

Episode 26: Beyond Broscience: The Toxic Truth About SARMs

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TRANSCRIPT

Hi everyone, welcome back to the Tox Lab. I'm Rebecca. I'm Rob. This week we're looking at a rather different sphere of science: bro science. We're going to be looking at some of the compounds traded in locker rooms and on bodybuilding forums, and trying to drill into some of the risks and toxicity that come with those compounds.

A few weeks ago we had a request asking if we could look at performance-enhancing drugs. Performance-enhancing drugs are an absolutely massive area. There are toxicologists who dedicate their entire career to detecting drugs in Olympians and things like that. We thought we'd narrow it down and have a look at one or two compounds in particular.

Let's try and focus it in a bit and we're going to be looking at some compounds called SARMs. Have you ever come across SARMs, Rebecca? I have had them pop up in a case recently, but before that I'd never heard of them. So what are SARMs?

Well, SARMs are selective androgen receptor modulators. They're drugs that are designed to act a bit like anabolic steroids. And really the pitch is that you can get all of the muscle-building and power without the hair loss, mood swings, or various parts of your anatomy shrinking. At least that's the premise.

They were originally developed as medications. The plan was to try and treat things like osteoporosis, muscle wasting conditions, but they never got FDA approval. And now they're sold as workout supplements, as research chemicals, sometimes under catchy titles like hard bulk and alpha mass. And how do they work?

Well, they bind to androgen receptors in the same way that testosterone does. But in theory, they're selective. They mainly activate muscle and bone and shouldn't activate the prostate and things like that. So today we're going to dive into what happens when SARM use goes rogue and enters the bro science sphere.

We're going to look at some mislabelled products and also some case reports as well. So Rebecca, why don't you dive into our first paper? So the first paper we're going to look at today involves illegal products containing SARMs in Italy. The aim of the study was to purchase products on the internet in 2022 that were being targeted at consumers based in Italy and see what they contained.

So they selected products from two different websites and purchased 13 food supplement products in total. These all claimed to contain SARMs. To identify what was present, they used LC-MS/MS and then NMR for quantitation to work out how much of each SARM was present in each product. When looking at the retail websites, seven out of the nine they looked at stated that these products were for research use only and therefore not for human consumption.

But they all reported information on dosages, phases of a bodybuilding plan, and when you should be taking them. Some websites even linked to quite reputable sources like PubMed and the NIH website, and to papers talking about SARMS and their effectiveness. As part of the study, they also looked at social media and how SARMS are being talked about there. And there seemed to be three main themes that they saw.

So there was the obvious exchange of information among users talking about means of administration and stacking with other substances. And it was often bros giving advice to beginners. Obviously a lot of these products were also being sold in plain sight on social media platforms and private channels, including Telegram. And from comments on Reddit and things like that, it seems the research only tag doesn't hamper sales and people are still willing to go out and buy these and give them a go.

And looking at Google Trends for SARMS in Italy from 2013 to 2023, there was growth in Google searches from 2018, peaking around 2021. So onto the 13 products that they'd purchased. They visually inspected each one. Most of them contained "research only" on the label, but then also had dosage information, which is quite counterintuitive.

When looking at the SARMS that were present in each product, the stated SARM was present in approximately 70% of samples. This included ostarine and ligandrol. Cardarine was also present, but this isn't a true SARM; it's a PPAR agonist, and we'll come onto that a bit later. Twenty-three percent of the products had a different SARM present and 30% of them had an undeclared pharmaceutical substance detected, and this ranged from selective estrogen receptor modulators like tamoxifen.

Testosterone was present in one of them along with tadalafil, and epimetandienone was present in three samples. So there was quite a range of different compounds in there that weren't SARMS, including some anabolic steroids. Clearly, if your logic is "I'm going to buy SARMS because they don't have the risks of steroids", then finding that you're actually purchasing steroids is going to be a problem. Tadalafil, that's a PDE-5 inhibitor similar to Viagra, right?

Yeah. I know we probably shouldn't laugh. The idea of a product being sold as a testosterone booster or steroid and actually just making it feel like it's increasing your testosterone by dilating certain blood vessels, I do find quite amusing. So when looking at the quantity of SARMS in each of the products, four of the samples contained 80 to 95% of their declared content, three samples contained 60 to 80%, and one was highly under-dosed.

