Episode 401: Berberine Is NOT Nature's Ozempic

With Dr. Martin Katz, Dr. John Gildea and David Roberts

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David Roberts:

Hey, everybody. It's David Roberts, and you're listening to the Mara Labs Podcast. And today, I have Dr.John Gildea, Dr. Martin Katz with me. Welcome, gentlemen.

John Gildea:

Hello.

Martin Katz:

Hello, hello.

David Roberts:

And we're going to be talking about berberine and specifically comparing it with Ozempic, which we've written a blog article about that, but also it's in the news. And really, both of them, where it's the new year, people are wanting to lose weight and they're probably looking maybe to be starting Ozempic and I want to talk about maybe why that may not be a good thing for them, depending on their situation.

But really, what Ozempic does and how it regulates weight loss, but also berberine because berberine, in the news, there are dozens of articles now calling berberine nature's Ozempic, and I don't think it is but we want to talk about that. I want to hear from you guys what you think now I've biased your opinions with mine. But also... No, I'm just kidding, you guys... We've already talked about this.

Martin Katz:

We have strong opinions.

David Roberts:

You're welcome to share them here, Martin.

John Gildea:

Safe space here.

David Roberts:

But also, what is the mechanism for why berberine leads to moderate weight loss? So let's dive in. And really, let's maybe start with the first thing. What's going on with berberine, and what are the mechanisms at play, and what's going on with specifically its benefits? Let's talk about all the benefits and then what's going on with weight loss. Who would like to start?

Martin Katz:

Do you want to start with mechanisms, John?

John Gildea:

Yeah, so I think the one thing that's clear from the literature is that there's been a number of studies that lower A1C, and that's just a measure of your total amount of glucose that is in your bloodstream. It's a very good measure for averaging over I would say a month, maybe a few months.

Martin Katz:

Three months.

John Gildea:

Three months?

Martin Katz:

Three months, yeah. So that's how long the red blood cell lasts in the system. It's about three months and so it's glucose is very good at glycating things and that's why it's so dangerous at elevated levels. So it glycates the kidneys, it glycates nerves, it glycates heart, glycates everything including red blood cells. And the higher the glucose level is, the more it glycates and, therefore, you can see what's happening over a three-month period with this hemoglobin I would say.

John Gildea:

Yeah, so that's a great place to start because it's saying that even normal amounts of berberine probably taking even moderate amounts of it on the long haul does decrease A1C so it's behaving like starting an exercise program. It's very similar. You're lowering how much glucose is in your circulation over a period of time and so it's a good place to start saying it seems to be pointing in the right direction. And then the other thing that I know from reading a number of papers that it's AMP kinase activator. So AMP kinase activation is it's activated when you fast.

So we can also say that it's probably pushing in the right direction in terms of natural weight loss. If you just restricted what you're eating, you get AMP kinase activation. So berberine activates AMP kinase, a natural compound that's inside your cells that's part of metabolism. Lipoic acid or thioctic acid also activates AMP kinase and is known to cause weight loss too. So in that case, it's acting like a natural version of weight loss. And then I'd say the last mechanism is it says c-myc inhibitor so there's a direct inhibition of c-myc.

Martin Katz:

C apostrophe M-Y-C.

John Gildea:

Yep. It's an oncogene and it's known to be a major component of what's called a glucose response element. So it's a transcription factor that sits down when glucose gets high and turns on genes that up regulate glucose metabolism. And so blocking c-myc kind of blocks that. And I think the idea there is that it pushes you back towards oxidative metabolism. So I think for those three reasons, it's pushing correctly and like a natural movement if you started exercising. It's moving things in the direction that you would want to for weight loss.

Martin Katz:

Yeah, that's interesting, John. Sorry, David. Yeah, a couple things there. What most people think of exercise is you're mostly burning sugar. And what people don't realize is you're actually mostly burning fat through all stages of exercise until you get into the high zone five, which is really pushing hard. And you may be only have about 30 seconds of that, and that is likely primarily sugar anaerobic, which is how again, cancers like to work as opposed to the fatty oxidation. Fat is zone two through zone four, which is pretty awesome and so you're going to get this fat oxidation when John says oxidative utilization, energy utilization is mostly fat.

