

Episode 79: Kava - Tradition, Benefits and Toxicity

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Transcript

Welcome back to the Tox Lab.

I'm Rebecca.

I'm Rob.

A few weeks ago we spoke about kratom and its overlap with kava and we asked if you wanted us to do an episode on kava and we had an overwhelming response from people asking us to talk about this topic. So this week we're going to be taking a look at kava and we're not talking about cava, the Spanish sparkling wine.

Although that is great. But instead we're going to be talking about kava, with a K, that comes from parts of the South Pacific. But before we dive too hard into that, Rebecca, when does a wellness product stop being a wellness product and start being a drug?

That is a good question. The first thing that comes to mind is kind of when it becomes addictive and when it moves from being like solely beneficial to maybe having more harms associated with it.

Interesting.

Okay, so it's nothing to do with whether it's psychoactive or not. I mean, that is a good point, it's just the things that came into my head first. It's a bit of a philosophical question, isn't it?

But for example, I can go into a supermarket and I can buy chamomile tea and that might help me sleep.

Yeah. And nobody sat there thinking chamomile tea is a drug.

True. I could go and buy valerian tea and valerian has got recognised pharmacological properties that lead to relaxation.

Maybe that's still a tea. If I make something out of kava Root, for example, at what point have I crossed a line?

It's a very good question.

I think you're right.

I think some of this is determined not by the compound, but probably by society's view of the compound. And so this week we're going to be looking at kava. kava is not new. kava has got a long, rich history, but it has become, in recent years, a wellness trend. And as we said a few weeks ago, we were talking about how it emerged with kratom and how it's become almost synonymous with the kratom movement. And I guess the big question here is, is kava a wellness product or is kava a more traditional drug? Before we dive into today's episode, if you want to stay up to date with our content, you can find us on Instagram at @the_tox_lab. We also have a page on LinkedIn and we're fairly active on there. And for those of you who don't use social media, but still want to get in touch with episode suggestions or comments or episodes, you can use our new website and we can be found at the Tox Lab dot co dot UK. And we also have a very exciting announcement in a couple of weeks on the 9th of

June is the day where the EU DA, EU Drug Agency, released their annual report. And very excitingly, we are planning to do our very first The Tox Lab livestream on the evening of that report dropping. It may or may not go well, we will see. But the plan is that we are going to go live on YouTube. And if people want to come along and listen to us unpack that report, then please do.

Yeah, we'll put more details about the timings on our socials.

So what is kava? Well kava is derived from a plant with a complicated Latin name that I can't say. But the literal translation is intoxicating pepper. And it has a long, rich ceremonial history amongst a lot of Pacific Island cultures. So quite a wide area, actually, across parts of the Pacific, places like Fiji, up as far as Hawaii, in fact. So there's quite a wide area of cultures that use kava. And it's traditionally a water based extraction.

You take this cultivated plant. You dry and grind up the root and you mix this root in water. There's a ritual that comes with it.

It's often quite a social experience. And people consume this as part of these rituals. And it's pharmacologically a really interesting plant. It contains a lot of compounds called kavalactones. And this is where the overlap was with the kratom products we discussed a few weeks ago. And kavalactones, there's a range of them. I think there's maybe 30 or something that have been identified.

There's maybe six most abundant ones. And these compounds have really, really interesting pharmacology.

They don't just do one thing. They seem to have an effect on GABA-A. But they also seem to have an effect on sodium channels and calcium channels. They may have an effect on monoamine oxidase as well.

So they're really complicated pharmacologically. And what is complex as well is different cultivars, different versions of this plant have different kavalactone ratios. So even though they all come from the same plant, actually different varieties can have different effects. The general effects are that it's quite social, that it leads to relaxation. And also interestingly, people describe a tingling or a numbing of the lips and the mouth as well.

And it's not associated with violence.

