

[00:00:00] **Mike T Nelson:** Welcome back to the Flex Diet Podcast. I'm your host, Dr. Mike T. Nelson. On this podcast, we talk about all things to increase your performance in the gym, add some more muscle, and improve body composition, all without destroying your health in the process. And today, this one fits exactly within that wheelhouse.

[00:00:24] We've got my buddy Dr. Hunter Waldman on the program today. We're going to talk all about the use of ketones, metabolic flexibility, and a supplement called astaxanthine, which you may not have heard of before. You may recognize Dr. Hunter Waldman from the FlexDiet certification. Inside of it, he is one of the experts talking about metabolic flexibility and his research.

[00:00:57] He is currently an assistant professor at the University of North Alabama, and we get into talking about the use of ketones, especially ketone esters, to potentially enhance different aspects of performance, and especially related to potentially cognition under higher levels of fatigue. So if you're looking at athletic performance, or even just in the gym.

[00:01:25] We all know that as you have higher levels of fatigue, you get a little bit more tired. It's harder to stay present and make good decisions. Could the use of ketone esters be beneficial in these circumstances? What's cool about ketone esters is you can literally be in a state of ketosis within about 15 to 20 minutes of consuming them.

[00:01:50] As a side note, I've been... Extremely interested in the use of ketone esters for, man many years now. I remember on Facebook the other day there was a little thing that popped up that I was on a panel at ISSN, I think seven years ago now, with Dr. Lane Norton, Dr. Dom D'Agostino, myself, and we were talking about the use of ketone esters, salts, and the ketogenic diet in general.

[00:02:17] Also, I am a person who's helping at Tekton. So they have a new ketone ester. So I'm helping them with some science looking at what is actually going on with these ketone esters. So I may be biased in that, but wanted to include that for full disclosure. We'll include a link to all of their information there.

[00:02:40] And the great thing about the Tekton ketone ester is. It tastes actually pretty good. If you've tried any other esters, we talk about this on the podcast too, they are not very good at all. So how can ketones potentially be helpful? How does this relate to the concept of metabolic flexibility? And then how does astaxanthine relate to all of this?

[00:03:07] Astaxanthine is another compound I've been interested in for many years. I've presented to... At least one other company, I won't say who, but several years ago, they were looking at a fat burner, quote unquote, that was not a stimulant. And astaxanthin may have some interesting properties in there. So we discuss all of that too.

[00:03:30] So I think you'll really enjoy this podcast. And as a reminder, if you are looking for ways to increase your performance, become more robust, anti fragile, just generally much harder to kill, And your nutrition and training and sleep are, pretty decent. You've got those pillars down. Check out the PhysFlex certification.

[00:03:51] This is based on the idea of physiologic flexibility. How can you train the four areas? These are called homeostatic regulators. And your body has to remain constant. So one of them is going to be temperature. We know that humans are what they call homeotherms. We like about 98. 6, it's about 97. 7 Fahrenheit actually, and we can go into different areas of exposure such as sauna steam rooms, and you can get super crazy and submerge yourself in cold water, and there are some benefits to that.

[00:04:25] So think of this as expanding the areas of which your physiology can operate because of these specific adaptations. And it's my bias that as you expand these into these four critical areas, you will generally be able to recover faster. And you're just going to be a lot harder to kill. And one of those areas is expansion of metabolic flexibility.

[00:04:51] That's a B pillar number three, which is fuels. And this is also expanded into the areas of high carbohydrate use. Where you spin off a bunch of lactate hydrogen ions, and then also very high use of fat as a fuel with low carbohydrates. And this would be the use of a ketogenic diet or specifically ketones themselves as a fuel.

[00:05:14] So the physiologic flexibility certification opens September 18th. Go to [physiologicflexibility.com](https://www.physiologicflexibility.com). You can still get on the wait list. It will be open September 18th through September 25th. You can go to that same link if you are interested in enrolling in the certification then. Of course, we would love to have you.

[00:05:34] We've got some free gifts there for people who get on the wait list there. So go to [physiologicflexibility.com](https://www.physiologicflexibility.com) for all the information or hit me up with any questions you have. And enjoy this great conversation with Dr. Hunter

Waldman all about ketones, metabolic flexibility, and the supplement astaxanthine.

[00:05:56]

[00:05:57] **Dr. Hunter Waldman:** Hello. What's up Mike? How are you? I'm good.

[00:10:41] **Mike T Nelson:** How are you, doctor? Good. Good. You're so funny in calling me, doctor. You don't have to, especially with you being a

[00:10:46] **Dr. Hunter Waldman:** doctor as well. It reminds me of was it Fletch or was it spies like us? Were there like

[00:10:52] **Mike T Nelson:** Doctor. Doctor. Yeah, exactly. Where does it end?

[00:10:56] Yeah. Every time you email me and you say, doc, I'm like,

[00:10:59] **Dr. Hunter Waldman:** oh boy. I do it sometimes now just to almost annoy people. But yeah, I don't know. It's just almost more of a, for me I don't wanna say comic relief 'cause getting a PhD is a pain in the ass. But Yeah.

[00:11:13] **Mike T Nelson:** No, I get it. I get it. It's definitely it is always interesting when I meet people that you could tell it's just gotten to their head and it's yeah, we've all been there, buddy.

[00:11:23] So it's

[00:11:24] **Dr. Hunter Waldman:** all good though. Yeah. The funniest one I had years ago, my virtual assistant booked a hotel in Columbus, Ohio. I was down there for the, oh, the lead, f t ss to learn to train thing. Cool. And so I'm checking in and she's looking at the name and she's oh, okay. How are you today? And you could see her looking down, trying to find my name.

[00:11:43] She's Mr. Nelson. Oh, Dr. Nelson. I said, oh I'm good. And she's oh what are you a doctor in? And I said, oh, I did a PhD in exercise physiology. She's oh. You don't cut people up. I'm like no. I'm not a surgeon. Yeah. She's oh, and she looks so disappointed. She checks me in and she gives me my key.

[00:12:01] She's here's your key, Mr. Nelson.

[00:12:04] **Mike T Nelson:** That's awesome. That's great. My wife I tell people all the time, she constantly, if someone finds out I, I did a PhD it, it's great and all, but they'll say, oh, Dr. Waldman? And Erica's no, he's not, he is not

[00:12:16] **Dr. Hunter Waldman:** that kind of doctor. She keeps me humbled.

[00:12:20] Yeah. Anyways. Man, thank you for doing this. I appreciate it. You got some great stuff going on

[00:12:25] **Mike T Nelson:** now. I appreciate it. Yeah, thank you. You know it was funny, I was listening to your podcast with. Dr. Brianna Stubbs and we run Oh yeah. Run similar circles. We've never met or talked, but I've got some ketone work with Dominique Dom right now.

[00:12:39] And Brendan GaN. Oh, Andrew Knick and Oh yeah. It was interesting 'cause I was listening to that podcast and, she went off the radar for a little bit, especially with podcast. And she mentioned that, and that's been me too, ever since the PhD. Wrapping that up. I had done some podcasts then, but the p it was just so brutal and I needed Tom to get a balance again, so I just went off the radar and got rid of social media and just recently started bringing that stuff back, you and I had talked about that, but so this was my first podcast in probably five years.

[00:13:10] So I think your podcast is just bringing everyone outta the woodworks.

[00:13:13] **Dr. Hunter Waldman:** That's cool that, yeah. People probably figured out in the podcast. One of the things I like is that I just get to talk to really smart people, but questions that I have, 'cause like early on I was. You do the thing of oh, who's a big guest and how do I get distribution?

[00:13:28] How do I do all this stuff? Sure. And then I realized, like some of the interviews I was doing I just didn't like them. I felt like it sounded like everything else. And eventually, I'm like, I'm not making any money off this. I purposely chosen to have no sponsors, so nobody can tell me what to say or what to do.

[00:13:42] I'm like, I'll just talk to cool people that I wanna know what they're doing.

[00:13:46] **Mike T Nelson:** Yeah, great. That's awesome. And that's how it should be. If you, when I listen I listen to yours and I listen to Joe Rogan and

Huberman and these different individuals. It's really these people, you could tell they're genuinely interested in the people that they're bringing on.

[00:14:01] And it's not, doesn't sound to me, at least when I listen to all of you guys, it doesn't sound like it is you're pursuing a name, for the podcast. It is. You could tell that the. You as the podcaster that you're very much interested in the conversations that you're having. And that's always apparent to the listener,

[00:14:19] **Dr. Hunter Waldman:** oh, thank you. I appreciate that. And I think, people have an opinion of Joe Rogan. I like his stuff overall, but I think the fact that he just does whatever he wants and generally sounds interested in the topic Yeah. To me is just that's cool. Yeah. And the fact that, human's, the same way you could have two to three hour long conversations about science and some of those podcasts will be like some of the top rated podcasts.

[00:14:45] Yeah. Like that actually gives me a bunch of hope that people actually still care about

[00:14:50] **Mike T Nelson:** science. Yeah. Yeah. I hope so. I hope so. And podcasts is really, I've heard that science is primarily learned through communicate verbal communication. And I agree that to be true. That is true.