So that's, again, very, very positive. And the other thing that berberine certainly helps is glucose across the membrane, which is so insulin sensitivity and glucose across the membrane. So again, if glucose is in the system, glycating, all these things, that's a negative for the system and you get into the cell and used as energy or stored, but preferably used as energy because you're exercising now, that's extremely beneficial.

David Roberts:

So I wanted to drill down a little bit about on AMP kinase and how specifically its activation impacts metabolism, which then can impact weight.

John Gildea:

At least from my understanding of it is, is it's basically in the whole pathway of where you have proper energy metabolism is through using oxygen in mitochondria and so that system is regulated by a transcription factor that's in the nucleus called PGC-1 alpha. So whenever you're activating AMP kinase, you're also in a kind of a long-term adaptation. You're increasing PGC-1 alpha, which is increasing the fidelity of your mitochondria. So in general, again, it looks like exercise so an athlete's going to be able to get rid of their under-functioning mitochondria.

A lot of people don't realize that you can change your genetics. Well, exercise will do that. It changes the genetics of your mitochondria getting rid of the under-functioning ones. And the ones that are higher-functioning will divide and replace so you're able to utilize the oxygen more efficiently. And like Martin was saying, a lot of that exercise that we think of an athlete, he's running off of fatty acids and so you can exercise longer and stronger when you're competing with somebody. Of course, sprinting is another thing of how fast you move your muscles without the utilization of oxygen, but still you still have to recover.

Martin Katz:

And then the thing in sports right now is everybody's trying to fat adapt so that their muscles go longer with this endurance. But if you're at a higher level, there's almost no way to fat adapt to the point you don't need carbs. But still, primarily everybody's into this fat adaption.

David Roberts:

And we're kind of dancing around it, but you talked about mitochondria, fat adaption, and that fat is being used as ketones in what's known as the Krebs cycle. You're talking about oxygen usage. That's how where oxygen, we breathe it in, we breathe out carbon dioxide thanks to the Krebs cycle, which occurs in the mitochondria. What happens with ATP when AMP kinase is on? How does ATP modulate? How is it changed?

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David Roberts:

... modulate. How has it changed its processing?

John Gildea:

I don't know the direct connection to that, but in general, the lack of food consumption is what is activating that. But I think using up energy in general would activate the same thing, but it gets messy in

my head because when you exercise, you're actually mobilizing sugar from the glucose that's in your muscles, and that's a big component of why exercise prevents metabolic syndrome, insulin resistance, is that you have this giant glucose sink that's using up your glycogen stores. Insulin resistance, at least part of that pathway, is that you're saturating those stores. And then that insulin, the only place it has to go is to store it in fat.

And of course, the fat that's stored around your organs is the metabolic fat that's producing cytokines and is associated with all the dysfunction. It's not so much the flabby stuff that's on the outside or especially your legs and things. I don't have that super clear, black or white with ATP production, except to say that mitochondria, when it uses oxygen, that's making 36 ATP, whereas through glycolysis you're only making a few ATP. Then you're also making lactic acid, which is one of the driving forces for stopping activity. It'll make you stop from production of acid, CO2 production, which is also acid, and then you have heat, which those three things together make you stop exercising.

Martin Katz:

Yeah. I'm also not quite sure where you're going with that, Dave, but what I can say is, as Joan was saying, we have a lot of fat stored. We don't store much sugar, so we'll burn that sugar quite quickly. But if we're going at higher levels or even at zone three, everybody's bunked at some point with exercise. But again, there's a good amount of fat. And again, if we're eating too much sugar and not exercising, because we don't store much as glycogen, that sugar can be then stored as fat, and we increase the amount of fat in the cell and we decrease our insulin sensitivity, which further increases our glucose, which continues this pathway down. And that's where we get into trouble. But if we can reverse that by increasing fat oxidation through the use of berberine or exercise.