So they had dosing instructions on the back, but actually contained much less than they said they were going to have. And also, when looking at these products that they'd purchased, they contained lots of other ingredients alongside the SARMS that do have potential to cause harm depending on their purity or grade. Some of these did contain rice flour, and if that's not properly prepared you risk having heavy metals like cadmium and arsenic in there. And a lot of these capsules were gelatin-based capsules.

And again, if this isn't of a sufficient grade, there's a risk of transmitting things like prion diseases. And a lot of these were also coloured pills or capsules, but there was no mention of any sort of colouring on the label, and these weren't disclosed. So that is a potential cause for concern. A lot of excipients simply weren't stated on the label.

Yep. It's quite concerning, isn't it? A lot of the marketing, I mean, it's hard to express the marketing on a podcast, but to describe it, we are looking at very, very eye-catching marketing designs, aren't we? Alpha-bulk with a man covered in muscles, skulls, all sorts of, help me with a better word, Rebecca, masculine kind of marketing.

Yeah. It's designed to draw you in and make promises about what it will do to your muscle gains and things like that. So what's worse, no ingredients or all of the ingredients? Ooh.

They carry with them two different risks, don't they? Clearly taking products that contain lots of things that aren't in there is a problem. Probably somebody buying something that contained no active ingredient is a different kind of problem. Hmm.

And especially with those products that contained SARMs and multiple other pharmaceutically active ingredients, we don't know how they all interact and there could be significant risks associated with consuming all of those at once. Okay. So why don't we now move on to the next paper, a study looking at the safety of these compounds? So this next paper is a systematic review of SARMs and their safety.

So this group basically searched for case reports and clinical studies reporting safety data. This group looked at case reports and clinical studies where safety data for SARMs had been reported in healthy individuals. Jumping into the clinical studies, they managed to find 18, 17 of which were clinical trials. Across these, 13 unique SARMs were tested.

In total, 2,136 patients were involved, with 1,447 patients being exposed. Across these different clinical trials, the median age was 57 years and the median weight was 81.2 kilograms. Nine of these studies only involved men, four only involved females and the remainder were mixed populations. Some serious adverse effects were reported in six of the clinical trials, including chest pain and a maculopapular rash with a raised ALT, which is indicative of a drug reaction.

There were two cases of rhabdomyolysis, although these weren't considered drug-related. So I'm not sure how they made that determination. And other effects such as acute MI, cancers, pulmonary embolism were also all reported. So one of the things the big study looking at safety data did was it compared a lot of clinical trials, didn't it?

So as I said at the start, these compounds were originally developed and tested as pharmaceuticals. There were clinical trials using these drugs in various different illnesses. A lot of the dosages used in those clinical trials, let's look particularly at ostarine because that's easily comparable and is one of the more common SARMs, were between one and three milligrams a day. When we looked at that Italian paper, some of the forum dosage recommendations were between 10 and 30 milligrams a day.

So not only are there a range of adverse effects with SARMs at dosages of one to three milligrams, the black market use of SARMs is suggesting doses around 10 times that. Ten of these clinical trials reported raised liver enzymes as a complication of use. These ranged between one and two times the upper limit of normal and varied with each trial and with each different SARM that was being tested. A couple of the studies also saw decreases in HDL and decreases in total testosterone and SHBG.

And these are the effects that the marketing says SARMs don't cause, right? So it's quite interesting. Some of these studies also showed an increase in haemoglobin and raised blood pressure, which could potentially contribute to cardiovascular disease risk. Some of the individuals in these clinical trials were reporting acute MIs and coronary symptoms, so.

An increased cardiac risk is one of the things we see with more traditional anabolic steroid use. And a lot of the common symptoms seen in the clinical trial data were headaches, dry mouth, constipation, dyspepsia, nausea and upper respiratory infections. That's interesting. I wonder why that is.

I'm not too sure. So moving on to the case reports they looked at, they identified 15 manuscripts with a total of 18 different cases. Eighty-eight percent of these case reports described drug-induced liver injury following SARM use, all of which involved men with a mean age of 35 years who were reportedly using SARMs for muscle building and were described as being athletic or bodybuilders. And two were on active military duty.