[00:15:03] And To be able to talk. A lot of people aren't trained, you know this, but a lot of people aren't trained to read the research. They might correct just read the title and walk away with it, and that's what they're spewing. But when someone gets onto a podcast to listen to what we have to say we're able to take that research that we've read and make it digestible for the wider audience.

[00:15:24] And that's what's so attractive to me to listen to podcasts or be a part of 'em, is it really is an ability that we've been trained in to get this information out to people and hopefully a way that they can use, in a practical sense to improve their lives and in some manner.

[00:15:37] Yeah. And as it's a different skillset to go into something where you don't know a lot of the questions ahead of time.

[00:15:47] Yeah. And to be able to. Make intelligent conversation out of it versus if you're not really so deep in that area, you could probably buffalo your way through a presentation if you put enough time and effort into it and you had to Sure. Super polished up. I think you could get your way through it.

[00:16:04] But I also think people now are able to disseminate that and they look for, it's like the argument I made for years of like, why would I buy a CD for example, of a live band? If by definition it's not gonna sound as good as a studio, but you want to hear like those different interactions with the crowd.

[00:16:23] You want to hear the slight imperfections, you want to hear, oh, they did this solo just a little bit different. Yeah. Like I think you humans want those types of slight imperfections and variability in the system. Sure. Absolutely. Totally agree. Yeah. Tell me about what you're I know you've got a couple studies on you're working on now.

[00:16:41] Did you wanna. Talk about some of the ketones stuff first and then maybe some of the metabolic flexibility stuff after that.

[00:16:47] **Dr. Hunter Waldman:** Yeah, for sure. So our, I'm, at the University of North Alabama. I'm the director of our exercise biochem lab and our lab, I've got three doc students under me right now.

[00:16:58] Nice. Yeah. It, is, it's a lot. But mentoring them's been awesome. And then we've got a couple master's students and then a ton of undergrads. But my lab is primarily, we've got obviously multiple faculty members, but my lab's primarily focused on three separate areas. Right now. It's asked, Ashin is a big aspect which probably will dive heavily into today.

[00:17:19] Exogenous ketone work and, those studies we're wrapping up right now. We've already wrapped up. We're actually writing on, so I just had a meeting with. Dr. Dino and Dr. Egan and Dr. Knick. Nice. And they're all a part of this. So those studies, all great dudes too. Oh yeah. Brilliant. Super nice guys.

[00:17:36] Brilliant. I was the primary variable in the, so we did some ketone mono ester work and trained females, division one trained female. Step beyond your typical recreational athlete. And we were looking at physical performance and cog cognitive performance. My big argument right now based on a lot of the isotope work that's come out by Dear Love and, some of these Howard and some of these other ones, is that it, is clear that beta hydroxybutyrate is probably not a major contributor to muscle energetic demands.

[00:18:09] Which makes sense because from an evolutionary perspective, B h B was likely elevated during periods of starvation. Yeah. Low carbohydrate availability. And so the mu there's saturation kinetics with B H B. Whereas when you start getting anywhere between three and six millimoles, the muscle essentially like limits itself on how much it can take up.

[00:18:31] And that makes sense because if it could just oxidize all of that b h b, there'd be nothing left over for the heart or the brain, I would argue

[00:18:38] probably the greedy organs.

[00:18:40] That's right. A little more important maybe than muscle. With deer love's work showing that regardless of the concentration of B H V, I think they in that study it was like two and four millimoles and then multiple intensities cycling intensities, they looked at oxidation of B H B at the muscle level is only about 5%. So the argument then becomes, what's happening is it acting as a signaling metabolite? There's a lot of gene transcription, which is actually, I.

[00:19:09] To take a step back, the way I even got into the ASEs anthem world was all of my interests in exogenous ketones and happen to come and their effect on the mitochondria. I came across Ashin and its impact on the mitochondria and that led me down. So it's like same rabbit hole, but two different rabbits.

[00:19:28] And so yeah, I really fell in love with both of them. But on the, again, going back to the ketone work, my thought was, all of those ketones that all that beta hydroxybutyrate is likely going to either the heart or the brain or both. And so I wanted to design a study looking at some cognitive measures and so brought that whole team on.

[00:19:49] We wrapped up that work this spring. We've got two papers in one paper. We induce mental fatigue and we looked at several cognitive measures from low and high cognitive domains. Task switching, incongruent flanker, your ability to decipher and inhibit certain stimuli. Your reaction time did that pre and post following mental fatigue.

[00:20:11] We didn't find anything between the ketone, mono ester and placebo. That's obviously still, this is all in writeup right now. But the second paper that we did where we have, it's even more intense. We have all types of metabolic data and physical data physical performance data, and then we've also got additional cognitive measures in that found nothing between.

[00:20:32] For the physical performance, there was no detriment but no improvement. But the cognitive side is awesome. I'm super pumped to get that out. I think we're gonna submit that to M S S S E and we found that with the ketone mono ester that. Not only were there greater improvements in that with the keone mono ester, but that there were also improvements in cognitive measures just immediately post endurance exercise, which was pretty cool.

[00:20:55] And, the research is clear on that. But if you ingest the ketone mono ester, not only do you get an improvement in markers of cognition post-exercise, but they seem to be, there seems to be a synergistic effect when you take it, when you take ketone mono esters. 'cause the magnitude of change was even greater with the ketone mono ester.

[00:21:15] And so we've got that work again, in write up everybody's getting feedback on it. But we'll be submitting that hopefully in the next month on getting that work out pretty

[00:21:25] soon.

[00:21:26] **Mike T Nelson:** And in that one where you saw the cognitive benefits was, what were you comparing it to? Was it placebo and then was it another type of ketone ester and then the mono ester?

[00:21:35] Or was there just two groups?

[00:21:35] **Dr. Hunter Waldman:** Yeah, so it was ketone mono ester compared to ketone mono ester with, or excuse me, carbohydrate alone. Provided at one gram per minute of exercise. So they essentially did 60 minutes, they did 30 minutes of a graded exercise test. So we base that off their respective tmax.

[00:21:53] So they did 40%, 45, all the way up to 65%, if I remember correctly. Five minutes at each stage, looked at various markers at each stage, and that took exactly 30 minutes. And then they did a 10 kilometer time trial, and we had done all the familiarization. So the CV was real close or real tight. Nice. And but no difference in that 10 kilometer time trial.

[00:22:15] And, there's several reasons why we chose that, but no difference in those performance markers. But anyways, gave them a carbohydrate alone provided at one gram per minute or carbohydrate with the ketone mono ester. So they got a relatively low dose, 375 milligrams per kilogram of the ketone mono ester in addition to one gram per minute of carbohydrate.

[00:22:38] The argument someone could make is, they weren't calorically matched. But you, have to choose your poison. You could go that route, but, or you could go the route wheat went and, there's pros and cons to either one. And I'm sure I'm gonna hear it from everybody when the papers do come out.

[00:22:55] how do you know it wasn't from the additional calories and how do you My argument's gonna be still though, that we saw there are other studies,



Dr. Eagan, Brendan Eagan has demonstrated mitigated decrements to cognition with keto mono ester lemons and quinones, I think how you say that last name, have demonstrated the same thing with keto mono ester ingestion.

[00:23:16] No one's specifically set up a study to look at cognitive, though it's always been like a secondary measure and we really set out to make that like a primary focus of the paper. and, and look what we found. So I think it goes back to the hypothesis, which is if you can overcome the fact that when you elevate beta hydroxybutyrate, which subsequently lowers glucose output, it seems from the liver, but metabolic clearance rate when it comes to carbohydrate remains unfaced.

[00:23:48] And that's what Howard showed with her is with that isotope work, which is even though beta hydroxybutyrate will lower glucose output, If glucose is still in circulation and available, the muscle can use it. It that metabolic clearance rate is un untouched. So the thought was, let's overcome the reduction in glucose output by giving 'em an exogenous carbohydrate and the muscle has enough carbohydrate to oxidize well then that b h b, when it's provided, may go to these other sources thinking cognition and may exert an effect there.

[00:24:20] And that's what we found. Again, it has to go through the review process. And it's always, I'm excited of course, but it could turn out, they're like, you did everything wrong. But we'll see. I've got some brilliant other, as you mentioned, other, some brilliant researchers on this one.

[00:24:37] So we're flushing out any, potential limitations right now, and then we'll, get that out

[00:24:43] to everybody.

[00:24:44] **Mike T Nelson:** Yeah, and that's a good lesson in how you set up a study too, right? Because a lot of times there's no. Right or wrong, it's what question are you trying to answer? And by definition, people could argue and say, oh, maybe you should have done a, third group of just the ketone only.

[00:25:02] Yeah. But then you have to look at your stats. You have to look at enrollment. You have to look at how many people you're gonna get through the trial, your trial of exercises, not a walk in the park either. And then, as if you run that type of style and people start dropping out, that screws your whole statistical power.

[00:25:19] And then if you can't recruit enough people to finish it, now you're f for starters. And then you're back to where you were before.

[00:25:25] Absolutely.

[00:25:25] **Dr. Hunter Waldman:** and you, make a great point and always point out to people cost. Yeah, they, the su time, the keto mono ester is not cheap. Not cheap. These were three hour long trials.

