The Biochemistry of Human Metabolism and the Complex Process of Aging
A Special Interview With Georgi Dinkov
By Dr. Joseph Mercola

Dr. Joseph Mercola:

Now, I want to jump to a really complex concept that is antithetical to almost every conventional medical person. And that is the concept of reductive stress. And I actually remember viewing a podcast you were on with Tucker Goodrich and Cate Shanahan where you were discussing this concept. And Cate's a pretty sharp woman, she's one of the first people I ever interviewed about the dangers of linoleic acid. But she just couldn't get her head behind this concept. She was just adamantly opposed to reductive stress as a concept even. And she didn't believe it, didn't believe it. So, it would be really helpful to understand, because this is really mind-bending, and it absolutely turned my world upside down once I understood this thing, with respect to what I thought and believed to be the truth about, really, the fundamental way that we age in an accelerated fashion.

It's believed to be oxidative stress, and then further refined to be oxidative stress in the mitochondria. And yes, because that's where most of it occurs, but when I wrote my book "Fat for Fuel," it was totally mixed up. I thought fat was the cleanest fuel. And it turns out no, the cleanest fuel is when you have reductive stress minimized, because reductive stress – Now, first of all, we'll define it in a moment, but it actually is what causes oxidative stress. So, to understand, you have to understand what is oxidation and what is reduction.

So why don't we go over this simply, because this is a complex topic and I suspect many of you will need to listen to this a few times to get it, or you can just fast-forward if you don't want to. But in my view, it is really foundational to understanding what's going on. And once you understand how to combine these other components, you can easily refute any of the arguments that people have against us because it's so solid and really explains at the fundamental subcellular molecular level in the mitochondria what's going on and why it's going on. And it's pretty straightforward once you understand the basic concept.

Georgi Dinkov:

So, I guess we can start with the rate of living theory, which is really underpinning this whole concept of oxidative stress. Currently, pretty much every doctor you try to talk to about aging, they'll tell you that, look, the higher your metabolic rate is, which means the quicker the electrons move from food towards oxygen, which is the final acceptor of electrons, the quicker this process is. Basically, the faster you will age because there'll be higher oxidative stress. You'll be producing a higher amount of reactive oxygen species (ROS). But if you look at the actual data, and actually this is even in the medical books, and I sent you Wikipedia pages about this, it turns out it's the exact opposite. Reactive oxygen species get – Yes, they are generated from oxygen, but it's actually when you're not shuttling the electrons fast enough towards oxygen, when these electrons build up in various chunks of this process, whether it's the Krebs

cycle or the electron transport chain. And these electrons, which are coming from food, you have to do something with them. And the body has-

Dr. Joseph Mercola:

Let's stop here. What you just said is a profoundly important statement, and I am wondering why this isn't more widely known, because I was searching for this information and I never found it. I couldn't find it anywhere. I was trying to find out where most of these ROS generated in the mitochondria, and it's not clear, but if you understand the concept, you can see it. So how did you understand it, and what is the reason why this isn't more widely known or certainly accepted?

Georgi Dinkov:

Well, I think the main reason is that basically if you use the various search engines, they're going to give you what the majority of the websites are writing about. Just like the AI (artificial intelligence), the ChatGPT bot. If you try to argue with it on a specific medical topic, it'll just argue blindly, to the depth that a specific concept is what medicine says. And no amount of evidence you produce will convince it otherwise. It'll say, "This is my motto, that's all I understand." So, if 99% of the websites in medical presentations and studies are saying, "Oxidative stress happens only in the context of high oxidative metabolism," then if you search Google, then the first five or 10 pages will be, basically, statements along that line. But if you look at what a reactive oxygen species is, you'll see that it's actually oxygen that has been reduced, in other words, oxygen that has gained an electron.

