: Like mini foods.

Sydnee: [titters]

Justin: [chuckles]

Sydnee: And it's been pushed that way for quite a while, like this is a natural alternative to opioid—to an opioid. But I mean, it is in the sense that like Percocet is an alternative to Norco.

Justin: Sure.

Sydnee: You know?

Justin: Yeah.

Sydnee: Heroin is an alternative to fentanyl.

Justin: Yeah. There are all sor—there are different things you could do.

Sydnee: So, because of this, because as it became more popular in the early 2000s, more people were using it. And there were—and let me be really clear, there—it has been implicated as one substance present in a number of overdose deaths in the US. However, these are almost always polysubstance situations. So to say that it alone is the problem would be an overstatement, right?

Justin: Mm-hm.

Sydnee: Like we don't—we don't know—we didn't know that certainly back at this point.

Justin: Right.

Sydnee: But we were starting to see some potential for abuse, there was some concern. It only makes sense that if mitragynine and 7-OH are opioids, then there could be all this concern. So in 2012, the FDA issued an alert basically saying, "We don't know what these are exactly, but they're unregulated, they're being sold out of truck stops."

Justin: Mm-hm.

Sydnee: "We need to look into this."

Justin: Yeah!

Sydnee: It is possible that we need to schedule this and effectively ban it, right?

Justin: Right.

Sydnee: If you make something to schedule one substance in the US, there is no legal use for it, so you've banned it.

Justin: Right.

Sydnee: So, there was a push to do this, and in 2016 specifically, there was a move to schedule it. And the FDA was pushing this all along, the FDA, the DEA were saying, "We are concerned about this. This is going to be a problem. Maybe it's not a problem yet, but it's going to be a problem."

Justin: Okay.

Sydnee: So, there was a move to schedule it back in 2016, and it was halted by the lobbying group, the American Kratom Society.

Justin: Oh, good, they sound good.

Sydnee: [chuckles]

Justin: I like the sound of this.

Sydnee: I looked into the American Kratom Society.

Justin: I bet they're cool.

Sydnee: I don't, Justin, I don't really know. All I know is that they started back in 2014, and they only made 200 bucks in revenue. And if you look fast-forward to their last year, 2024, that's recorded, it was over four million dollars they are doing. Like you just look at these graphs in the last few years, they have—

Justin: A lot of money in the—in the kratom—

Sydnee: The American Kratom Association is bringing in a lot of money to lobby for kratom use. And they must have been successful, because they reached out to say, "Hey, no, no, no, don't schedule this." And they were supported with a letter from 51 members of congress.

Justin: Mm-hm! A bipartisan group—

Sydnee: A bipartisan group from 51 members of congress who got together—

Justin: Nice.

Sydnee: Yeah, to say please don't… please don't schedule—

Justin: "It's really important that you not do this."

Sydnee: Yeah.

Justin: "For this incredible miracle food is helping everybody. Don't say it's a drug!" [chuckles]

Sydnee: And here's what they said, "As our nation continues to combat the public health crisis of opioid abuse, the federal government has invested significant resources to develop alternative pain management strategies." And so they—kratom is part of this basically. This study led the researchers to apply for a patent identifying the kratom extract metragynine as a useful treatment for other addictive drugs besides opiate derivatives.

And then if you do it as—if you schedule it, "We won't be able to do this," right? Once you schedule it, you can't study it. You're done. And it's interesting because at this moment, as I'm reading the story of kratom, I didn't know this was an effort. Because as a result of this in 2018, the FDA said, "You know what? We don't have enough data to know what to do with this, we're just dropping it." So they let it alone. Let it go.

Justin: Great.

Sydnee: Let it go, let it grow, let it be sold at Speedway. And—

Justin: And this was—this—which FDA was this though? Because I think we should be…

Sydnee: This is 2016 to 2018.

Justin: All right.

Sydnee: Yeah.

Justin: All right. Cool.

Sydnee: There you go. So, the problem here, I think that this is a nuanced issue. And man, that's tough, isn't it? Right? Especially in this day and age, when you have a nuanced issue.

Justin: Ooh.

Sydnee: So—

Justin: Not a—yeah, not in a climate for nuance.

Sydnee: No. Kratom definitely, and specifically—let's be specific, 7-OH has potential for abuse. And we're—there's studies I'm going to tell you about that say this. But have we had great success with criminalizing substances of abuse in this country?

Justin: I would say no, Syd.