[00:25:36] We collected I ran some salivary markers. So you're talking about a life cost as well. Yeah. Looked at salivary cortisol between the different trials and stressors and obviously looked at some capillary blood markers, but that's not cheap. And so you start getting into money and time and and with the ketone mono ester only group, the argument for me is from a, because we're looking at this with trained athletes, I don't know how many athletes are just going to take a ketone mono eter and nothing else unless you start getting into the like, keto only group of people that are out there.

[00:26:10] And that's fine. But your typical wor the athletes that we're working with, they're going to take some type of carbohydrate, whether it be a deflated Coke or a Gatorade. So we are really trying to mimic real sport nutrition guidelines with the one gram provided per minute of carbohydrate. The keto mono ingest it, 'cause it'd be very likely that they would co ingest those.

[00:26:32] But again, not only what you pointed out, but I'm not married to the research that we do. I'm, it's, none of these are hills. I, know where my biases li lie. I do, I am biased in the work that I do but I'm aware of that. I try and control for those. Of course, I'm pumped about exogenous ketones.

[00:26:52] I wanna see some cool stuff from it. So much of the research now is just Eh, boring. Yeah, it is. And that's what it's showing right now. And but some of the stuff on mTOR signaling, potential, glycogen recovery, again, the cognitive side some of the oxidative stress signaling from exo or mitigation from exogenous ketones.

[00:27:13] there's still a lot of stuff to be done with it, but from the performance standpoint if you ask me right now, and, Dr. Stubbs really said it beautifully, it's probably, that's probably, a wrap in terms of is it really gonna have an effect? So now we need to start looking at it in other aspects of co ingestion spec.

[00:27:31] Another area I'd like to check it out with would be like, caffeine. That would be very cool. 'cause I think they would work real nicely together.

And then so anyways, we'll see. We'll see. But yeah, it's just, research is fun. It's fun to be able to talk about the results and get some cool findings out there just see what happens with it.

[00:27:49] And obviously the, Cox paper that was published a long time ago Used pretty high level cyclists. Yeah. And used carbohydrates with, I believe that was the mono ester that was used that too, from Vita's group.

[00:28:01] **Mike T Nelson:** Again, they only saw, if I remember right, 2% increase. But man, you could argue in, that population, that's pretty damn significant.

[00:28:10] **Dr. Hunter Waldman:** And in higher level athletes, I think Dr. Egan was the one who said 2% he. Talk a lecture at Ohio State, and he demonstrated that, someone would look at a 2% increase in and say, it's not much of a difference. But when you're talking about almost Olympic style type athletes, Olympic level is huge, 2% is the difference.

[00:28:30] It was the difference in like 10th place and two second or third place. It's, huge. You're talking about the podium and not podium. So those, were elite athletes that the Cox Group recruited for that study. again, context is so important when you start talking about findings methodology and, whether something works or doesn't work.

[00:28:52] **Mike T Nelson:** Do you think on the, what are your thoughts about the mono ester versus like the butanediol version? Because, and this is public knowledge and, conflict of interest. I may be working very soon or probably will be by the time this comes out with one of the, ketone companies who has a different ester.

[00:29:09] So for people make their own decisions based on that, whatever. Any thoughts on the mono ester versus the Butanediol version, because I know H V M N has switched over for reasons we don't have to get into, but They're pushing the butanediol version. You've got the mono ester, you've got these different esters that are coming out now.

[00:29:31] I'm just curious on what your general thoughts are. 'cause Yeah, I think for consumers it's super confusing, right? Because you hear Esther and, used the, mono ester early on from H B M N and it tastes horrific. Yeah. Like it tastes pretty bad. Yes, it does. And it's quite different from the butane dial

[00:29:50] version too,

[00:29:51] **Dr. Hunter Waldman:** it's a great question. I always stick, go back to the mentors that I have and look at what they've done. And I'm, looking at potentially doing some work. I've been put in contact with H V M N and, potentially gonna do some work with them in the next year or so. I haven't seen enough data to really have an opinion yet on if you should go one, one way or the other.

[00:30:12] I think we still need a lot of data on the different types of esters. Dom was talking about a trimester that it was in his fridge, and I haven't even seen any data on a trimester, so I'm like, there's just all types of stuff that are all types of potential data and research that's underway that we don't know anything about.

[00:30:33] And so right now with, so the, on what I can say is, and it's not even Esther related, is that the ketone salts, which are much more available to the public and cheaper, those don't really seem to have much of an effect other than giving you a GI distress. And so I usually turn people away from that. It's very hard with the ketone salts to get.

[00:30:58] Beta hydroxybutyrate levels above. Right now, there's a theoretical threshold of about 1.5 or higher, may even 2.0 millimoles of B H V and concentration to have an effect. And we think that might be a, at for physical performance, just based on what studies are out there that have found in effect. it's always been above 1.5 to 2.0.

[00:31:20] In cognition. We got our girls up, our females up above 2.0 and found some cognitive effects, but when you look at the ketone salts, they're not touching that. So it's gonna be within the realm of the esters. But in terms of an opinion on the different types, I'm just, there's again, for me, it's, I don't really have an opinion just yet.

[00:31:39] I, think there's still a lot of more, a lot more research to be done on that area. Before I can have much of an opinion there.

[00:31:47] Yeah, I

[00:31:48] **Mike T Nelson:** always ask this question too. Any thoughts about the, taste of 'em during the study? I did a, it wasn't published, but some stuff with the care institute were, we had three groups.

[00:31:59] We had the ketone ester and we were using the old mono ester from H V M N at the time, fasted, and then a high carbohydrate day. So they would

come in, do a two K on the rower under those different conditions. And it was interesting because, again, anecdotal not published data, but one or two people hit a PR on the fasted.

[00:32:19] No one hit a PR on the ketone group. However, we did a stroop test and we tried to do just some really basic cognition type stuff. And just r p e, a fair amount of people reported that they felt better and some of the Stroop scores and some of the cognition stuff was a little bit better. And then most people hit PR on the higher carbohydrate day.

[00:32:41] And we did that over a couple different groups, but. Even just getting them to take the, mono ester was Yeah. Was quite interesting because the, faces that they made of what did you just make me do? Were very

[00:32:53] interesting.

[00:32:53] We've I

[00:32:54] **Dr. Hunter Waldman:** mean it is extremely bitter. So when we were trying, we, I pilot, tested the taste along with some others trying to figure out for the placebo, trying to figure out an appropriate placebo.

[00:33:07] And so it is very bitter, very acidic. I've heard people call it jet fuel. I don't know what jet fuel tastes like. I just know that the ketone mono ester is man, it is very hard to get down. With that said, there, we have been able to figure out placebos that mimic it to enough of a degree that when we do an exit interview with our subjects and say, which treatment did you get?

[00:33:33] More than half will usually either say they don't know or they guess wrong. And

[00:33:38] so the way we've been able, oh,

[00:33:39] **Mike T Nelson:** that's pretty good. Yeah.

[00:33:40] **Dr. Hunter Waldman:** The way we've been able to do that is the biggest one is there's a, it's called true bitter blocker that you can add to the ketone mono eter. And I cannot remember the company, it's, they're based out of

[00:33:53] Pennsylvania.

[00:33:54] Yeah. Is it a masking agent for

[00:33:56] flavored houses used? That's exactly it. And we've been able to figure out that nice little balance there. Add a little arrow route to the placebo, give it a ma it, if you do too much, it's way too thick. But if you do just enough the correct amount, it gives it this the same mouth feel.

[00:34:14] And it is enough of a match between the two that are, like in this past study we did for the spring, only four of the subjects correctly guessed the treatment. So that's still four out. Yeah. That's good. We did 12 total, but that's that you were talking about a third. Yeah. But it is tough, for those who've never done it or tasted It it is very very harsh supplement to, to ingest.

[00:34:41] Yeah. I'll have to look to see what I know. Martin Gal just published a study on the ketone mono ester and I Read it the other day. Again, I can't remember what they used for a placebo on it, but yeah, that is one of the downsides of doing those, kind of studies for sure.

[00:34:56] **Mike T Nelson:** Yep. Oh, very cool. So what's up next for the kind of the ketone area? Are you still looking more at. Cognition after doing some type of physical tasks,

[00:35:08] I'm guessing. Yeah, I think again.

[00:35:11] **Dr. Hunter Waldman:** Alright, so we know, yes, it's with cognition and knowing that the ketone mono ester is so expensive, it just is it's, very costly if someone was to really incorporate it into their r typical training routine.

[00:35:26] So one thing I wanna check it out a with against and compare the two is against caffeine, caffeine's very cheap. It's also better. So I think making, being able to match the two in terms of taste won't be too hard. And looking at this very cheap, established ergogenic aid even for the cognitive side, established among a lot of military studies and compare that to the ketone mono ester, I think that's where the lab, in terms of the ketone work we're doing, that's where the lab's gonna head.

[00:35:55] Again, that's where I was talking with H V M N about some research down the road. I think that's what we're gonna look at. Then again just going back to an earlier question, you said what else the lab had was looking at. We're also involved heavily. I've got doc students on our ashin and then we're looking big time at some confounding slash variables slash influences on female substrate oxidation rates.