Now, electrons, by their nature, are a reductive species. Basically we – A food is a donor of electrons, a reductant. Oxygen is an acceptor of electrons, an oxidant. So, if you have a buildup of electrons, this means that you are in a state of excessive reduction, or at least higher than optimum. So, these electrons have to do something, the body has to do something with them. You're giving the body electrons either from food or through lipolysis or the cortisol generating amino acids from your muscles. Ultimately, all of these things get converted to energy. And the way energy works is, it's a flow of electrons. So, electrons ideally should be paired at the very end with oxygen through complex IV of the electron transport chain, and if that does not happen, then [the] molecular oxygen floating around, these electrons can actually attack it and reduce it by an electron or two and generate these very reactive species-

Dr. Joseph Mercola:

Well, let's stop here because this is complex and you said, "these electrons floating around." So, I'm assuming they're floating around in the – because there's essentially five complexes-

Georgi Dinkov:

Well, they're moving, I shouldn't say floating. They're actually moving along the steps of metabolic chain-

Dr. Joseph Mercola:

Right, so complex I, then II, then III, IV, V. And in that process, and you'll go in in a moment, if you don't have those cofactors, it gets stopped and flown backwards.

Georgi Dinkov:

Exactly. So, if they can't go forward, they can build up. And when they build up to a certain point where it becomes toxic for that specific step, the step will say, "I have too many. Send it backwards." And then by sending them backwards, basically, they can interact with the molecular oxygen, which is always there, but it's only useful if it's used at the last step, which is the cytochrome C oxidase. At any other point, oxygen coming into interaction with these electrons is asking for trouble. It's basically similar to the peroxidation of the polyunsaturated fats. You can either degrade them oxidatively, which is still not preferable because we're going to talk about oxidative stress, reductive stress, but if they don't get properly metabolized, they can get attacked by these reactive oxygen species, and create a degenerative free radical or basically a toxic aldehyde.

So, the same thing happens with these electrons. When they're not meeting the oxygen at the very end, they build up at complex I or III usually, and then this excessive buildup of electrons, the body has to do something with it. And when it loses control, when these electrons build up too much, then they start leaking through the mitochondrial membrane and start combining with molecular oxygen and creating reactive oxygen species. However, these oxygen species are not oxidative. They're not oxidizing agents anymore. They have accepted either one or two electrons. so they're actually reductive species.

So, the hydroxyl radical, which is the most powerful one we produce, and the superoxide anion, which combined these two are probably responsible for 90% of the reactive oxygen species. Both of these are reductive agents. They are one electron reductive agents. So, they can attack the DNA (deoxyribonucleic acid) in our body. They can attack the polyunsaturated fats, they can attack various enzymes, including the actual electron transport chain enzymes that are there, or the cardiolipin, which is part of the electron transport chain IV, but they're not oxidants themselves.

Dr. Joseph Mercola:

I thought cardiolipin was a fatty acid embedded in the inner mitochondrial membrane, and it is not [crosstalk 00:08:16] specific complex-

Georgi Dinkov:

It's part of complex IV.

Dr. Joseph Mercola:

I thought it was part of the cristae that convolutes-

Georgi Dinkov:

Yes, but complex IV cannot work without combining with cardiolipin. So cardiolipin is crucial to the final step of oxidizing cytochrome, which is being reduced by complex III. And so, without cardiolipin, complex IV will not work. So yes, not fused with it, but the final step of accepting the reduced cytochrome C from complex III and oxidizing it to complex IV requires cardiolipin as present. And cardiolipin, since lipin is in the name, is composed of lipids. And if we eat too much PUFA (polyunsaturated fatty acids), you get too much PUFA in the cardiolipin, and all of these reactive oxygen species, they're highly reactive, but they're not oxidants. They're actually a reduced form of oxygen.

So, they're highly reactive. They can wreak a lot of havoc, but the very reason they're present there is because there was an excess of electrons to start with. And an excess of electrons is by definition a reductive state, that is at the core. So, having a high amount of excess impaired electrons means you were in a reductive state, or reductive stress, if you want to call it. And only then you can have the oxidative stress – I mean, the creation of the reactive oxygen species, which for some reason became termed "oxidative stress," as if it was the oxygen causing this. It's not the oxygen causing this. Oxygen by itself floating around in the mitochondria does not do much damage, as long as the electrons, in other words the reductants, are flowing along the line as-

Dr. Joseph Mercola:

It's just like the carbs in diabetes. Carbs are getting unfairly vilified. They're just like an innocent bystander. The marker-

Georgi Dinkov:

Innocent bystander, yes.

Dr. Joseph Mercola:

-of the damage that's going on. But I just want you to highlight – you sent me this email this morning, my mind was just spinning, because I never knew this was true. When these cofactors – we'll talk about that next in a moment – they're diminished and the electrons can't flow all the way to complex IV to get attached to oxygen, that's like 0.1% ROS production, 0.1%. Whereas if it goes backwards, reverse flows and [is] blocked, it's 3% to 4%. So, this is such a massively important concept to get.