The majority of these cases involved the use of a single SARM, most commonly LGD-4033, which was found in eight of these cases, RAD140 in six of them, and enobosarm, which is ostarine, which was found in three cases. These were commonly being taken daily. The mean duration of SARM consumption before symptoms presented was approximately 6.7 weeks.

And where reported, the mean time from discontinuation of the SARM to symptom onset was about 14 days. The majority of patients presenting with drug-induced liver injury had a raised bilirubin and a hepatocellular pattern of liver injury, so raised ALT and AST. That was the initial picture, but then they sort of developed cholestasis and had a subsequent rise in ALP.

A couple of these individual cases had quite interesting presentations. So a 36-year-old male who was a competitive powerlifter ruptured his Achilles tendon while playing dodgeball, and that was attributed to his SARM use. Another one of these cases was reported in the systematic review.

I managed to actually find the paper for it. This case involved a 43-year-old male who was a sports coach presenting to the emergency department with epigastric pain, myalgia, severe headache and brown urine. He had cycled approximately 120 kilometres the day before he presented to the emergency department. They found that he'd taken ostarine a day before at a dose of 20 milligrams, and cardarine, which is a peroxisome proliferator-activated receptor delta agonist, in the four days leading up to this at a dose of 20 milligrams per day.

So cardarine isn't a SARM, as Rebecca says. It's got that really long-winded name that I'm not going to try and repeat. Peroxisome proliferator-activated receptor delta agonist. That's the one. And it activates a pathway that leads to fat loss.

So the theory with cardarine is that it increases fat burning and helps you reduce your body fat. This, like SARMS, was originally trialled as a medication and never made it through clinical trials. Rat data saw an increase in GI tumours, I think. And so it never made it through clinical trials for human use.

So he'd bought both of these on the internet and was taking them approximately 10 days before he presented. On admission, his BP was 135 over 70 with a heart rate of 76 BPM. ECG was normal, but his abdomen was quite painful. He had raised liver enzymes, both ALT and AST, but a normal bilirubin.

His CK creatine kinase was raised and this increased several hours later, which was a sign of his rhabdomyolysis worsening. So his muscles were breaking down. And he was treated with IV hydration. He experienced continuing muscle pain and had weakness for about 15 days.

But his labs were normal after about two weeks and he'd completely recovered six weeks after the event. And during his stay, blood, urine and hair samples were taken for toxicology and the white powders were also sent for testing. So this is quite a complicated case, isn't it? He had quite an extreme exercise history.

Whilst clearly people do extreme cycling like that fairly often, people also develop rhabdo and things like that after extreme exercise even in the absence of SARMS. In this case, he also had a liver injury. Yes, yeah. So that's perhaps less likely, although I guess rhabdo could potentially have contributed to some of that as well.

Yeah, it's an interesting case, isn't it? So the powders were sent for testing to determine what was present and how pure the substances were. They tested positive for ostarine and cardarine. The purity of the ostarine was 28%, but the cardarine was 100% pure, which I thought was quite impressive for stuff bought online that they hadn't put other things in.

And this is obviously an estimate based on, I think, peak area, so it's not an exact science. Both ostarine and cardarine were found in both blood and hair. Ostarine was found in the blood at a concentration of one nanogram per millilitre and cardarine was found at a concentration of 403 nanograms per millilitre.

In hair, ostarine was found at a concentration of 1,105 picograms per milligram and cardarine was found at 146 picograms per milligram. And interestingly, ostarine was only present in the urine at a concentration of 88 nanograms per millilitre. They didn't see any cardarine. Cardarine is extensively metabolised and is only present for approximately five days.

And the sample was sent 10 days after he'd claimed to have finished taking them, so it was not surprising they weren't seen. I do believe they saw metabolites including cardarine sulfoxide and cardarine sulfone. So when looking at hair analysis, often they'll do segmented analysis to work out long-term use and whether usage has changed over time.

Based on the hair collected, they weren't able to perform segmental analysis. But comparing the levels seen to cases from doping controls and drug trafficking, the measured concentration of ostarine was much higher in this case than would suggest infrequent use. So it seems like he'd been taking it a lot longer than he said

he'd been taking it for, and potentially at higher doses as well.