[00:36:20] So those are like the three big metabolic flexibility in a sense, if you wanna call it that. I, think like yourself, I've expanded that thought a bit beyond just metabolic flexibility. There's, so many other founder confounders that come in and, impact that, but yeah, those are like the three directions of the lab right now.

[00:36:41] Interestingly, they all come back to mitochondrial health. Which is really at the focus. If you said, Hey, hunter, what is the primary research? if you had to sum up your research, what would it be? I would say I'm primarily interested in practical interventions, whether it be exercise, nutrition, mitigating stress, improving sleep, whatever it might be.

[00:37:01] And I'm interested in these practical interventions and, how they might improve medic mitochondrial efficiency, mitochondrial health, and a, because our lab is so applied, yes, we can do a lot of different blood analysis, but I wanna, again, to make it practical, I'm interested in just, easy things.

[00:37:18] It might be just cardio respiratory measures or cardiometabolic measures like blood pressure and body fat. But substrate oxidation rates is a big part of that as well. Just simply looking at, Hey, how well do you burn fat and carbohydrate at different intensities? So that kind of summarizes what our lab is trying to accomplish hopefully before I take the old dirt nap.

[00:37:39] We'll see.

[00:37:41] **Mike T Nelson:** Oh, that's great. And obviously we initially connected on, you're in the flex diet cert with the interview we did back in the day about metabolic flexibility and stuff too. So yeah. Give me your, I'm super curious now, you said expanded thoughts on metabolic flexibility. So give me your expanded thoughts.

[00:37:58] I'm super curious.

[00:37:59] **Dr. Hunter Waldman:** Yeah, I used to think of metabolic flexibility just as, and it still sticks to the name, which is, how well your ability to oxidize either this substrate or this substrate pending what the mitochondria or what you're exposed to, whether it be exercise or stressors, whatever it might be.

[00:38:18] And then that's kinda where it stopped for me at the time as a doc student. And now later on looking at metabolic flexi. First off, the biggest question is what, how do you quantify metabolic flexibility? Yeah. What is that's like the, That was being posed to me early on. Not directly, but the way

the questions I was getting asked, and I came to this thought myself, which was what is considered metabolically inflexible.

[00:38:46] So if we go to the extremes, you could look at, you could argue insulin resistance type two diabetes. You could go to the other extreme though, and. People will mention maybe like ketogenic diet as a way to become metabolically flexible. You can also make yourself metabolically inflexible, I would argue if you follow that chronically, because then you essentially impair mitigate the glycolytic system.

[00:39:12] And we've seen that, we've seen reductions in pyruvate dehydrogenase and that whole complex. So that's right. So you can also become metabolically inflexible, this other extreme. And that the, so then you start trying to cut, if it's a spectrum, you start coming on in into the spectrum and saying, okay, so where exactly does metabolic inflexibility happen?

[00:39:32] Because it's hard to talk about metabolic flexibility if you don't have a definition that you can quantify. Yep. And so that's really where my brain, when I mean expanded, that's where I'm at now, which is, and it's not just looking at how well the mitochondria or the cell itself handles substrate oxidation.

[00:39:51] It being. As a result of exercise, because that's where a lot of the early research was. Now it's expanded for me, looking at all the different type of stressors. So psychological stress, physical stress looking at sleep. If in a sense, sleep can be a stressor. Someone could argue sleep, could be a stressor.

[00:40:11] You're going, if you're getting enough of it, I know it's a restorative period, but eight to 10 hours in a fasting state you definitely can see transcriptional factors and enzymes and proteins like m p k upregulated. M P K is a stressor. Stress protein that in caloric deficits will be upregulated.

[00:40:28] So we can see some upregulation, A M P K so anyways, just environmental stressors and you can start combining those and get what are called dual stressors, like physical and cognitive stress. And then looking at how those impact metabolic flexibility. And Anyways it's just, it's, it went from me thinking of metabolic flexibility and just how exercise impacts it to now it's okay, we really need a working quantifiable definition for it.

[00:40:52] And there are many more factors that impact it other than just exercise. And again, that's just me just growing up, a lot when we had talked years ago that's where I was a doc student and I'm getting older and hopefully



learning a little more every year, and I'm, I've got great mentors that, that help me see things that I wasn't seeing at the time.

[00:41:11] Yeah. And I don't know how, if it's changed for you, since we've last talked or because that's how one of the ways we connected was over Facebook talking about Yeah. Metabolic flexibility. Has it changed for you in terms of your

[00:41:22] thoughts on it? I think so. I.

[00:41:26] **Mike T Nelson:** God I was looking at this the other day.

[00:41:28] I'm like, oh my God. I started looking at this 16 years ago, I think now when I started my PhD. Yeah. And at the time I was like, metabolic, what? I like same. That was my first question you had too is wasn't that just how normal humans work? If, show me the metabolically inflexible people and then I might care because it means it can be changed and Yeah.

[00:41:48] So happens. So lots of disease processes do that. And then the definition was, the thing I was trying to finish my PhD dissertation on was, fine scale variability across different physiologic systems from heart rate to r e r. So our hypothesis was if we baseline someone, we get 'em into the lab, we do their VO two max, we baseline them to a.

[00:42:09] Max amount of work, put 'em on a steady state treadmill. We have a breath by breath metabolic heart looking at r e r. So we're looking at what percentage of fuel that they're using. Like most of the textbooks at that point, even now would say it should be, 0.7 5.75. But if you've done enough metabolic tests it's a 20 minute test, you get bored and you just start staring and you feel like you're in the matrix looking at all these numbers going across the screen.

[00:42:35] And you'll see like r e r starts moving around 0.7, 8.7, 6.7, 4.7, 3.75. And then the next person you'll see 0.7, 5.7, 6.75, 0.75, like it doesn't move much at all. Because some people would argue like, that's just the machine. It's the variability in the system. And there is some of that. So our argument was, That fine scale variability change in r e r under a constant low intensity exercise is a marker of metabolic flexibility.

[00:43:05] And that might be a non-invasive way without pulling bloods, without doing anything else to try to get at, who's more metabolically flexible than somebody else. So long story short, we did that, we published it we only did a, basically a gauge r and r on it showing that it is repeatable.

[00:43:21] And my thought is, I'm sure maybe you were similar once you graduate, get your PhD, you're like, yes, I'm done. I'm out. Woo hoo. Yeah. And you just assume people will read your research and someone will, go out and test it, right? Yeah. So I assumed someone will read this and go, Hey, that's ingenious.

[00:43:37] Let's see, does it actually show that it is, it's a stable measurement. Does it actually show it's metabolically flexible or not? And no one's ever done that. And every time I present the idea to people, they're just like, I. Eh, and I'm like, man, I'm not going back to school to look at this again.

[00:43:51] I'm out. Yeah. Least someone else will do it. Yeah.

[00:43:53] But in terms of expanded definition, lately, probably starting maybe eight years ago, similar to you, I was like, okay, so if this works for metabolism, what about if we scale up as like a human organism? What does that look like? And so the concept I came up with is, physiologic flexibility.

[00:44:14] How well can you change depending upon different, stimulus? And then the next question for me was, okay, great. What systems am I even gonna bother looking at? There's bazillions of systems in the human body. So I said, okay, if you're survival based, what systems does your body 100% have to hold within a fine range?

[00:44:34] So I came up with temperature pH fuels, and then c O two. You could get into some, molecular ones and some other stuff beyond that. But my argument then is, okay, if your body has to hold those constant, can we build a more physiologic headroom or buffer space within each one? Because we know all those have the ability to be, adaptation.

[00:44:57] Whether it's heat declamation, you can get used to cold, whatever. And so I just called that, physiologic flexibility, and so I have a certification that goes through each four of those areas of how can you increase the physiologic overhead in those. My argument is that once you have your basics covered, like sleep, exercise, nutrition, this would be a framework then to look at how can you become a more resilient organism.

[00:45:22] Yeah. How can you be dropped into other environments and still, perform

[00:45:27] well at that point? There's a lot of just based off that, and I've checked that website out and obviously listened to you talk about this on some

of your other podcasts, but, so many factors play into what you're talking about, like the idea of hormesis, some stress is good.

[00:45:42] Yeah.

[00:45:42] **Dr. Hunter Waldman:** And too much is bad and not enough is also potentially bad as well. And getting into allostasis and allostatic load and these are concepts that people even in the exercise science generally haven't heard of or thought about. And yeah, what you're talking about summarizes all of that.

[00:45:59] It's also interestingly where a lot of the acids anthem research that we've done, it's is with that mindset what you're talking about, these different concepts in mind. Yeah, it's fascinating.

[00:46:08] Yeah. Yeah. Yeah.

[00:46:10] **Mike T Nelson:** And last part on that is that, I like the word adaptive homeostasis better than hormesis, which again, is getting down and like really splitting hairs.

[00:46:21] Yeah. Because the definition of hormesis would imply that there has to be some cell death in order to trigger that process. But as we know, you can do things to the body without actually having to damage the cells and they can still get a positive adaptation, which would be more adaptive, homeostasis.