Georgi Dinkov:

The higher your metabolic rate, the more easily these electrons flow from food to oxygen, the less oxidative stress – I know it's a misnomer, but let's use it – the less oxidative stress you're going to have. The slower your metabolic rate, for whatever reason, this immediately translates into buildup of these electrons combining with oxygen and creating these reactive oxygen species, which for some reason, medicine has called "oxidative stress." It's not oxidative, it's a damage caused by excessive state of reduction. It's too many electrons that are unpaired.

And even the Wikipedia articles that I sent you said that the determining factor for most of the creation of the reactive oxygen species is the NADH (reduced nicotinamide adenine dinucleotide) to the NAD (nicotinamide adenine dinucleotide) ratio, NADH being the reduced form, NAD+ being the oxidized form. So this ratio, which also controls the speed of metabolism of carbohydrates, because the rate limiting step is pyruvate dehydrogenase. When you're in the oxidized state, in other words, NAD+ predominates, then pyruvate dehydrogenase works well. And then basically, these electrons start flowing through the Krebs cycle and also the electron transport chain and [then] meet the oxygen.

When NADH predominates, which means you have too many electrons – that's what NAD does, it accepts the hydrogen, so now it's carrying an extra electron. So, when you have too much NADH, [that] means you have too many electrons that are not meeting oxygen properly, this buildup of electrons creates these bottlenecks, either [in] complex I or complex III, mostly. I mean, it can happen in the other ones as well. And then something has to happen with these electrons. Two things can happen, actually. One is increased synthesis of the reactive oxygen species. Second is the body uses these extra electrons to synthesize fats. So, you can view obesity, or at least extreme obesity, as a desperate mechanism to get rid of electrons that are coming from food but are not getting properly – In other words, you're not combusting the food properly.

So what happens with it? Well, you store it, right? That's the only thing that the body can do. And the second thing – and by the way they always happen hand in hand, always happen together, is whenever you have obesity or severe overweight, you always have high amounts of reactive oxygen species, because those are the only two things that the body can do with the extra electrons. It cannot simply evaporate them, though there's some research on grounding that I think it can actually help get rid of the excess electrons.

Dr. Joseph Mercola:

I was going to ask you about the grounding, if that was-

Georgi Dinkov:

I mean, I think it's promising.

Dr. Joseph Mercola:

Because to me it superficially appears to be another reductive stress because it's a source of electrons, and that's the issue: an excess [of] electrons.

Georgi Dinkov:

Well, some studies are saying [that] when they measured the electron potential of the blood, they didn't measure NAD to NADH ratio but, basically, they said that when people were grounded, they were actually losing the excess electrons.

Dr. Joseph Mercola:

Oh, interesting. Okay, because the information I was studying before suggested it was the exact opposite. But it makes sense. Like if you're dissipating static electricity, you're grounding.

Georgi Dinkov:

Exactly. Precisely. The static electricity is an excess of electrons, right? So you're discharging them somehow. So really, basically, like I said, the two things that a body can do with excessive electrons, which by definition is a reductive state, or let's call it reductive stress, is dissipate [them] through either synthesizing fats or creating these reactive oxygen species, not that the body wants to, but if the electrons are not being processed properly, they will react with molecular oxygen and create those reactive oxygen species, which then the body has to somehow deactivate, and it's got a number of different enzymes. Or you can take antioxidants. But the whole point is, before you even get to that point, why bother taking all of these substances if the whole problem from the very beginning was the metabolic rate, the metabolic process, was not working as fast as it should have?

So, the way to get rid of oxidative stress, paradoxically, is to increase oxidation, to increase the metabolic rate. That's really the ultimate antioxidant, it's improving metabolism. Now if that doesn't work or you're not doing it for whatever reason, sure, antioxidants can help by neutralizing many, if not most, of the reactive oxygen species. But if you haven't addressed the blocks that are the reason for these reactive oxygen species, this means they'll always be produced. So, you always have to be taking antioxidants. Really sounds like a suboptimal thing. It's like, I keep cutting you with a knife and instead of really stitching up the wound, I'm going to give you painkillers so you don't feel that the wound is there.