It's not like alcohol. It tends to be more of a relaxing experience. And what is interesting when you look at these traditional cultivars of kava is recognising that they have different effects. And so you get these noble cultivars, as they're called. A noble kava is what's traditionally used in ceremonies, the social kava. And then you also get these other varieties. And these are actually called two-day varieties. And it literally means two days because these have got a heavier effect.

The effects tend to last longer. They're generally described as a dirtier feeling. And so you get these different classes of kava. And so it's not one standardized thing. So there has been a very big review of kava and its use. And so we thought we'd dive first of all into that review paper because it really does unpack quite a lot of the detail that comes with kava. So this paper reviewed the literature on kava from 1980 to 2022 to look at the broader health outcomes, prevalence patterns, social and cultural uses, economic impacts, and policy considerations of kava. And they included 197 records in this review. So in terms of prevalence of kava use, 47% of reports involved use in Pacific Island countries and a third of them involved use in Australia. When looking at benefits related to use, they looked at randomized controlled trials, observational studies, and case reports. And 92% of these reported benefits relating to improved mood, relaxation, or reductions in symptoms of depression, anxiety,

stress, and insomnia. Some of the less frequently reported effects included anti-cosidogenic effects, anti-craving properties of kava, and effects on adiposity. But these were all reported in less than 6% of the records. And this is where we're starting to see kava move from a traditional ritualistic consumption to entering this wellness space, where it's suddenly seen as perhaps an alternative to alcohol or another way of relaxing a natural alternative to harder drugs, perhaps. And some of these effects were significant. Eight randomized controlled trials observed significant reductions in anxiety symptoms among those who consumed kava compared with the placebo. 35% of the records reported no serious adverse effects or withdrawal symptoms, suggesting it was well tolerated among users. Moving on to the harms related to its use, 4% of reports related to harms found that kava consumption negatively impacted driving ability and behavior, but 6% of records found that kava did not impact on cognitive performance and driving ability. So there seems to be a bit of a debate around this. So the question here then is, actually does it have any impairing effect at all? I think it's really unclear and the studies just don't seem to agree with each other. So I think that's an area that needs further exploration. 43% of the records reported cases of harm associated with liver damage or failure, and these were sometimes serious enough to require a liver transplant. And we're going to look at liver failure a little bit more later on. So kava has become controlled and bans have been put in place on the sale, distribution and medicinal use of kava in Europe as a result of the severe instances of liver toxicity. And these kind of started in the early 2000s. So in New South Wales and Australia, the trade and consumption of kava was banned between 2007 and 2021, but prohibitions were removed in 2022. Germany had also banned kava, but had overturned this in 2014. I remember when that happened in the UK, because there was a health food shop in Brighton that would sell kava in smoothies. And I remember overnight, it's suddenly disappearing from the shelves because of that ban linked to hepatotoxicity. And in the UK, the law has never been repealed. Kava is still banned for human consumption in the UK. Kava has also been linked to demopathy, which is skin condition characterized by rashes, itching and scaling. And heavy kava use in Aboriginal communities has also been associated with signs of nutritional compromise, including reduced BMI, abnormal lipid profiles that resemble those with anorexia nervosa and scaly skin. The dermopathy is interesting because I don't think it's really understood what causes it. It does seem to be a thing. I think it's believed it could be to do with interactions with cholesterol metabolism.

Oh, okay. So there's possibly all sorts of things going on under the hood in terms of what happens to your lipid profile with kava. When looking at social and cultural reasons for kava use, which I find quite interesting, they managed to find 25 records on this and 60% reported on the use of kava in social settings as a recreational activity to aid social bonding in unity or for developing or maintaining alliances. 16% discussed kava use as means of asking for forgiveness or to aid in conflict resolution. And 8% discussed kava as a social lubricant and its possible use as an alcohol alternative, which we have discussed. They also talked about social status in relation to kava consumption and how men or those of higher social status or age were permitted to use kava and how participation in kava ceremonies may demonstrate strength and endurance and facilitate their ascent in social ranking. 56% of reports highlighted the cultural reasons for kava use and the solidification of one's cultural identity and connection to their country and maintaining traditions. So you can see a lot of the literature related to kava use. It looks more at its traditional uses in these Pacific Islander communities mostly. But more recently, we've started to see Western commercialization. Traditionally, we were talking a peeled root, as I say, a water extraction.