[00:46:39] Yep. Again, that gets into the research and Kelvin Davies is the main guy who, goes with that theory. So Yeah. But again, it's always fascinating to me how the adaptability of the human organism almost never gets lost. Yeah. I worked for a cardiac medical device company for many years, and we'd have patients that would be in, class three, heart failure with their lungs half full of fluid.

[00:47:03] And the heart's like the size of a basketball. But it's still in that phase, still trying to adapt and do the best that it can. And in a couple cases where we put in devices to resynchronize the actual pacing of the heart, the beating the heart actually re remodeled back down to a smaller size in Oh wow.

[00:47:20] Many of the cases, which to me was just fascinating. Yeah. 'cause a lot of the eps, electrophysiologists, cardiologists I talked to, they're like, eh, they might do better, but their heart's not gonna change in size. And at some point if you have enough damage, it won't. But if you can get at it right before you start

having fibrosis and a bunch of damage, it's crazy to me with the right stimulus, how much adaptation you can still get out of the human body, even in the worst

[00:47:45] case scenario.

[00:47:46] **Dr. Hunter Waldman:** For sure. I think maybe like yourself that's a, that case maybe not that extreme, but is what attracted me to xFi an undergraduate student. Yeah, totally. Is the just. The, how amazing the human body is. Someone could look at someone who's extremely obese and insulin resistant, type two diabetic and maybe not think twice about it.

[00:48:06] And I look at that and think, man, even though, and they might smoke and everything else and look at that body and think it's still functions, it still has all these different processes that allow it to function and adapt and potentially even reverse itself to the other side of the spectrum if done correctly.

[00:48:24] So physiology, it's fascinating. I just love it.

[00:48:28] Yeah, I gotcha.

[00:48:30] **Mike T Nelson:** Similar, I'm always amazed at the range. If I put sugar in the gas tank in my car, I'm not gonna make it around the block. But you could live on seven 11 Slurpees for several months and still be upright. Yep. You're not gonna be the best functioning human on the planet or the other end of the spectrum where we talked about that 2% difference in elite athletes, like these minuscule changes make. Big differences on that end too, just the range of it, or I just coined a term I call human dynamic range is just

[00:49:02] **Dr. Hunter Waldman:** Fascinating. That's a good term.

[00:49:03] **Mike T Nelson:** Yeah. Yeah. I like making up terms now I figured I screw it. I'll just make up my own terms and whatever.

[00:49:08] Yeah. I keep doing it. I

[00:49:09] love it. I'm gonna have to make a list of them. I'll credit

[00:49:13] when I use them. Yeah. Yeah, so let's talk about asthe. I started. Following some of that research. Oh man, maybe it was a 10 or 10 plus years ago, I saw a talk, I can't remember the Japanese fellow at I S Ss n talking about asan thing related to eye fatigue.

[00:49:32] Oh yeah. And I was like, man, this doesn't make any sense, and his, the thought process was the eyes, the muscles of the eyes produce a lot of reactive oxygen species because of how much work they're doing all the time. And that astaxanthin can help quench, some of these free radicals.

[00:49:49] And so I started looking at it and I found a bunch of really early rats or mouse data showing up regulations in fatty acid use. So at the time I was really looking at, supplements for how can we up upregulate the use of fat for fuel related to, metabolic flexibility, which, everyone's looking for better body composition, all that stuff, forever.

[00:50:09] But I was like, can you do with the something that's not a stimulant? Or, massive uncoupling agent like D M P, which has a side effect of like death. It's probably not so good. Probably not. Yeah. And not reversible. Yeah. And there's some very interesting studies on rats. I think it was interaction of a CCPT one enzyme, which is basically allowing more fat to flow through the mitochondria.

[00:50:31] And so I kept following that and following it and I've tried a bunch of experiments with it. And then they had some human studies that came out that were like, eh, not as impressive. And then I was kinda like me. And then I talked to Dr. Karen at is s n last year again, and she was telling me about all the new work they've been doing and some of the update of the studies.

[00:50:49] And I was like, oh. Because it was one of those things where the research just kept accumulating, right? So you've been around long enough that you'll see people get super excited about a thing and there's a whole bunch of research and then it just drops off a cliff and no one ever looks at it again.

[00:51:03] Where the research on this kept. Going up and up and there's yeah. A lot more interesting things that you see

[00:51:07] now with it.

[00:51:08] **Dr. Hunter Waldman:** Yep. Yeah, we, and we can definitely go down whatever rabbit holes you want for those who are listening just to talk about what is, as Anthony Yeah. What is it? We should duck up there.

[00:51:19] Yeah. Because a lot of people, when I talk to 'em about AST is Anthem. They were like, they don't know how to pronounce it. Yeah. And they've never heard of it. And I was at a conference and someone didn't know

how to say it, and so they called it AZT tax and they kept referring to it as that. I was like, no, that is not, yeah.

[00:51:37] That is not a good

[00:51:38] shortened version. Let's come up with

[00:51:39] something else. Yeah. All so taking a step back, let's get a global view. There are probably 10,000 plus phytochemicals that exist. That we're aware of vital chemicals being plant chemicals, and most of these have some type of antioxidant properties.

[00:51:56] And it's very tough to talk about antioxidants without talking about oxidative stress or oxidative eure and free radicals. And we can talk about that and give a quick overview of those. But these antioxidants within that is a subclass of carotinoids and that we think there's probably, give or take a thousand different types of carotinoids.

[00:52:15] And within that subclass for those who are unaware of carotinoids they're different from other antioxidants. They're hydroxyl containing, which is oxygen and hydrogen. A lot of times they are converted into vitamin A, but they are pigments that give fruits and vegetables. They're color. So yellow, orange, red, anything mangoes, sweet potatoes, carrots tomatoes, anything that has those colors.

[00:52:41] Those are the OID families that are allowing them to have that color. They are very powerful in terms of being able to prevent oxidation. Astaxanthin, almost, I couldn't say it, asan. Astaxanthin is unique in that it is a carotenoid, but it's not found in plants and fruits and vegetables. It's actually found in crustaceans like lobster and crab.

[00:53:06] It's found in soil. It is found in microalgae and yeast and it's also found in salmon. And I've heard people make the argument if you eat enough crab and lobster, and always have to stop 'em and tell 'em, if you've ever seen a lobster or a crab on the beach or in a tank, if you're gonna eat one, they're not red.

[00:53:26] They turn red when you cook 'em. It turns out that most antioxidants, phytochemicals, carotinoids, they're bound by proteins, and those proteins only release 'em when they're heated up. So you find a lot of astaxanthin in the shell of crabs and lobsters. And what happens to a lobster when you cook it?

[00:53:46] It goes from gray to red. Why is that? The heat degraded that protein that was binding astaxanthin, and then that allows astaxanthin to express itself. But even still, you don't eat the shell. So really the main place that you're gonna get it, if you are gonna get it naturally, not talking dietary supplementation, is going to be from salmon.

[00:54:07] Now there's two different types of, there's all types of salmon, but there's farmed and wild farmed salmon is actually has a gray muss. And because people aren't attracted to eat gray salmon, they're fed pellets that have synthetic astaxanthin in it. Ashin comes in several, in three different stereo isomers.

[00:54:27] It comes in the three R, three R three s, and then three s, three s. And for those listening, you can start really getting down the chemistry rabbit hole on this, but, and we don't have to go there. But I usually, when I explain it to my students, I'm like, you have a left and right hand.

[00:54:42] It's the same thing. It could be like two left hands, two right hands, or left and right hand. The stereo isomers are just. Saying the configuration of the chemical either looks the same or it's been flipped, whatever it might be.

[00:54:54] Yeah, I call 'em like, they're like a mirror image of each other.

[00:54:56] Yeah, exactly. If you write 'em out on paper, they look the same. But if you hold it up to a mirror, you've got two, two

[00:55:01] different images now. That's exactly right. And the synthetic form is actually the three R three Ss. Generally the three R three Ss and farm salmon have a very, have a much higher ashin content than wild salmon because they are fed this concentration concentrated form.

[00:55:19] However, it's the synthetic Assan anthem, which is not nearly as powerful as natural astaxanthin. So the natural astaxanthin three s three Ss is what you find in wild salmon of all types and really came to the forefront of research. It was some fishermen had. Essentially come up to a researcher, and I do not remember his last name but they were trying to figure out a way to have healthier salmon, healthier fish.

[00:55:49] And so he recommended they start feeding a masses anthem. And for those who don't know, you probably know what a salmon is, but you may not know it's lifecycle. And at the end of their lifecycle, they travel over 900 miles. Crazy. They travel so over 7,000 feet of elevation. And when you talk

about, and they don't eat the whole time that they do this, they don't eat interesting.

[00:56:10] They don't eat. So they are the ultimate endurance athletes. And so they're one of the main animals you can study for oxidative stress and reactive oxygen species production. And what they were finding in the salmon is that, They are somehow able to preserve their ability to oxidize fat and maintain this healthy muscle tissue even after not eating and having traveled all this way.

[00:56:35] And they were able to find out that it was astaxanthin that protects the muscle, protects their ability to burn fat, utilize fat. And to go back to what you were saying, you were talking about the the mice data. We know one of the things that happens now, you can see this in an obese population or you can see it just in an athlete that is exercising for a long period of time.