It's not really the solution. You're just masking up the problem by taking continuously the antioxidants. Now, it doesn't mean that it's not a valid approach. Say if you have a lot of PUFA, or if you've been under oxidative stress for a very long time. But it's not the actual solution to the problem. The solution is [to] improve metabolism, so the electrons go where they should be going, that they don't build up.

Dr. Joseph Mercola:

And that's exactly what Ray Peat's work is all about. The fundamental core is pro-metabolic work, to improve your metabolic rate.

Georgi Dinkov:

The analogy he gives is with the light bulb. Light bulb is between the two poles of a battery. We are the light bulb, and the intensity of the light is the intensity of our metabolic rate. And the intensity of the light depends on how quickly the electrons can flow from one pole to the other through the light bulb. If, let's say, the light bulb is made of the conductor that has very high resistance, then the light will be dimmer and they're going to be producing a lot of heat, and eventually the light bulb will burn out. But the light bulb works best when there is very little resistance and the light is as bright as possible, which means the electrons are facing very little resistance in this object that is staying on their way between food and oxygen, the two poles of

the battery. So the less resistance, the less problems we're causing to the electrons on their way from food to oxygen, the healthier we will be.

Dr. Joseph Mercola:

Yeah, that's just amazing. So thank you for sharing that. It was just brilliant and it was actually pretty well simplified. I mean, it's a complex topic, but you did a magnificent job of simplifying. That's the best I've ever heard you say it. And so, I'm sure anyone listening to this is really excited about learning how to reduce the reductive stress. So, let's go over the big ones, and maybe rank them as the most important. Would PUFA elimination be the most important thing to reduce the oxidative stress? Or reductive stress, sorry.

Georgi Dinkov:

Well, I think a very immediate thing you can do is take some oxidizing agents. If you have a buildup of electrons that are not meeting oxygen, things like quinones, like coenzyme Q10 (CoQ10), which is by the way, a component of complex II and III. Sometimes you get buildup of electrons because of coenzyme Q10 deficiency. Guess what? Taking statins reduces your ability to synthesize coenzyme Q10. So, you will think that people taking statins will have higher amounts of reactive oxygen species, and that has been confirmed universally, among many other issues that people taking statins face.

A reduced molecule cannot accept electrons, but it can actually neutralize the already formed reactive oxygen species. So really, the better thing to do is to take the oxidized version, which will help prevent the buildup of electrons to start with, and that will also potentially eliminate the problem when you – See, this is a fat. Remember the antioxidants, once you take them in the reduced form, they only address the reaction of your species. They don't address the other pathway to which the body gets rid of excess electrons, which is the synthesis of additional fat. While the quinones, the oxidized molecules, the oxidizing agents, will actually solve the problem at the very beginning, which is, if there is a block somewhere along the steps, most quinones can actually take this extra load of electrons to themselves and relieve the block a little bit.

Dr. Joseph Mercola:

So, another quinone would be vitamin K2, right?

Georgi Dinkov:

Yes. Vitamin K2 is a quinone. Methylene blue, which you mentioned in your email, is another one.

Dr. Joseph Mercola:

Oh, methylene blue. Well, I guess we could talk about it now. I'm a big huge fan of methylene blue.

Georgi Dinkov:

I mean, it's a quinone-like molecule. It can accept two electrons. And basically, it can be cycle redoxed, so you can donate them to another portion, right? Then come back, pick up another two.

Dr. Joseph Mercola:

Is it the parent molecule for hydroxyquinone?

Georgi Dinkov:

Quinine is-

Dr. Joseph Mercola:

Quinine. Hydroxy-quinine. Yeah-

Georgi Dinkov:

Quinine is the parent molecule for hydroxychloroquine, which was used for COVID.

Dr. Joseph Mercola:

No, but I thought – Wasn't the quinine a non-staining derivative of methylene blue?

Georgi Dinkov:

Let me see.

Dr. Joseph Mercola:

That was my understanding. They got the quinine that was developed specifically because they didn't-

Georgi Dinkov:

Yes. They were isolating the quinine molecule and the person who discovered methylene blue then patented it for malaria. It was like a German scientist I think in the 1860s.

Dr. Joseph Mercola:

It was Paul Ehrlich, I think.

Georgi Dinkov:

Yes, exactly. So, they're structurally similar. I didn't know actually – See, I learn something new every day. Yes, they're structurally very similar, but the quinine is colorless, while the methylene blue in its oxidized form is actually [a] very deep kind of blue.