Sydnee: Right. So, when you see some of the names, some of who—who some of these 51 members of Congress are. It might surprise you if you're thinking, well, why wouldn't you want to stop this? This is dangerous? This is addictive? This could hurt people? People could die? All true. Making it illegal, though, doesn't always help.

Justin: Right.

Sydnee: Right?

Justin: Okay.

Sydnee: And so that—so, when you look at that bipartisan group, some of them are just very much like this "just say no" crowd. But like I think like Bernie Sanders was one of them. So, then you have people who were trying to be thoughtful about our approach to substance use and, you know, the legalization of drugs or not in this country.

Justin: Yeah.

Sydnee: Right? And so, it is nuanced. The problem, though, is that by the time they're having this conversation, the cat's out of the bag.

Justin: Right.

Sydnee: And if people were going to get addicted to kratom, that's already happening. And it's growing in popularity. So, we see there's all these studies that have been done about like they—they actually looked to like Reddit forums to see how many mentions of kratom. And in the last few years, it's just exploded. People everywhere are talking about kratom and, more specifically, the 7-OH.

Now, why is it more popular? The reason it's more popular is the same reason that every other opioid they've made has been popular, because it's addictive. They took the most potent part, the 7-OH, and they put it into pills and gummies and powders and drinks, and all kinds of—and if you look, there's tons of products, you can buy them online. They look pretty and they're flavored, like they're everywhere.

Justin: Yeah.

Sydnee: And they're usually sold as an energy supplement?

Justin: Yeah…

Sydnee: And weight loss is tied to it, so like they're hitting on the things that they think most people will want to buy. It's natural, that's what they all tell you. It's natural, so no problem. Now, that right away is a problem. I would say there's a—there's a lot of problems here. But the idea that it's natural being in its favor is already a fallacy. But it is probably not economically feasible for all the companies. And there are multiple—I mean, this is a multiple billion-dollar industry now.

Justin: Mm-hm.

Sydnee: There are multiple companies making these various things with kratom in them and 7-OH. There's no way they're going and harvesting this plant and getting it from the plant. You know what I'm saying?

Justin: Yeah.

Sydnee: It's not feasible.

Justin: Doesn't seem right.

Sydnee: You couldn't.

Justin: No.

Sydnee: So instead, you just make it in a lab.

Justin: Yeah.

Sydnee: So I mean, and just like we did with Fentanyl, right? Fentanyl isn't from a poppy. Fentanyl is synthesized in labs.

Justin: Mm-hm.

Sydnee: It's a very potent opioid that's synthesized in labs. That's what they're doing with 7-OH, they're just making 7-OH. It's not natural anymore. So even that claim has kind of fallen by the wayside.

Justin: Doesn't see—I don't know, this seems bad, Syd. I don't think it's a good idea to do it.

Sydnee: Well, so what we—a bunch of studies have been done in a hurry in the last few years to look at 7-OH in terms of abuse potential and addiction. And what we know is that it does have a very high affinity for those new mu-opioid receptors. That's the stuff that will make you feel high when you do an opioid, right? Like, they do this stuff.

We know that—there are several studies they do in animals. It was interesting, I was reading descriptions of all the different ways to see like a

self-administration study they do with rats. Like if a substance has abuse or addiction potential, then the rat will go back and try to put it in itself. Like it will try to get the substance on its own.

Justin: Mm-hm.

Sydnee: There are studies where they'll look for like pain. It does appear to have in rats, it appears to help with pain. So, you know, if you're in pain, you may be more likely to want it. In drug discrimination studies where they were looking at it compared to morphine, the rats were going for this over the morphine.

Justin: Hm.

Sydnee: Meaning that its abuse potential is probably higher than morphine at this point. It looks like it has a stronger affinity than morphine. We think that as much as you might get addicted to morphine, you are more likely to get addicted to this.

Justin: Oh.

Sydnee: This is what we think—we think. This is all early. Basically, it has a high potential for abuse, is what we know based on these preclinical rat models so far.

Justin: Mm-hm.

Sydnee: So, when these supplement compa—and they're not supplements. When these food companies, when these fun… fun truck stop favor companies are—

Justin: Party favor companies!

Sydnee: When these party favor companies are talking about how their sales of this have exploded, and people really love it, and that people have been—

Justin: It's because you're selling drugs! [chuckles]

Sydnee: It's because you're selling drugs. It is. I mean, that's what you've done. You've taken something that had a teeny, teeny bit of addictive potential. And I would say you could make the argument that when people are talking about pure kratom, the plant, eating those leaves, I don't know that there's enough of the addictive substances in there to make you addicted to the plant. Do you know what I'm saying?

Justin: Yeah.