[00:56:56] But the mitochondria, so I'll take another step back and talk about oxidative stress and free radical production. So there are several places that you produce free radicals. And what is a free radical? It's just a molecule with an unpaired electron. It can get, it can be more than that. But for the sake of this talk, we'll just stay there.

[00:57:14] And it's produced in several sites. We know it's produced in the mitochondria. There's some debate right now as to if that's the primary site during exercise or not. It's produced outside the mitochondria and the cytoplasm. It's produced by endothelial cells, and we can talk about that as well 'cause there's some cool stuff there from Anthem.

[00:57:32] But it's produced in all these different areas when it's, when free radicals it, they all originate from something known as superoxide and or singlet oxygen. Singlet oxygen is literally just oxygen that's missing an electron. And one of the things that happens is when it's produced in the mitochondria, it is able to immediately escape the mitochondria and start reacting with D n A mitochondrial d n a and changing the form of mitochondria.

[00:58:01] It's able to interact with lipid membranes and proteins and degrade these things, which is not a good thing. So anyways, one of the other proteins it can interact with is carnitine, a sealed transferase one. So the carnitine system. And for those who are unaware, your mitochondria, the way they're able to oxidize different types of fats is they have a transportation system, the cat system, carnitine system that will take these fatty acids and bring them inside to be used as a fuel.



[00:58:30] But these free radicals, when they're created anytime metabolic rate is increased, these free radicals will attack that CAT system. That carnitine system. And what we end up seeing is we see a reduction in someone's ability to burn fat. And again, this can happen in someone who's at rest if they're really obese or overweight due to ceramides and DAGs and all these other, and disruptions to the insulin receptor substrate.

[00:58:57] But in even a healthy person, if metabolic rate and metabolism is high enough, this can also happen to you as well. And so Astaxanthin has a unique ability due to its structure, which is different than the other carotenoids. It has polar ends. It's it, if you can picture a chain, At the end of both sides of the chain are two balls, and it is the perfect size and length that it's able to embed itself into any bipo or bilipid membrane.

[00:59:27] So think of like your mitochondria. Your mitochondria has two membranes, an outer and an inner, and ashin is able to take its ends and put 'em in the membrane. And then it has this chain that connects the two ends that actually sits in the, in between those membranes. And it can do that in cell membranes.

[00:59:44] It can cross the blood retina barrier you were talking about. The silly scary muscles, which can control contraction and lengthening of the muscle or the eye muscle. It can cross the blood brain barrier and it increases its concentration and content in hippocampus and prefrontal cortex, and we can talk about that.

[01:00:02] And so it's able to scavenge these free radicals outside of the membrane. Inside the membrane and on the inner membrane. And so usually if you take vitamin C, it's water soluble. It can only scavenge in the aqueous or rec cytoplasm. Section. If you take vitamin E, it's lipid-soluble, so it's gonna scavenge within the actual lipid area of the membrane.

[01:00:30] Butis, anthem's able to do it all and it's got a mu, it's much more powerful than these other beta car. These other carotenoids. One of the problems with the carotenoids is that if taken in too high of a dose, they can actually go from antioxidants to pro oxidants, which is an issue. And astaxanthin, we've not seen any negative effects from supplementation with astaxanthin.

[01:00:52] Doesn't appear to become a prooxidant even in high doses. And its ability to quench singlet oxygen, its ability to take on these high electrons, these high energy electrons and mitigate free radical production is really impressive. And there's research that's come out in 2023 because one of the big things from

the athletic community is, Whether or not taking antioxidants actually impairs exercise training adaptations.

[01:01:18] And we're not seeing that with astaxanthin. In fact, again, some of the 2023 data has demonstrated that its ability to upregulate mitochondrial antioxidants glutathione catalase, superoxide dismutase. It's doing this through a transcription factor known as NRF two. We could talk about that as well.

[01:01:37] But it's not mitigating the training adaptations. There was a cool study that came out with hi in Ashin versus no Ashin and finding a lot of cool adaptations in the HI hit group with ashin. Whereas the HI only group experienced because it was so frequent, they actually went backwards. And this was a mouse model, but they went backwards due to excessive oxidative stress.

[01:02:00] And that was not experienced in the group with Astine. And so it's just It's a really a phenomenal antioxidant. And the more I study dietary supplements, the more I, the less I take. I, there's only a couple, I take whey protein, creatine vitamin D three, and I've added astaxanthin based on what I've read and the research that we're doing.

[01:02:19] I've added astaxanthin six milligrams a day to my regular stack and that's it. So it's interesting how fish oil plays there too. Yep. So there's fish oil. Man I am a proponent of fish oil. There's an argument as to whether it should be fish oil or carola oil, and people gonna say

[01:02:38] why.

[01:02:38] **Mike T Nelson:** That's my next question.

[01:02:39] **Dr. Hunter Waldman:** Yep. So if you look at the fatty acids that were primarily focused on between krill oil and fish oils, d h a D cosa, h noic acid, and E P A I, cosa pen, NOIC acid a lot of benefits to e p A and d H a. In fish oil, it comes in the triglyceride form and in krill oil it comes in the phospholipid form.

[01:03:01] And for those listening, it's like, what is he talking about? Just understand the phospholipid form found in krill oil. It's able to penetrate it, we'll say it's more bioavailable to the cell. Interestingly, there's research coming out now that shows that ashin, when paired with fish oil, specifically fish oil it seems to enhance the effects specifically for cognitive function.

[01:03:25] And that's really interesting. Now the mechanisms are not known yet on that. Those have not been fleshed out. We just know right now, That astaxanthin and e p a and d h a when taken together, which makes sense 'cause that's what you would find in natural salmon muscle. But when taken together, there's a synergistic effect that's happening there.

[01:03:45] And there's research coming out that's showing that the mechanisms are not understood. There's an argument of, okay, if, if krill oil is more bioavailable in terms of the fatty acids that are in there and krill oil, it's red, it has sampan in it. Shouldn't we take that? And I always tell people I.

[01:04:04] Her oil is made up of less than 1% astaxanthin. So yes, it is in there, but it's in such a small amount. I don't know if it's actually meaningful. So yeah, I think if, going back to your original question, do would I recommend fish oil? I think context dependent for sure. Especially as we age and we know the data coming out on anabolic resistance and fish oil, potentially being able to reverse that.

[01:04:26] Yeah. Or enhance our ability, the anabolic signaling Pathways protein kinase B and mTOR. I definitely think that it's there. I'm not taking it yet, but when I talk to people, especially over 35 it's one of the main it's, or if they're suffering with any kind of dyslipidemia or cardiovascular disease markers or elevated inflammation, visual is one of the first things we get to talking about.

[01:04:49] Yeah.

[01:04:49] **Mike T Nelson:** And that's for people really wishing to push the envelope. My recommendation for many years was, Eh, curl oil. I agree. The bioavailability is better, but if you look at the price and you look at the amount that you would end up with at the end, it becomes a little bit cost prohibitive.

[01:05:07] I think, especially when I've run blood spot tests on people and like the E P A D H A is in like the absolute crapper, yeah. They're just like so low. They're Omega six is so high. Yeah. I'm like, if you really wanna push the envelope, take a bunch of fish oil and then just take astaxanthin separate.

[01:05:25] Yep. That's my

[01:05:25] go-to, yep.

[01:05:26] **Dr. Hunter Waldman:** And that's what I recommend as well. Honestly the promising data with astaxanthin to, to put it in perspective, We in general recommend PE individuals that study this, depending on the benefits that you're looking for. Because it does change a little bit based on the data.

[01:05:42] Right now, if it's cognitive, if it's for eye health, skin health or performance, it's gonna range somewhere between four and 12 milligrams a day. And so again, I take six milligrams, I hit that middle middle mark. But in order for you to get, so for one milligram of astaxanthin, if the main food source is gonna be salmon, you have to eat somewhere, depending on the type of salmon, somewhere between six to 12 ounce filet to get one milligram.

[01:06:12] Which is a lot of fish to get one milligram of it. So if we're saying you need to take six milligrams, You're getting up to a really, a lot of salmon every single day. So yeah just from a practical standpoint, it makes sense to just take it as a dietary supplement. The biggest thing is making sure you're getting it from someone who's sourcing it from yeast or microalgae, where the environment can be controlled.

[01:06:37] One of the ways that algae going back to the hormetic theory algae, it's green, but when it's stressed, It actually will produce it will synthesize astaxanthin and it turns red. It's again, to protect itself from pH changes in pH, changes in temperature and acidity. So individuals that understand this, like Astor Real and Dr.

[01:06:59] Hecht, and that's part of her company that she works with as a scientific affairs manager there, and she's brilliant. They're able to control for that. Whereas most, 95% of dietary supplements that are producing astaxanthin is the synthetic form. And we go back to the synthetic form. It's not nearly as powerful as the natural source that you can get from, again microalgae salmon.

[01:07:24] But yeah, definitely supplementing with it makes the most sense. It'd be very tough to get it from the diet if you were

[01:07:29] to eat that every day.