Dr. Joseph Mercola:

But if it's reduced, it's colorless.

Georgi Dinkov:

It's colorless, exactly, yes. And there is a company doing research with reduced methylene blue that has now developed an anti-aging cream that you apply to your body and, basically, by improving the metabolism, by improving the flow of electrons, they're saying they're capable of reversing skin aging in humans.

Dr. Joseph Mercola:

Yeah, I remember reading that. That was in Nature, it was pre-COVID. It was like 2018, I think, that paper. But methylene blue, you wouldn't want the reduced version normally because it's not going to help reductive stress. But the beautiful thing about methylene blue, and this is where I was hoping you can clarify this for me, is because it can be oxidative or can be reductive.

Georgi Dinkov:

Yes. You can go back and forth. While most of the antioxidants, if they either donate or accept [an] electron, they're done. So, they're going to have to excrete them and get a new one. But methylene blue can go back and forth for a long time. I mean, the half-life, I think, is like 36 hours.

Dr. Joseph Mercola:

No, I think the half-life is closer to 13. My understanding.

Georgi Dinkov:

I will send you a study which showed that while in the blood it is. In the blood, it is. In tissues, it builds up and even at very low doses, you can actually get it at up to two days to basically stay there.

Dr. Joseph Mercola:

Wow. That is interesting, though. A lot more questions on methylene blue then. We're going to go into other ways. I mean, you mentioned the quinine, coQ10 and vitamin K2 and methylene blue, like quinine or quinone. But we'll talk about niacinamide and vitamin B2 because you want to stop those – The reason the reductive stress is going is because the electrons are flowing backwards in the electron transport chain. And many times, that's due to reduced cofactors like NAD, NAD+. But this is the question, if those cofactors aren't present, my understanding is that the beautiful thing about methylene blue, if anything can block those complexes, including cyanide or other-

Georgi Dinkov:

Nitric oxide. Yep.

Dr. Joseph Mercola:

Nitric oxide. It could block [inaudible 00:21:36]. So, whatever's blocking it, it doesn't matter because methylene blue just transfers the electron straight to oxygen, no matter what the heck's going wrong with those electron support chains. So, it would seem to me, it's kind of like the ultimate solution for reductive stress. Am I confused on this?

Georgi Dinkov:

Yep, it is. No, you're absolutely correct. Even vitamin K or the simpler benzoquinone, of which coenzyme Q10 is a derivative, they can only work at specific steps of the electron transport chain. I think coQ10 is complex II and potentially complex III. I think vitamin K is complex II. However, complex I and complex IV, we don't know of any other quinone that can actually take care of them except methylene blue.

So at any point, actually, even in the Krebs cycle, if there's a problem with the Krebs cycle, methylene blue can serve as an emergency oxidant. In other words, [it] can accept these electrons. If you have a buildup of succinic acid and you don't have the necessary cofactor, FAD (flavin adenine dinucleotide), which is derived from vitamin B2, methylene blue to the rescue. It can actually go even there and accept those electrons and allow basically the electrons to continue floating through the electron transport chain. So yes, methylene blue is probably the most universal quinone that is nontoxic to humans, at least in the dosages that are used clinically, that can probably resolve most of the metabolic problems associated with the buildup of electrons, or reductive stress.

Dr. Joseph Mercola:

So, would it be fair to say that you believe it could be an important supplement for almost anyone?

Georgi Dinkov:

Methylene blue, in combination with niacinamide, is probably the ultimate metabolic over-the-counter therapy you can do.

Dr. Joseph Mercola:

Oh my God.

Georgi Dinkov:

Without taking thyroid or anything else that artificially increases it.

Dr. Joseph Mercola:

That is fantastic. So then, the practical issue becomes the dosing. I've settled on a maintenance dose of about 15 to 17 milligrams, unless I'm going to have – Now methylene blue is rapidly

augmented and synergized with near-infrared radiation, which is 70% of the photons from the sun are near-infrared. Or you can get a near-infrared sauna. So ideally, you'd want to combine it with near-infrared. The reason I say this is when I go into my near-infrared sauna or doing the sauna, I'm doing a higher dose, like maybe 25 milligrams. And if I'm sick, I go up to 50. So, what do you think is a good dosing for methylene blue?