Now you can get capsules, you can get gummies, you can get drinks containing kava. The extracts are often done using solvents rather than water. And actually a lot of the hepatotoxicity concerns emerged after the Western commercialization. So I think there is a possibility and maybe we'll unpack this a little bit more that that could be related to some of the liver disease that was being seen. Why

don't we look at one of these cases in a bit more detail?

So a 46-year-old male from Australia was referred to the emergency department with a three-week history of fatigue, dull right upper quadrant pain and profound progressive LFT derangement. He had a past medical history of hypertension, depression, gastroesophageal reflux, active smoking and had a history of previous alcohol misuse disorder. He was also prescribed a variety of medications and had recently started taking paracetamol for his right upper quadrant pain. When looking at his history, he had consumed 10 grams of kava daily for five weeks prior to his presentation to assist with sleep, which was stopped two weeks prior to his admission after his LFT derangement was discovered. On examination, there was no evidence of jaundice or signs of chronic liver disease. There was no evidence of hepatosplenomegaly and his abdomen was soft and non-tender. He had a raised ALT of 1,546 units per liter, a raised AST of 920 units per liter and his gamma GT was also elevated at 493 units per liter and these are all markers of liver dysfunction. He underwent further investigation to determine the cause of his liver damage, including autoimmune and viral screening, which were all normal and his paracetamol was also measured, but this was also within normal limits. A notary sound of the liver showed normal liver architecture with a normal biliary tree and no evidence of portal or hepatic vein thrombosis and other causes of acute profound transaminitis. So these raised liver enzymes were ruled out. So it was thought that the kava had induced liver injury based on the temporal association between the kava ingestion and the symptoms developing.

So let's unpack this. A man takes a lot of kava, then develops liver injury. And the cynic amongst you would just say, well, that could just be coincidence.

No other cause was found. And to be fair, this case is one of many. Lots of cases have been reported of liver injury following kava use. And it's a classic biochemical picture of drug-induced liver injury, isn't it?

What's going on? So there does seem to be something in it, but what I think is much less clear is what. And there's a lot of debate about what causes the liver injury. And I think there have been a few case reports of liver injury following more traditional kava use, but it does seem that the rate of cases did skyrocket when modern extraction methods started to be implicated. So it is suggested that perhaps the extraction method, whether that solvent extraction or whether they're perhaps using more of the plant, so leaves, may have an effect.

This is currently up for debate. Is the reason for like an ethanol or a solvent-based extraction to do with yield for like commercialization versus traditional?

I believe so.

It's just more efficient.

Yeah, you get more out of it. But the hypothesis is you extract a different kavalactone ratio, which might be why it's more harmful. There's a few working hypotheses as to what exactly is going on. I think one of the theories is that some of the kavalactones produce reactive metabolites similar to paracetamol metabolism. And therefore it's hypothesized that people who have got reduced glutathione stores might be more at risk. And what is interesting then is if that is the case, kava is often marketed as an alcohol alternative. And so in individuals who have got an alcohol use disorder and want to come off the alcohol onto kava, they may actually be more at risk of liver injury as a result of that reduced glutathione reserve. kava has also been shown to inhibit some of the cytochrome P450 enzymes. So if you're taking other drugs alongside that, you could then be altering their metabolism and building up toxic intermediates, for example, which could then precipitate a liver injury. And the idea that somebody might well be using other things, possibly other herbal things alongside kava. I

mean, we know some herbal substances, if you inhibit the metabolism of them can be toxic. So actually that's entirely plausible, isn't it?

That there could be some overlap with other compounds as well. I think all in all, the absolute cause of this liver injury is unclear. Interestingly, you had mentioned earlier, hadn't you, that countries like Germany had banned it because of this liver injury risk. Subsequently, they reversed that ban because the strength of the association was perhaps not as strong as originally thought. So why don't we look at another case then?