David Roberts:

Or both.

Martin Katz:

Well, again, preferably. I almost never talk solely about one thing. I'm always about the holistic approach. And exercise for me is medicine for sure, as is nutrition, but the two together are extremely beneficial in production of ATP and getting out of that fatigue syndrome.

John Gildea:

It's funny, that really brings up a great point of when you take berberine, because it's just like metformin. You probably don't want to take it right before exercise. That's mimicking fasting. A lot of those studies are done at UVA where if you block all of oxidative stress, you block a lot of the benefits of exercise. So taking a very strong antioxidant right before your exercise is not a good idea. Recovery is different. You want to do it afterwards. I'm pretty sure this might be a little bit of a stretch, but when you take metformin, it's a complex one inhibitor in the mitochondria, so you actually decrease your VO2 max when you're on metformin. And that's part of the side effect of that, of why you feel tired if you're not metabolically stable. And then they make you stop taking metformin to do a VO2 max study.

Martin Katz:

Yeah, I mean a lot of people, because of the whole mTOR craze, were taking metformin and realizing that their exercise capacity was slightly diminished. But again, I think when you take it, it can be very telling or helpful.

John Gildea:

Yeah, in the case of a person who's metabolically deranged a little bit, then it makes sense to take that because it's long-lasting.

Martin Katz:

Yeah. I think we encourage people to take berberine in the evening. Is that right?

David Roberts:

Yeah. Biggest bang for the buck would be evening, but that you can take it, I mean, people do take it around meal times as well.

Martin Katz:

Sure.

David Roberts:

So one other benefit of berberine, and then we can get into the Ozempic, but that you didn't mention John or Martin, is the anti-aging benefit. Can we talk about that a little bit?

John Gildea:

I think the most consistent anti-aging strategy is calorie restriction. I think that might be part of what exercise is as well, is you're using up excess energy that you've ingested, so you have that slight deficit there. So I think it's going to mimic fasting in some way.

Martin Katz:

Yeah. I think another thing we didn't talk about, which likely plays significantly into longevity, is the health of the gut. Berberine certainly has been used for thousands of years, certainly over in Chinese medicine for the health of the gut. So you're improving the health of the gut. That's a good thing. But you don't want to keep berberine in the gut for too long or for too much of an extended time. It's more for an acute treatment. So that's why I think our product's really good in that way, is it helps it get into the system.

David Roberts:

Well, one of the studies that you put me onto too, John, you said it was one of your favorite anti-aging studies. This was several months ago, so lots happened since then, but it's the one with the mice study where they gave the mice chemotherapy and then gave half the mice berberine, and they lived 80% longer, and with the thought process there being helping with the senolytic.

John Gildea:

Yeah. So chemotherapy is known to massively induce the number of senescent cells in your body. So berberine, that's the easiest interpretation of that study, is that you're clearing those senescent cells.

David Roberts:

One other study that I just pulled up was, it's entitled Berberine Ameliorates Obesity in Inducing GDF-15 Secretion by Brown Adipose Sites, and how basically, the study is on lowering body weight through-

Martin Katz:

Brown fat.

David Roberts:

Yeah, through berberine, which I'll put a link to that in the show notes.

Martin Katz:

Brown fat, just so is this again through mitochondria? Because that's again, the benefits of brown fat.

David Roberts:

GDF-15, are you familiar with that?

John Gildea:

I think it's the same benefit of cold immersion, is you get uncoupling response from your white fat. So that's what brown fat is, is instead of turning energy into heat, it's dissipated. It produces heat. Did I say that right? So there's an uncoupling of the mitochondria. Instead of just making ATP, you're basically blowing off. By uncoupling it from ATP, you produce heat, and that's what brown fat is. So if you turn up that furnace, it's like having big muscles and that it's using up glucose all the time. And that's a good strategy in general.