Georgi Dinkov:

Have you seen the – So several human studies are testing methylene blue for Alzheimer's disease.

Dr. Joseph Mercola:

I have not seen that.

Georgi Dinkov:

There are more recent ones-

Dr. Joseph Mercola:

If you could send it to me, great, because I'm interviewing Dale Bredesen real soon.

Georgi Dinkov:

Yeah, two of them actually. There's a company in the UK that patented a slightly modified – really a salt of methylene blue. It's not a different molecule. It metabolizes into methylene blue in the body. But in order for them to patent it, they have to change the molecule somehow. Anyways, they created this methylene blue-like molecule, and they've been studying for Alzheimer's since 2011 or '12. And they found out in the most recent trial that it reverses the symptoms of Alzheimer's in 80% of the people.

Dr. Joseph Mercola:

Oh my gosh, that's crazy. It’s not surprising-

Georgi Dinkov:

Well, there's a plateau. Yeah. There's a plateau of the benefits. More than 18 milligrams, which is kind of where you're cutting it off as well, more than 18 milligrams did not produce more benefit. So, there is definitely a plateau. Yeah.

Dr. Joseph Mercola:

Wow. That is, can you send me that stuff?

Georgi Dinkov:

Yeah, yeah. It's a remarkable study.

Dr. Joseph Mercola:

And I'm just doing muscle tests and stuff to figure it out. But when you're sick, I think there's a massive benefit for taking a higher dose.

Georgi Dinkov:

Higher doses combined with red light, because then it creates the photodynamic effect, which is a combination of red light and methylene blue. Creates singlet oxygen species, which is part of the reactive oxygen species, and those are extremely toxic to viruses and to bacteria. Pfizer has patented the photodynamic therapy with methylene blue and red light for cancer, and they're saying, “There's no need-”

Dr. Joseph Mercola:

Really?

Georgi Dinkov:

Oh yeah, I'll send you the patent. They're saying they've been – I think they patented 10 years ago. They said, "Oh, we've been giving people these toxic chemotherapy drugs and radiation, but really the mechanism of action that we're after is we’re increasing reactive oxygen species and killing the tumor cells, because they're more vulnerable." They're saying, "Is there a way to do this in a less toxic way? Oh, look, methylene blue, red light, combine the two." And they're saying, "This is our patent." And I'm surprised the patent was granted, but they said, “Look, we know about methylene blue and red light for killing pathogens, but we are patenting it for cancer.” And of course, they created a slightly modified version of methylene blue, just like that U.K. company, and the patent was granted. Pfizer has a patent on using methylene blue and red light for treating cancer.

Dr. Joseph Mercola:

Wow. So, do you have any concerns for taking higher doses for people? Because it appears, especially for long COVID or any condition where you have this massive fatigue, which is obviously related to the metabolic rate, but as a short fix, a sort of a Band-Aid while you're addressing the other issues such as the macronutrient ratios and revising the diet, that [a] higher dose of methylene blue would be useful for energy, maybe in the closer to 50 milligram range? Interestingly-

Georgi Dinkov:

I think the ideal thing is to combine it with niacinamide and keep the dosage at about 15 to 18 milligrams.

Dr. Joseph Mercola:

Of course, we haven't talked about this. It's on our list, but man, niacinamide is a no-brainer, and it's almost free. But-

Georgi Dinkov:

Up to a dose of about 100 milligrams, single dose, is probably okay with a big caveat. That person is not taking anything serotonergic. Methylene blue is a relatively strong monoamine oxidase type A inhibitor, which means it's going to decrease the degradation of serotonin, which means it's going to increase the buildup of serotonin. So, if you're taking anything that contributes to the serotonergic tone, it's potentially dangerous. [There are] multiple case studies published of people going to the hospital in shock, and methylene blue is the preferred treatment for shock, because it rapidly recovers the blood pressure and the perfusion of the tissues, which are dying because there's no blood supply.

But they noticed that, since they give a very high dose between 100 milligrams and 400 milligrams as a single injection, they had cases where people went into serotonin syndrome because they didn't know – because when somebody comes in critical through the door, you don't always know what medication they're taking, right? People went into serotonin syndrome and there's a known interaction of methylene blue with SSRI (selective serotonin reuptake inhibitors drugs). If you go to even CVS or Rite Aid pharmacy and tell them, "Hey, what medication should I not take together with methylene blue?" The first thing they'll say is SSRIs. I've already tried at the local pharmacist.