So this is a case of an 18-year-old male who'd presented to hospital with severe vomiting after a night out with friends. He had reportedly consumed 15 cups of kava tea but denied other drug or alcohol consumption. In his case, he had no preexisting chronic kidney disease but was found when he attended hospital to have an acute kidney injury. He had an abnormally low urine output and had clinical signs of mild dehydration. He also had a normal blood pressure on exam but was bradycardic and had a prolonged QT interval. He was previously well with no recent illness or significant past medical history. He had not been taking any supplements or medications. And he is a Pacific Islander background in a consumed kava recreation near a party which had been obtained from a local health food store.

And he'd also used kava before. A CT scan of his abdomen showed bilateral perinephoric stranding which is inflammation of the fat that surrounds the kidneys. But the kidneys were of normal size with no features of obstruction. The urine drug screen was performed which was negative for amphetamines, cocaine, cannabis, benzodiazepines and opiates. And he was treated with IV fluids to improve his urine output but his creatinine continued to rise from 223 micromoles per liter on admission to 970 micromoles per liter 96 hours after his presentation. A kidney biopsy showed acute interstitial nephritis with patchy interstitial inflammation and edema. And there was some mild tubular injury and the glomerular and vessels were all normal. And due to the temporal association of the kava tea and the acute kidney injury, kava was thought to be the cause again. And this case is even weirder, isn't it?

If we're not sure what might be causing these sporadic cases of liver injury, I don't think we've got any real clue as to the mechanism in this case. I mean, I guess it's possible that it's just a coincidence that something else caused it. But again, most people don't randomly develop acute kidney injury for no reason at all.

There's normally a reason behind it. And kava has been reported to cause rhabdomyolysis, which can then induce an acute kidney injury, but this wasn't seen in this case. And this seems to be the first report of kava-induced acute interstitial nephritis. They did manage to test the kava tea powder, the individual brought it in, and it was found to contain four different kavalactones without the presence of any additional substances. So it does just appear to be kavalactones in what he was consuming. And I think this just shows how possibly kava can be fairly unpredictable. Assuming that was the cause in this case, perhaps it's not. But if it is, it seems to have come really out of nowhere. And it's interesting that he has consumed kava before with no ill effects. So is it just the ratio of the different kavalactones in this tea versus what he's consumed before?

Possibly. I can't help but feel like we're missing something in this case.

I know.

It feels like something's off.

Now we have got one more case to look at. And this is perhaps the weirdest of all of the cases in which kava has been implicated in harm. A 36-year-old male was found dead in his bathroom next to a

10-millilitre syringe which contained 7.5 mils of yellowish liquid. There was a tourniquet tied around his arm and needle marks were also found alongside several suicide notes. He had been suffering with long-term depression and had previously been in psychiatric care for this. And he had no known history of substance use. An autopsy was performed which showed agonal pulmonary edema and brain edema but there were no pathological changes to the major organs. And based on the pattern of injection marks it was thought this was the first time or one of the first times that he'd attempted to inject something intravenously. The syringe unfortunately was not available for toxicology testing but samples were taken for analysis and kavalactones were detected in femoral blood by GCMS. The concentration of the six kavalactones that they detected ranged from 0.13 milligrams per litre to 2.7 milligrams per litre and were much higher than those found in pharmacokinetic studies. They're also quite similar to one other reported case involving a kava-related fatality but this case also involved a head injury. So it's impossible to determine whether that concentration of kava was the cause in that particular case and whether it would have occurred without the head injury. kavalactones are not thought to cause significant respiratory depression. So even though they're sedating and relaxing there's not really reports of people losing consciousness or stopping breathing or anything really significant. If all that syringe contained was kavalactones it does suggest that there might be a potential sealing a potential toxic effect if enough is consumed. In general, most of the time people aren't injecting kavalactones of course so maybe that has a role as well. There was also ethanol present and it was elevated although I don't believe it was significantly elevated to account for the death but they couldn't obviously determine whether it was that he'd consumed alcohol alongside injecting the substance or whether because of the extraction method he was also injecting ethanol. We can do the maths, can't we? Because it was a 10 mil syringe and there was seven and a half mil liquid remaining. So if he had injected two and a half mil of pure ethanol probably wouldn't detect very much of that, would you?