Sydnee: Do you see the distinction I'm making?

Justin: Yeah. Nature and its infinite wisdom provided the exact right dose for us to keep on truckin'.

Sydnee: Yeah! And so, probably people in the fields would chew those leaves and then were able to go home and not go into withdrawal, and desperately need more of the leaves.

Justin: Yeah.

Sydnee: But now we've taken the very active part and purified it, and so you will need more of it. And that's what we've seen, is that in those same studies, they definitely saw intoxication syndromes when you took it, withdrawal syndromes when you stopped it, craving and seeking behaviors to get more of it. It's just everything we know about opioids.

Justin: Yeah.

Sydnee: Everything we know is true about 7-OH. And anywhere from—these are the studies that I found. Anywhere from 1.7 to 10 million people in the US are trying it in a year. We have—so, a lot. We have no idea, because there's so many different formulations of it, and it's so widely available. The people who are using it, it seems to be like the average user, the demographics are like white, middle class.

Initial, it was slightly more women, I think, because the initial preparations were marketed for like weight loss. And that usually is targeting women over

men, and energy. And now I think it's just white, middle-class people are using it. They also—I mean, anybody could, but that's generally the demographic. And they're usually using it multiple times a day. And they usually continue to use it because they get sick if they stop.

Justin: Drugs.

Sydnee: Right. So like these are—I feel like we're like walking backwards into something we already knew.

Justin: Yeah.

Sydnee: It's really weird to watch this happen backwards. It works really quickly. That's another thing that people find attractive about it. Like within 45 minutes, you're probably feeling the high.

Justin: The high! Again. [chuckles]

Sydnee: Yeah. Because it's—because it's an opioid. We have no idea how much of it is in any given product. So, there are tons of TikToks you can watch where like pharmacists will go around and buy various kratom and 7-OH products off the shelf, take them home, and use their gas spectrometer to like measure how much metrogynin or 7-OH is actually in this product. And it is wildly variable—to, you got ripped off because you just bought some gummies that have nothing, to, oh, no, it has way—it has 200% more than you thought it did.

Justin: Right.

Sydnee: Which could lead to overdose. It also, a lot of the preparations are cut with other random things, like Benadryl is in there for whatever reason. Some of them have been cut with codeine, which is, you can't just legally buy that over the counter.

Justin: Right.

Sydnee: So, we don't know what's in any of these supplements. You have no idea what you're getting or how much of it you're getting. Seven states

so far have taken action on their own and banned it. And 17 more have age restricted it. Which means, by the way, that everybody else hasn't even age restricted it.

Justin: Kids, come get your drugs. [chuckles] I guess.

Sydnee: And I get—I really do, I think it's—my initial reaction was ban this stuff, ban this stuff. Why don't we ban this stuff? And I had to really do some soul-searching, because the way that it is being sold and marketed, I disagree with vehemently, because it's just a profit thing. They're selling over-the-counter opioids for profit. And so, the motivation is going to be to sell as much as possible. There will be no safe—no safeguards, no guardrails on this. But banning it cannot be the solution either, right?

Justin: Well, certainly not right now. I do not trust the US government to be a… you know, respectful, sort of, you know, responsible… instrument in terms of that. You know, I certainly don't trust them to regulate anything.

Sydnee: And I think that if there was a pathway for mitragynine or 7-OH to be used as medication-assisted therapy for the treatment of substance use disorder, which, I mean, perhaps there was at one time, it's gonna be really hard to… I mean, how do we walk this back, now that it's available everywhere? I don't know how you—I don't know how you do that. And I would also argue we have good MAT, we have buprenorphine.

Justin: Yeah, we have other things that can do this.

Sydnee: Right, and there is no advantage, if your argument is, well, but this is natural, it's from a plant, that's not a good argument here. We have substances that help with this.

Justin: Yeah.

Sydnee: And do not create euphoria, which is the goal, because then people can function on them.

Justin: Yeah.

Sydnee: If you're taking something all day long that's gonna alter you, it's gonna intoxicate you, how can you, you know, how can you have a family or a life or hobbies or friends or a job or, you know, go to school or any of the stuff that you might want to do with your life? You need… not to be intoxicated. So, that's the—that's the skinny on kratom. I would not recommend it. I would not recommend it to somebody who's trying to kind of self-treat for substance use disorder, to try to reduce their use of other opioids.

I would not recommend this substance for that at all. I would not recommend buying any of these over-the-counter, unregulated, whatever they are. You have no idea what you're getting. I would encourage you, if you do have young people in your life, if you have children or other—if you're a guardian of some sorts, if you have—please educate kids about this. This is gonna be at parties.