Dr. Joseph Mercola:

Yeah. But I've interviewed Francisco Gonzalez-Lima, who's supposedly the top methylene blue researcher in the United States, he's at the University of Texas, and I had this question, I asked him, “The dosing?” They have the researchers. I don't know if you realize this, they have not studied doses below 0.5 milligrams per kilogram.

Georgi Dinkov:

Really?

Dr. Joseph Mercola:

Yeah. I said, "Well, what about lower doses? Why not lower?" "We don't know. We haven't studied it." Which was shocking to me, but – 0.5 milligrams, that would be, so it's-

Georgi Dinkov:

Like 40 milligrams, 50 milligrams for most people.

Dr. Joseph Mercola:

Yeah, yeah. But I was doing 15. I said, I think it's like 0.15 or maybe even 0.2, not 0.5.

Georgi Dinkov:

Two great studies that I'll send you. One of them, remarkable. You can send it to him, I'm surprised he doesn't know about it. Methylene blue trials for suicidal depression, impermeable to any treatment, and another one for psychosis. So, the psychosis trial is really interesting. They had several groups. One of them, they gave methylene blue at a very high dose, 300 milligrams daily, and they said, "This is the active group." But because people who are taking methylene blue, they know they're taking methylene blue, so in order to properly blind them, we're going to have a "placebo group," which also gets methylene blue but only at the 15 milligrams [inaudible 00:29:22]. Guess who had the biggest benefit? The placebo group.

Dr. Joseph Mercola:

Geez. It would have to be a serendipity research, this trial. It wasn't by design.

Georgi Dinkov:

Yeah. I mean, it's just the 300 milligrams [that] had some improvement but not statistically significant. Placebo got worse, and the 15-milligram group got their psychosis cured. And in another study, probably by the same researchers who said, "Okay, 15 milligrams methylene blue, there must be some magic to it. Let's try it for depression." In two weeks. In two weeks, 15 milligrams of methylene blue got rid of treatment-resistant depression.

Dr. Joseph Mercola:

Oh my gosh. So, Georgi, I've listened to many dozens, it's probably coming up on a hundred of your podcasts now, and I've heard you talk about methylene blue, but I've never heard you strongly endorse and recommend it like you do niacinamide. Well, why is that? Why aren't you talking about it more?

Georgi Dinkov:

It's just that a lot of people – I'm concerned because, like you said, 40% of women of childbearing age are taking SSRI drugs. Many men are as well. I don't want to sound too – because it can be – If you're taking a lot of SSRIs, and a lot of people take it in the high dose too. I know a lot of people who are only on SSRI drugs, and are already showing up jittery and confused, which is like a precursor to serotonin syndrome. These are symptoms of that. They need a very little extra help to get into serotonin syndrome, which by the way has [a] 30% to 40% mortality rate, definitely not something I want to be involved with.

Dr. Joseph Mercola:

Okay. That explains it.

Georgi Dinkov:

I love it as a molecule if you know how to play with it and use it wisely. Unlike vitamin K, which you can abuse as much as you want, and it has no known side effects. But of course, at the expense that it's much more selective. While methylene blue, being the proverbial power drill, can resolve all of your problems, but you have to be careful with it.

Dr. Joseph Mercola:

Wow. Wow, I was not expecting this. This is fantastic. Man, this is great. One thing I wanted to mention, that Gonzalez-Lima mentioned to me, is that pretty much everyone, everyone, should have it in their emergency cabinet. I mean, you don't have to take it, especially if you're concerned about the serotonin syndrome, but if you get a stroke or heart attack-

Georgi Dinkov:

Oh yeah. Yeah.

Dr. Joseph Mercola:

-you are out of your mind if – It is the first thing you should reach for and swallow, 100%. And what would – assuming that you're not on an SSRI, if someone had a stroke, what would you dose, 50 milligrams or 100 milligrams?

Georgi Dinkov:

Even a single milligram will do great. There are multiple animal trials, which if you translate the dosage, comes down to less than 15 milligrams, single dose. Any dose over a milligram and less than 15 milligrams, I think, will do just fine. There was an in vitro study, which showed full reversal of aging in human cells. Unfortunately, it wasn't in vivo. And that study showed that the optimal concentration for anti-aging benefits, which means for longer-term consumption, is about 100 nanomoles per liter in most humans.