So if berberine is increasing the metabolism of brown fat, that's what it's doing. It would tend to heat you up. So classically that's the lumberjack phenomenon-

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John Gildea:

Classically, that's the lumberjack phenomenon is you're exercising outside in cold weather. Over time you adapt by making more brown fat and that actually heats you up. And so if you're not outside and not exercising a lot, some of the chronically cold people that are out there, strangely the treatment that would help you the most would be to go into cold. It's just kind of ironic that you're cold all the time, but you really should do cold plunging.

David Roberts:

Yeah, and interestingly swimmers would fall into that category as well. Exercise in cold.

John Gildea:

Yeah.

Kind of like whales.

David Roberts:

I Resemble that comment.

John Gildea:

Well, the people that I went to a prep school and we had very good swimming team and they were notorious for the amount of food they ate and still stayed skinny, which was kind of astounding.

David Roberts:

In college, my friends would not say that when we would eat together, they were like, you're not eating, you're feeding. Because I'd have a plate, like a mound of food. Anyway, but yeah, you certainly burn a lot of calories too if you're swimming four hours a day. So let's move on to... So basically there are some mechanisms at play with berberine, AMP kinase, this brown fat, but really it's very different than Ozempic and the GLP one. And let's dive in there. It's New Years. It's the 8th of January, people are thinking, Hey, it's a great time to lose weight. Maybe I should get on Ozempic. Martin has some strong opinions on that, which we want to hear. But let's get into the mechanism first.

John Gildea:

I think in general, GLP-1 is a peptide that's released when you eat and it's degraded by DPP-4. It's a known digestive enzyme. And I think the interesting, right off the bat, the conundrum there is DPP-4 is associated with a healthy gut. So the idea of a healthy person Inducing GLP-1, and then it being short-lived, is kind of opposed to the idea of what nature is doing. So you're providing... It's basically GLP-1 agonist, but that it's not degraded. And so that's the strategy. And the drug that was before GLP-1 agonist is to inhibit DPP-4. And that has lost a lot of its thrust, I guess you would say. And that's because it's shown in larger studies to cause celiac disease. Because then you don't degrade gluten. So lots of issues.

Martin Katz:

We're dumbfounded.

David Roberts:

Wow. Wow. Yes.

John Gildea:

Yeah. And then GLP-1 increases. It's known to increase insulin secretion. So if you're not eating excess glucose, you're not hyperglycemic, berberine doesn't increase insulin. So if you are eating lots of glucose and you take berberine, it's known to cause an increase in insulin secretion. So you still need to have good behavior while taking berberine or else it will act like Ozempic in that you get prolonged insulin secretion. And I think the benefits, maybe we should talk about some of the benefits is that-

Martin Katz:

Of which one?

John Gildea:

So Ozempic decreases your appetite, and that's what most people... If you're on a high carb diet and you're constantly getting ghrelin secretion, you're hungry all the time. You get a reprieve from that, and that feels pretty good, I'm sure. And then along with that comes some of the side effects of nausea. Only, nausea bombing gastroparesis. You're not emptying your stomach. So there's a lot of side effects, but there's no doubt that people are losing weight.

Martin Katz:

Yeah. The studies are very positive on Ozempic or Mounjaro, the GLP-1, you can just look them up and get the names. But there are some true benefits even when you're studying or looking at heart, there's some heart benefit to that. Is that secondary to the matter? Is that secondary to the weight loss? The studies are quite mixed on that. So I don't think there's a... Well, I know there's not a direct correlation between the Medicaid, taking the medication and decreasing heart disease at this point, it's likely more related to the weight loss and the fact that that's happening. And that's a true benefit. And there's a lot of people out there that do need to lose weight. And with that weight loss, they have decreased medication usage. And that's a true positive. They may feel better about themselves. I get people in my office chronically who have struggled with weight for many, many years.