Justin: Yeah.

Sydnee: I'm sure it already is. This is gonna be the new party thing to do. This is salvia. Do you remember when salvia came out and everybody said this is the new legal weed that you can buy on the internet?

Justin: I just want you to know, babe, you have never sounded more young and relevant than when you said,"This is gonna be the new party thing to do."

Sydnee: [chuckles]

Justin: Because I want all the parents to know that Sawbones is where you can find out about all the good party things to do.

Sydnee: [titters] Shut up.

Justin: [chuckles]

Sydnee: I'm just saying like there're gonna be kids at parties—

Justin: It's the new salvia! It's the new party thing to do!

Sydnee: When salvia first came out, it was like, "Well, it's legal. It must be fine. And it's also, it's just weed." And then when people did it, it was a potent hallucinogen!

Justin: It's not just weed.

Sydnee: No!

Justin: It's a super mega bad idea. [chuckles]

Sydnee: So—

Justin: It's a super mega bad idea.

Sydnee: And I feel like this is the new—and the problem is, at least with salvia, it wasn't going to cause respiratory depression.

Justin: Mm-hm.

Sydnee: With this, if people don't know what they're doing, I mean, you can overdose on this. And it's not nearly, at this point, it is not to the level of fentanyl. I'm not—I'm not making that claim. Certainly, we should be more concerned about these other issues—

Justin: Fentanyl of course is the old party thing to do, and now this is the new party thing to do.

Sydnee: But I think—here, can I—one last analogy before we're done?

Justin: Yeah.

Sydnee: Every—when vaping became a thing—

Justin: Mm-hm.

Sydnee: Everybody agreed pretty quickly like, well, smoking's worse, and maybe vaping isn't good for you, but smoking's worse for you. So, let's just chill on vaping, right?

Justin: Right.

Sydnee: And that was kind of the—that was the—everybody just said, yeah, that sounds good. Like, you shouldn't do either, but if you're gonna do one, vape. And the problem with that has been, vaping is so much more socially acceptable among young people now than smoking was becoming. I think smoking was kind of becoming a thing you weren't supposed to do, right? Vaping is cool and fun, and you can hide it really easily, and the barrier to entry is way lower than it is with cigarettes.

Justin: Are you sure that's still true? Like—

Sydnee: Everybody's vaping?

Justin: If it was cool and fun years ago? Maybe it's not even cool and fun anymore. Are you sure we still know what's cool and fun? What if vaping is like—what if the listeners are like, "*Vaping*?!"

Sydnee: We have friends with young kids who are vaping.

Justin: Yes, around us, and we're like, "Get those vapes away from the kids?" And they're like, "It's their vitamins! They need it."

Sydnee: No! They're trying to get them to sto—no, they're not letting them. I'm saying that I think the barrier to entry to vaping is so much lower than cigarettes, that a lot more people were onboarded to vaping—

Justin: And the social pressure is obviously different.

Sydnee: Yeah. And what I'm saying is, I think that kratom is sort of filling that hole in this space. The barrier to entry for kratom is going to be super-low, because you can buy them everywhere, and they look like fun gummies that give you energy. And they're—it's the same kind of plant that coffee, is

it's a family—coffee family plant. So it's like, "Ooh, super caffeine," and it is not that!

Justin: It's not super caffeine! Make sure you talk to somebody this week, just like, "Hey! I know kratom sounds fun, but it's a drug." [chuckles] If you tell one person this week, maybe two, that kratom is drugs.

Sydnee: We need to regulate it. I would—I—prior to this, I would have said we need to ban it immediately. I do not feel that way. It hasn't worked. We shouldn't have banned things, it didn't work. It just makes more things that are worse than the new thing. So, we need to regulate it. It shouldn't just be sold at truck stops. It is dangerous.

Talk to your kids or young people in your life about it. And if people need treatment for substance use disorder, please see a medical professional who can help them—help you through that process, to medications that have already been tested, that are—we know what they are, they're regulated, and we know that they work, and we have evidence to do so.

Justin: Thank you so much for listening to our podcast. Thanks to The Taxpayers for the use of their song "Medicines" as the intro and the outro of our program. Thanks to you, Sydnee, for being here, and thanks to the listeners, and thanks to everybody. That's going to do it for us for this week on Sawbones. Until next time, my name is Justin McElroy.

Sydnee: I'm Sydnee McElroy.

Justin: And as always, don't drill a hole in your head.

["Medicines" by The Taxpayers plays]