[01:07:32] **Mike T Nelson:** And I would assume sockeye salmon, because they're more red color, would have more astaxanthin

[01:07:37] in it. Correct? Yep. Yep.

[01:07:38] **Dr. Hunter Waldman:** Brilliant. A ab absolutely. It, it has, based on what I understand, it has the highest concentration of astaxanthin, of natural astaxanthin.

[01:07:48] But it's still, you still have to, would have to eat quite a bit of it every day. Yeah. I still eat a ton

[01:07:52] of it. Yeah. Kinda like creatine. Yeah, that's right. Yeah. Yeah. You can get it from meat, but you're talking like multiple pounds per day to get a couple

[01:08:00] grams. Yeah, exactly. That's a great comparison there.

[01:08:03] And I think AST does Anthony, because it's incorporated into the cellular membrane.

[01:08:07] **Mike T Nelson:** If you're looking for kind of a maximal effect, like creatine, you would need a loading phase of, would you say, two, four-ish weeks maybe? Or longer for it to accumulate into the body.

[01:08:19] **Dr. Hunter Waldman:** Yeah, great question.

[01:08:20] The data on, so that's data that we need still in terms of do you need a loading dose? And how long does it take to saturate the actual cell itself? Because the data that we do have, we know there's acute data where people have ingested 40 milligrams up to a hundred milligrams, no toxicity effects.

[01:08:40] But again, we're not really sure if you set, if you take 40 milligrams of astine within about eight hours, it, we see that it has, it's. We see that in the blood from the red blood cell, but that doesn't mean what you find in your blood or plasma doesn't necessarily reflect what's going on in the cell.

[01:09:03] Yeah, so we don't have the data as of right now to say you should or should not load it to get the mitochondria and cell membrane fully saturated. But we do know, based on the data that's out there, if you take anywhere from six to 12 milligrams a day, you can definitely start to see cognitive effects, skin health effects metabolic and performance effects within four weeks.

[01:09:26] So there's clearly within about a four week timeframe of just taking it. And that's no loading. I would not consider six to 12 milligrams a day. Lo a loading phase. And again, about that four week timeframe I can definitely start to see effects there.

[01:09:39] Interesting. What is your thoughts on, so one of the things I do before I go on a kiteboard trip is one of the things I've added within the past.

[01:09:48] Probably three years is actual AST asan thing. And from talking to Dr. Karen last year, and again this year I've upped my dose. I started initially at three grams, then I went to six, then I went to nine. Three milligrams. Yeah. Yeah. Three milligrams, yeah. Now I might try the higher end, maybe 10 or 12.

[01:10:05] Yeah. And my thought process is that there may be some protection for UV potentially related to the skin because I'm very fair skinned. Obviously I still wear sunblock. I wear full clothes when I'm outside, but I'm kite boarding, down south, like staring at the sun for, five hours at a shot.

[01:10:23] And then also, I haven't seen any direct date on this, but any thoughts on potentially mitigating concussion with potential stabilization of the blood brain barrier or, yeah, some of the neuro aspects? Again, my thought being that I. I don't know what the potential upside is, but I know the downside, there's not much of a downside other than cost.

[01:10:47] **Mike T Nelson:** Yeah. And if I'm gonna do something where I'm gonna try to, jump 20 feet in the air, there's some bad shit that could go wrong, right? Yeah. That's right.

[01:10:54] **Dr. Hunter Waldman:** That's right. I assume there's no, I'm not familiar with Kiteboard. I have an idea, but I'm assuming there's nothing to catch you if you land hard.

[01:11:02] Yeah. It's the good and bad. Obviously, you're using the kite and if you ride and you throw the kite directly above you real fast, pull the bar in, it'll literally yank you straight up off the water. Yeah. So there's this little divis that measures it, and I'll go from, on the surface to, 15 feet, sometimes in a second and a half.

[01:11:19] It feels like the

[01:11:19] **Mike T Nelson:** hand of God came down and just threw you in the air. You're, man, the great part is if you, yeah, the great part is if you do it right, you can move the kite and you can, land super soft, but, If you screw something up or you start moving the kite fast and it's out in front you can just, but get drop like a sack of potatoes.

[01:11:37] Yeah. Let me hit

[01:11:38] **Dr. Hunter Waldman:** the skin side. Yeah. And then we'll talk about the cog cognitive side real quick. You're absolutely right. When you look at the data on Ashin and skin health there, there's enough data there now that cosmetic products are adding it to some block.

[01:11:52] **Mike T Nelson:** Yeah, I've seen that. It is very impressive. And those are, the data that's out there is all at the higher dose. It's been around 10 milligrams a day that those subjects, human subjects have been taken. There is some mice data as well where they, as bad as it is they would burn the mice and there was a group of placebo, group of ashin and the group that got as.

[01:12:14] The burn recovered quicker.

[01:12:17] **Dr. Hunter Waldman:** And I guess I'll take a step back and explain. One of the things that happens when you're exposed to UV radiation is that radiation can actually come into water knock ahy, and your skin is full of water. Obviously, hydration's a big part of that. But UV radiation can knock a hydrogen off.

[01:12:35] And what you're left with is a hydroxyl radical for those who are unaware. Hydroxyl radical is a free radical, and it is the most damaging free radical that you produce. Not good. Those hydroxyl radicals are then your lipid membranes in the skin and the dermis. Specifically, these polyunsaturated fats are highly susceptible to oxidation by those hydroxyl radicals, and we know one of the reasons that you age in terms of wrinkles.

[01:13:03] From a, an appearance standpoint is those hydroxyl radicals have a real nice ability to go in and disrupt those polyunsaturated fats that maintain the integrity of the skin. UV radiation also activates something known as matrix Metallo proteases probably best to think of those as like little scissor proteins.

[01:13:23] And what they do is they go in and they just literally just start breaking collagen down. And so there was a group to, I think it was 10, 10 milligrams a day for 16 weeks. And then a group that got placebo or astaxanthin. And the group that got astaxanthin had their less wrinkles. And this was done by a dermatologist that looked at them and assessed them pre and post, but they had less wrinkles.

[01:13:44] The skin was more what we'll say rigid in terms of its ability to look tight. And we know that one of the things astaxanthin does as well is it increases what are called fibroblasts in the skin, which helps rebuild broken down skin. Then it also increases collagen synthesis. So in an earlier study I had talked had

mentioned about the mice being burned, the mice that had received these skin burns, the group that got acid as Anthem had not only did they recover faster from the skin burns, but there was less scarring afterwards as well.

[01:14:17] And so when they ended up what they call sacrificing the m, going back and looking at 'em there was a lot, there was significantly greater collagen in that skin compared to the placebo group. And so we know that astaxanthin has quite a role in terms of skin protection. Again, as you mentioned, it is at the higher dose.

[01:14:34] And then from a concussion standpoint, astaxanthin is one of the only nutrients that we're aware of that can cross a blood-brain barrier. You've got ketones, you've obviously lactate glucose a couple others, but astaxanthin can cross that blood-brain barrier. And so we know it saturates the hippocampus and the prefrontal cortex.

[01:14:53] Two reasons that's important. The hippocampus, because the hippocampus is highly susceptible. Again, the brain is filled with polyunsaturated fats. Talking about oxidation you start getting in free radicals and inflammation and you start to go down the rabbit hole of dementia. Specifically the mitochondria within the brain.

[01:15:12] One thing that happens to 'em. So mitochondria are very dynamic. Obviously, you know this, they're able to grow if they're healthy and get really big, they're able to splice off aspects of 'em if they're dysfunctional. And but when they become dysfunctional, they actually will turn into what are called donut mitochondria.

[01:15:33] And so they actually form, they look just like a donut. That's not good. And in fact, in the hippocampus, You can see that taking place when someone is developing Parkinson's or dementia or different types of dementia. But Parkinson's and MS. And astaxanthin has a, an ability to go in there and stabilize those mitochondria and prevent reactive oxygen species, mitigate inflammation and keep aspects of the hippocampus healthy, keep the prefrontal cortex healthy.

[01:16:00] And the prefrontal cortex plays a significant role in your ability to coordinate movement, choose movements and conduct any kind of, I would say, gross motor skills. And so from the concussion standpoint, I'm not aware of much data on that. But you were asking what were my thoughts on it? It would make sense to me that you would have I, in my head, I would have probably have a couple things on hand.



[01:16:24] I would have asin, I would've taken ahead of time just because we know it can cross a blood-brain barrier. One of the things that happens when you are concussed is that blood brainin barrier breaks down its ability to oxidize certain nutrients also goes down and there's significant inflammation that all of a sudden takes place within those cells.

[01:16:44] So as is Anthem, if it's already there and saturated, those mitochondrias specifically would be able to mitigate that inflammation process. But I would also have some type of probably ketone on me, exogenous ketone that I could take right afterwards. A lot of people it, I think the N F L's a great.

[01:17:00] Example of this, of where they'll give individuals Gatorade after a concussion. And the problem now that we know is that all of that glucose, most of it doesn't cross that blood-brain barrier. And what does cross is probably increasing inflammation. And so beta hydroxybutyrate would have a opportunity there to help mitigate that inflammation from a concussion.