I have a couple of young ladies who sensibly eat quite well, one who exercises a significant amount, and she continues to struggle with weight and to the point where she's ready to give up. She hasn't realized the long-term effect and long-term take on this. She wants a more quick fix to the point where she's... Again, ready to give up on all the positives. And so we had a long discussion about that with both of them. Risk benefits, and this is where I feel like it's imperative that we talk to our patients about this ratio of risk versus benefit and really talk to them about understanding the very high importance of behaviors. Because there's a couple things. One is with that weight loss comes lean muscle mass, which is the last thing you want to lose. So some studies suggest as much as 30, 40% lean muscle mass loss with these medications. So along with weight loss comes this very, very detrimental muscle mass loss. And then-

John Gildea:

With GLP-1s?

Martin Katz:

With GLP-1s. And then-

John Gildea:

I've heard higher than that too.

Martin Katz:

Yeah. And then the very significant concern of this gastroparesis, which again is working well, it's decreasing ghrelin, which is this hunger hormone. But let's go back to the gastroparesis. If you have a procedure, any procedure coming up, and they're putting you either into general anesthesia even for colonoscopy, your risk of aspiration goes up dramatically. The study suggests, at this point, certainly it's seven days, probably 14 and even as high as a month. And again, these drugs have not been around very long.

They're pretty short-lived medications, and so we haven't been studying them for a great amount of time. So yes, they seem beneficial in a certain population. And should we be using them possibly, maybe even probably if the benefits strongly outweigh the risks. But in most individuals who are looking at it for weight loss, I would question that. And again, that's me sitting here who's doing very well with nutrition and exiles and yada, yada, yada. But I mean, I would say that if we can change the healthcare system to really put more emphasis on helping the patient understand their intention and behavior change in life coaching, I think we would be going-

David Roberts:

Well, and that's well said and needs to be said because these GLP-1s like Ozempic, it's hit the culture. It's in this Instagram. There are articles in Forbes on Ozempic being... Berberine being nature's Ozempic. There's ads everywhere. And even Weight Watchers, you heard in the news last year, Oprah Winfrey...

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David Roberts:

In the news last year, Oprah Winfrey, who's big on the board of Weight Watchers, investor in Weight Watchers, a longtime supporter of Weight Watchers, has been on a GLP-1 for weight loss. And Weight Watchers is actually including the... What's the other one? Wegovy?

Martin Katz:

Wegovy, yeah. I mean, they're all semaglutide, yeah.

David Roberts:

... in their program, in the Weight Watchers program now.

And so there does need to be sort of this, okay, maybe it might be okay. But you need to work it out with your doctor and just don't look at it as, hey, I want to lose weight, I'm going to get on it, on one of these, because there are costs.

Martin Katz:

Just so you know, semaglutide is a lot of these. Rybelsus is oral. Ozempic is injected. So just trying to understand the difference with all these there. They're basically semaglutide. There are other GLP-1s though.

David Roberts:

Yes. So I want each of you to answer this, is berberine nature's Ozempic? John?

John Gildea:

Yes. They're a completely different mechanism I would say they shouldn't really be compared. The GLP-1 is, I'm sure there's a category of people where losing a big chunk of weight makes sense, if, like Martin said, they're going to be engaged in behavioral work. If that gets them to the gym, if that starts them exercising, it gets them out of their horrible mindset, you and your doctor are going to decide that. But just thinking that it's a free pass I think is wrong thinking.

Martin Katz:

Yeah. I mean, I would say categorically absolutely no it's not. I mean, you were saying is exercise nature's Ozempic? And no it's not. And similarly, I'd say berberine is not.

And I think I mentioned this, I don't know if I have, but not only are you losing lean muscle mass as soon as you decide to stop Ozempic due to cost, which it's extremely expensive if you use Wegovy or Rybelsus as a weight loss medicine, it's hundreds of dollars a month. And so if you decide to stop, the weight gain has been shown to come right back. Unless, again, you're understanding the importance of

exercise and how you're eating and what you're eating and your intention towards that, which is imperative in my books.