Yeah. So I think lots to take in there, right? There's this big market, potentially growing market of supplements claiming to provide you with muscle gains without some of the negative side effects. And yet there's also a body of evidence that says these compounds actually do carry with them quite a lot of adverse effects.

Even at doses much lower than that, which is being used by individuals seeking muscle gaining benefits. It's really, really tricky, isn't it? I think this isn't an endorsement, but if your sole aim is to gain muscle fast, anabolic steroids just do incredible things in terms of their physiological effect, yet clearly carry with them a lot of negative side effects, a lot of downsides. And I can see why people might want to try an alternative that claims to have all of these perceived benefits, but none of the risks.

What I found quite interesting with the SARMs is that although they contain dosage information, they're all sort of advertised as research-only chemicals. And to me, that would put me off from taking something, but it doesn't seem to be deterring anyone from trying them out. I think the research label really is a sort of marketing device; it gets around certain medicines laws and things like that. I mean, it is a completely unregulated market.

The fact that these compounds are sold online quite freely, and I'm sure also in person in gym locker rooms and things like that, means that unlike the wider drug world, where there is an effort to try and control a lot of these substances, there doesn't seem to be too much control of SARMs outside of anti-doping within competitive sport. We haven't really mentioned that, but these compounds are all banned by the World Anti-Doping Agency. Yeah, I think they were banned in 2008. Completely reasonably, but within the non-competitive market this is completely unregulated.

Anabolic steroids are controlled under the Misuse of Drugs Act. I don't think SARMs currently are, although I could be wrong. So do you think people who use these compounds are necessarily aware of the risks? No, I think it's one of those where people aren't necessarily going to talk about the negatives behind SARM use.

And I feel like unless it's happened to someone, you're not necessarily going to know that there are quite significant risks associated with their use, but it's definitely something people need to be aware of if they are going to go down that route and take them. Yeah, for sure. It is a really tricky world because behind a lot of this, sometimes there's quite a lot of body dysmorphia and underlying psychological things going on as well. Yeah, it's like with anything: when there's a perceived quick fix, that's always going to come with some risk.

And it's just important to keep in the back of your mind that if someone's promising you something that's going to help you build muscle really quickly, there will be negatives that come with that. Yeah, for sure. Based on that safety data, they certainly don't appear to be the safe alternative to steroids. Possibly safer, maybe.

Yeah. But certainly not safe. One of the other possible complications here, of course, is that people don't always use just one substance, do they? Often, if they're going down a route of chemically assisted bodybuilding, they may use other compounds to help, as we saw with the case using cardarine to help with fat loss.

You might see people using clenbuterol or stimulants and things like that to also bring up metabolism. Previously, we've talked about 2,4-DNP on this podcast, haven't we, which is a very different compound but can also be used in that sphere. There's probably quite a lot of polydrug use as well. Yeah, and I'm definitely aware of, for example, ostarine and cardarine being sold in a mix together to promote muscle gain and fat loss in one.

One stack. They call it in the gym sphere, I'm told. So should we be worried? Just thinking in terms of the rise in kind of social media influences and gym influences and young people wanting to aspire to a particular phenotype.

Yeah, I guess with them being advertised so widely and freely on social media, you are going to get a younger generation wanting to try them and not considering the risks associated. And it's something that

does need to be considered. Okay, so in summary then, there are an awful lot of products out there claiming to be a safe alternative to steroids. There's a huge amount of variation in what's actually in them versus what's actually listed on the side.

There's a huge amount of online dosage data, which is much higher than what was used in clinical trial data. And clinical trials were stopped because of the adverse effects. So I think it's really hard to conclude that SARMs are a safe alternative to steroids, and clearly they carry a lot of risks. So I think we're going to wrap it up here.

I hope you've enjoyed listening this week. Do give us a like, give us a follow, share with your friends. You can find us on Instagram at @the_tox_lab. We also have a LinkedIn page called the Tox Lab where we post about each new episode.

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So you can email us at thetoxlab@gmail.com. And we'd love to hear from you over there as well. All of the papers we talked about will be linked in the description of the episode below. So feel free to check them out if you want to have a read into any of these topics a little bit more.

Hope you all have an amazing week and we'll see you next time. Bye.