Yeah.

A lot of unknowns, definitely. I think this is a really weird case. I don't again really have a good mechanism here, do we? We know that kavalactones were present in the blood sample. We know that the individual has died. Beyond that, we're putting two and two together and hoping we get four but maybe we're missing something.

Yeah, it's just another massive unknown.

So where does that leave us? I feel like after reading around kava for this episode I have more questions than answers about the mechanisms in which it can cause toxicity and whether it is truly responsible and whether there's a specific kava latone that plays a bigger role in these cases than others.

I think you're right. I think there's an awful lot that isn't known here about kavalactones and kava in general. Are modern extraction methods more dangerous than traditional ones?

Possibly, unclear. Is kava really all that toxic at all?

Or are these cases coincidence? There's probably some truth to the liver injury but to what extent? And how much of that was overlapped with other things possibly is a really big question mark. And of course, where countries have gone and banned kava outright because of these concerns, often a lot of research then stops as well. So we may not have the answers for that. In terms of where we're at now in 2026, kava is definitely a thing. As I say, in the UK it is officially banned. There are at least one or two websites which will claim they can ship me kava. Across the US, it's certainly not banned. As we said last episode, being increasingly detected alongside kratom and being seen in the kratom scene. And it's potentially that area of these synthetic extractions where perhaps much higher concentrations of

kavalactones are gonna be encountered and things like that, where we might start to see a rise in these ill effects. If kavalactones do cause hepatic disease, for example, we might expect to see a rise in that as kava takes off in the kratom space.

But I think you're right. I think a lot of it's really unknown. Reading around it, it doesn't sound like it carries with it anywhere near as much risk as something like alcohol, for example. I mean, what's your view on kava control? I think it's a really tricky one, especially with something that has such like cultural significance that you've gotta be really careful as to where you control it because it plays an important role in so many ceremonies and funerals and weddings and graduations. And you don't wanna stop that, but you do wanna prevent harm. So it is a really tricky balance. We see this so often, don't we, in so many areas actually. I mean, coca leaf in South America or khat in parts of Africa. Cat itself probably relatively harmless on the scale of harms. Synthetic cathinones that derive from it, different issue. I do see your point though, that for something which has got such a rich cultural history, it does seem heavy handed to ban it. What's next for this quasi-legal wellness area?

No idea.

No, this is an area I've been thinking about. So we've seen, we've talked about kratom in the US and we're now talking about kava. There is a whole world of plants out there which have some degree of mild psychoactive effect. kanna is perhaps the next big thing to look for. And maybe we could do an episode on that in the future. There's certainly a lot of traditional kanna products that are now erring into this tincture, gummy, smoke mix, drink, severe, that perhaps kanna could be the next under the microscope. So really then to summarize, kava is a thing, it's got a rich cultural history. It may or may not lead to liver disease in some cases, and it possibly isn't free from toxicity. It certainly is psychoactive to a degree. It also doesn't seem to carry within a lot of the harms that quite a few other things seem to carry. The big question is whether the modern take on kava in terms of gummies and extracts is more toxic than the traditional kava. And I don't think that question's been answered yet. And I think really it's a case of watching this space and seeing what happens. Well, I hope you've enjoyed listening this week. Thank you again for being so vocal at suggesting we cover kava because we do really appreciate the feedback. In fact, I think the last few have all been listener suggestions. Well, as always, if you've enjoyed listening, do give us a like, give us a follow, jump on YouTube and subscribe to our YouTube.

That'll be great. Hope you all have an amazing week and we'll see you next time.

Bye.