And again, going back to that, John, you were saying, as though it's so easy and implicated and important and imperative that doctors sit down and talk to their patients about this. But guess what? We don't time. So I've made a conscious choice to take more time with my patients and explain these things. But guess what? You don't get paid for it. So if you look at my salary compared to most wage earners in family medicine, it's way down, and the reason for that is family physicians do not have time to talk to their patients. They get six to 10 minutes per visit. I take 20 to 45 minutes per patient. And so the only way we make money as primary care physicians is turnover.

So yes, you want to weight loss medicine, here's your prescription. I don't have time to talk to you about it. Figure it out.

David Roberts:

Good luck.

Martin Katz:

Good luck. And that's an unfortunate part of the system. But there it is.

John Gildea:

As you were thinking about that, I have interacted with so many people that are anxious right now. So that's sympathetic overdrive. That is the opposite of good vagal tone, where you're having smooth muscle movements through your whole digestive tract. That's a hallmark of health. And stopping that or slowing that is not a great idea.

And just for one instance, SIBO is known to be correlated, but you have bacteria that's supposed to stay in your colon where you have two layers of mucus. It's designed for your bacteria to be there. You stop smooth muscle contractions or even slow it down, that bacteria is going to slowly be moving backwards up your digestive tract and there's a host of problems that are associated with that.

So it's literally the opposite. If you exercise, that's what heart rate variability is. You balance your sympathetic parasympathetic, it's just incredible. You can make it even better by doing some yoga and breathing exercises. But thinking that you're going to cheat the system by pushing it in the opposite direction of health is not a good long-term strategy.

Martin Katz:

I hope everybody caught that when John was comparing GLP-1s to slowing down the gut, as to what anxiety does. And we know through numerous studies what anxiety does to the gut. It's just impressive. Robert Sapolsky wrote a great book. And many, many people have since explored anxiety, what happens to the gut, it slows it down And what that does to not only the bacteria, but the health of the gut is important.

And so you look at this now GLP-1 which is not being inhibited by DPP-4. And some people are on both meds, DPP-4 antagonists and GLP-1 agonists. And again, one of my hallmarks of health and longevity, outside of exercise, nutrition, sleep, hydration is absolutely the microbiome, and obviously stress and stress management and all the things we talk about in my clinic.

David Roberts:

Well, you might've heard it here first people, berberine is not nature's Ozempic. And there's certainly some concerns if you are thinking about using Ozempic for weight loss. It's not the silver bullet that the popular media is showing it to be. So just talk to your doctor, work it out with them. And yeah, thank you-

Martin Katz:

Keep reading about it as well. I mean, your doctor should be discussing, you bet it doesn't always happen. So make sure you're reading both sides, not just what's coming out from the drug manufacturer or whatever.

David Roberts:

Yeah. And berberine can be a tool for weight loss. It's not at all the silver bullet either. I think the randomized control studies showed the meta analysis on different studies looking at berberine and weight loss, on average two kilograms of weight loss, which is something.

Martin Katz:

24%, I think it was.

David Roberts:

Yeah. So anyway, thank you gentlemen for discussing.

Martin Katz:

Just real quick, David. Currently reading a book about, talked about this, but Jim Clear's Atomic Habits. Just getting in, decreasing bad habits. He not only talks about improving good habits, but he talks about how to decrease bad habits. Atomic Habits by Jim Clears.

David Roberts:

Are you recommending this?

Martin Katz:

I am giving it a thumbs up, yes. Indeed.

David Roberts:

All right.

John Gildea:

Good for this topic because it's clear behavior trumps-

Martin Katz:

Behavior.

John Gildea:

... supplements or drugs.

David Roberts:
Behavior.

Martin Katz:
Behave yourself.

David Roberts:
Yes, exactly. Well said. All right. Well, thank you John, thank you Martin for talking about this. You've been listening to the Mara Labs Podcast. We'll be back next week with another episode. Thanks so much for your time.

Martin Katz:
Thank you.

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