[01:17:21] And there is some data to demonstrate that. So I think that would probably, if I was a kiteboard or going 20 feet in the air, I think that's, that would be my

[01:17:31] stack for that.

[01:17:33] **Mike T Nelson:** Oh, that's cool. That's pretty much what I do. The only one that I've added is up all my dose of creatine up to 20 grams a day.

[01:17:40] Yeah. Creatine's great too. So from Dr. Eric Raddon, we've had him on the podcast. Yeah. And again, human studies are very hard to determine what, how much creatine will saturate the brain. You've gotta look at M R Ss and some types of things because animals are much easier to study, invasively for those types of things.

[01:17:58] I do actually use a higher dose of C B D. There's some interesting data that it might be neuroprotective and there's a rat study or mouse study where they disrupted the blood brainin barrier. And the group that had C V D, the blood brain barrier stayed intact longer. But my thought being, yeah.

[01:18:15] Not much of a downside there. Yeah. Maybe there's some protection. 'cause once, as you said that blood brain barrier opens up. Man, you're into such a world of hurt now because you've got all this stuff that was normally kept out. Yep. Coming into a brain that's already got high levels of inflammation, already has an energy crisis.

[01:18:31] 'cause glucose metabolism gets knocked offline. Yep. And now you've got even more inflammation and it's just, it's

[01:18:37] A mess.

[01:18:38] **Dr. Hunter Waldman:** And you're, you're given context to the listener, which I think is really important because one of the things that you're saying, and I would wanna reiterate is you're talking about supplements that either they only either have an upside or at least no detriment.

[01:18:54] And That's correct. Creatine. There's really no detriment. Yeah. No detriment to creatine. Astaxanthin. There's no reported negative side effects to astaxanthin C B D. I'm I have to go with you because I don't know the research on that, but it sounds like no real down side effect to ccb d.

[01:19:11] Not much. So the ketone mono ester expensive. Maybe Dr. Stubbs though really demonstrated that the ketone mono ketone ester in general has very little GI distress. So really, you can throw that out the window. Other than expense for the ketone ester, then really no downside effect negative effect there.

[01:19:32] So anyways, just to the listeners, it's important that, you walk away with the supplements that we're talking about right now. They either have an upside or at least no detriment to performance or metabolic health or cognition. And that's really important to me because that's when I'm talking to other people about it, you have to weigh the pros and cons of whatever you end up ingesting.

[01:19:54] And definitely ketones. I've got all different types of ketone esters in my bag. I leave 'em in my car and, as soon as I, I'm able to, I would basically put myself in a high level of ketosis and then transition to a ketogenic diet and try to leave my ketone levels on the higher as opposed to the lower side.

[01:20:12] And

[01:20:13] **Mike T Nelson:** yep. Listeners are interested. I did a whole program for the care institute on the use of ketones, ketone ester salts, and a ketogenic diet for, potential t b i. So there's a, yeah, very smart whole, whole program on that if people want to go down that rabbit hole. Awesome. Thank you so much for all your time here today.

[01:20:31] I really appreciate all your knowledge and sharing everything with us. This has been awesome.

[01:20:35] I

[01:20:35] **Dr. Hunter Waldman:** appreciate you having me. Like I said, you pulled me out of the woodworks and I just looked down and saw it's already we're right at the end time. I'm like, man, we barely scratched the surface on some of this stuff, but.

[01:20:47] Mike I appreciate you man and you put out good work and look forward to hopefully getting a chat with you again.

[01:20:53] Yeah. And thank you

[01:20:54] **Mike T Nelson:** so much. I really appreciate that. We'll have to have you back on again for sure. Awesome. And if people, I know you're just on social media now. Yep. Tell 'em where they can follow you.

[01:21:04] I don't know if you have any openings for graduate students or anything like that. Anything you wanna promote, go for it. Yeah.

[01:21:11] **Dr. Hunter Waldman:** So we've got a couple different doc students, but two of 'em are in dissertation year. So if you're interested in some of the work I mentioned that my lab is doing, you can find me at the University of North Alabama.

[01:21:22] Just type my name in Hunter Walman, you'll come across my email address. Feel free to shoot me an email. And then I'm on Instagram. I just brought that back. I actually brought back Twitter. Then as soon as I got on, I saw how much negative talk was happening. I'm like, no, I'm not reintroducing this back into my life.

[01:21:39] So I re deleted it.

[01:21:40] **Mike T Nelson:** Yeah,

[01:21:42] I tried, I got my profile back just to say I got it back because then I kept getting banned for no apparent reason. And oh I have it now, and I've been trying to limit my social media, at least consumption of it. Yeah. And Twitter is still, I don't know, man, it's just dead last on the list.

[01:21:57] Yeah, I don't, I

[01:21:57] **Dr. Hunter Waldman:** know lot of researchers are on there, but when I try to look this stuff up I don't find any value added for myself personally.

[01:22:04] But yeah. Yeah. So I've got Instagram, that's my personal page that I use and really just brought it back for I don't plan on doing my own podcast, so my thought was maybe I can make the science that we do accessible to the everyday person and that doesn't do research.

[01:22:20] And so if you want to find me on there, please feel free to. And that's pretty much it for right now. Great. And

[01:22:27] how, what's your name on Instagram

[01:22:28] for everybody? Yeah, I think it is pro the username, so I'm We can find it. Yeah. Prof Waldman because Hunter Waldman and Hs Waldman were both taken, but who knows?

[01:22:38] So you can find me Prof, period. Waldman, you can find me on there. I'm sure if you just type in Hunter Waldman you'll see me pop up as well but yeah. Yeah, please feel free to follow. I'll follow you back.

[01:22:49] **Mike T Nelson:** Cool. Awesome. Thank you so much and I would highly recommend people check out your stuff. I know you've got a lot of stuff coming out and yeah, it's also a very good way, in my opinion, to get from researchers actually doing the research, explaining what's going on.

[01:23:01] I think that's always gonna be a good source.

[01:23:03] Yeah. Awesome. Appreciate you, brother. Cool.

[01:23:05] **Dr. Hunter Waldman:** Yeah. Thank you buddy. Appreciate it.

[01:23:09]

[01:23:09] **Mike T Nelson:** Huge thanks to Dr. Hunter Waldman for being on the podcast today. Really appreciate it. He's doing some really cool research, hoping we can look at some of the effects of ketone esters coming up again this spring possibly. I'm chatting with him about some potential study designs, which will be super interesting.

[01:23:30] And thanks again to him for all the great info, all the great research. And if you enjoyed the podcast here on astaxanthin also stay tuned for September 22nd podcast with Dr. Karen Hecht. We will talk all about astaxanthin only on that podcast. She is an expert in the world of astaxanthin. So you don't want to miss that.

[01:23:55] Also things you don't want to miss the Physiologic Flexibility Certification. Open again, September 18th through the 25th. If you want to learn how to become more resilient, more anti fragile, generally just much harder to kill, and your nutrition and training and sleep are pretty decent, this is the Level 2 to the Flex Diet Certification.

[01:24:18] Flex Diet Certification covers mostly nutrition and recovery via sleep, although we do have some stuff on walking and exercise in there. You have all of the basics, the Level 1 things that you would need to do for more muscle and better body composition. So once you've got that dialed in pretty good, the level two then is the Physiologic Flexibility Certification.

[01:24:43] We're taking those same ideas, but we're expanding it to you as an entire human organism. And the main question we're looking to resolve here is, once those are pretty good, where do you go next? Do you purchase a red light panel? Do you get supplements? Do you do hours and hours of zone 2 training because that's the thing?

[01:25:05] It gets to be very confusing and there's lots of, I'd say, sub niche programs in this area. There's some great stuff on breathing, there's some great stuff on temperature adaptations, but the reason I created this was I didn't find anything that pulled all of those four areas together in a system that makes sense based on actual research.

[01:25:29] When I was creating this certification, I think I ended up reading, God, well over 350 studies. So a bunch of them, sadly, never made it into the certification because they didn't fit. But it's actually based on real science and the cool part is you'll learn about the theories. You'll learn about the specifics, and it's broken down so you will know exactly what to do with that information.

[01:25:55] I found a lot of certifications, they tell you some good info, but you're left with kind of vague notions of what do you actually do with it this time. And here you'll know exactly what to do with it, and similar to the FlexDyed certification, it is led by what will be best for yourself or for the client.

[01:26:15] So it's a flexible approach. So go to the Physiologic Flexibility Certification at PhysiologicFlexibility. com It is open from September 18th through September 25th, 2023. If you have any questions, please reach out to me. Thank you so much as always for listening to the podcast. I really appreciate it.

[01:26:37] Big thanks to Dr. Hunter Waldman for sharing all of his wealth of knowledge and all the great research that he is doing. If you enjoyed this podcast, please forward it to someone you think may also enjoy it. Leave us a few stars or whatever you think is most appropriate on iTunes. And if you have even 30 seconds, leaving us a very short review goes a long way for us to get better distribution of the podcast, which as you've realized is just sponsored by me and the certification.

[01:27:06] So thank you so much. We really appreciate it. Have a wonderful day and we'll talk to all of you next week.

[01:27:13]

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