Of course, it depends [on] the volume of the human, right? Some people are bigger than others, but in most people, you can achieve that with daily dosages between 5 milligrams and 15 milligrams daily. So really, for me, the combination of all of these studies, the treatment-resistant depression, the psychosis, the Alzheimer trial, which found plateau at 80 milligrams, actually 60 milligrams, kind of tells me that the optimal dose is somewhere between 5 and 15 [milligrams], depending on the person.

Dr. Joseph Mercola:

Wow, wow.

Georgi Dinkov:

But any dose, any dose, even in the microgram amounts, if a person has a stroke or any kind of other acute event, any amount that can get into your bloodstream is probably going to be helpful.

Dr. Joseph Mercola:

All right. So, I was recommending a bit higher dose, but still significantly lower than the experts were recommending. I knew it wasn't 0.5 milligrams.

Georgi Dinkov:

[inaudible 00:33:07] doses-

Dr. Joseph Mercola:

That was the low dose. That was the low dose. They go up to 4 milligrams per kilogram.

Georgi Dinkov:

Yeah, because that's the clinically used dosage in hospitals, where if you go in the hospital in a shock, the dosage is by injection, 100 to 400 milligrams bolus, meaning a single dose.

Dr. Joseph Mercola:

That's great.

Georgi Dinkov:

Yeah.

Dr. Joseph Mercola:

Yeah. And the other thing, too, is that there's a lot of natural medicine clinicians who get methylene blue, and they're using it, but they use it in an IV (intravenous), and it's ridiculous. There's no reason to use an IV, just the absorption orally is close to 100%, isn't it?

Georgi Dinkov:

Yep. There's no difference. In fact, I've seen several animal studies that show that the bioavailability was a little bit delayed, but the total bioavailability is close to 100%. So, it is no reason to do IV.

Dr. Joseph Mercola:

Yeah. So, if you're dying from cyanide poisoning, yeah, go shoot an IV. But most people aren't dying of cyanide poisoning where every second counts. I mean, they could wait a few minutes and get 100%.

Georgi Dinkov:

Carbon monoxide poisoning, also, methylene blue is an antidote to that.

Dr. Joseph Mercola:

Oh yeah. Yeah.

Georgi Dinkov:

It's very dangerous.

Dr. Joseph Mercola:

Yeah. I mean, people die from it all the time. But if you just [inaudible 00:34:04].

Georgi Dinkov:

It doesn't smell. You won't even feel it. You just collapse basically. Or initially, you'll feel light-headed, but if you start doing that, [take] methylene blue immediately because that's probably the quickest antidote to almost any metabolic problem.

Dr. Joseph Mercola:

Okay. Wow. I knew there would be a lot of unexpected bonuses, and this was a huge one. I mean, this is a radical game changer. So, thanks for that insight, because I was just like, "Listen, when is he going to start talking about methylene blue?" I didn't realize it was this concern about the serotonin syndrome. On a podcast that I listened to, actually this morning, you were talking about the value of Listerine in changing the oral microflora to have some really powerfully beneficial effects.

Of course, Listerine, you were not recommending that because it's toxic as can be. But you're recommending a safer alternative that just happened to be a dilution of methylene blue. Maybe this magical 10 or 15 milligrams that you talked about, putting it into a liter of clean water and using it as an oral rinse. And you had also suggested adding some ethanol to increase it, which actually, you suggested putting in a quart of vodka.

Georgi Dinkov:

Quart of vodka, and you're going to be mimicking the Listerine without the side effects. Because some of the antiseptic effect of Listerine is very – it's because of the alcohol. Look at the contents of the label. I think it says 40% or 20% alcohol on the Listerine bottle.

Dr. Joseph Mercola:

Not ethyl alcohol. Is it ethyl alcohol?

Georgi Dinkov:

It could be isopropyl, maybe.

Dr. Joseph Mercola:

It's probably isopropyl, which is not good.

Georgi Dinkov:

It's not good. You don't want to ingest it. No, definitely don't want to.

Dr. Joseph Mercola:

I mean, I wouldn't even let someone put isopropyl alcohol on my skin with those alcohol wipe pads. I'd just use peroxide. Yeah. So you like that better? You think the ethanol would really help the – I was curious because methylene blue is absorbed so well into the tissues. Why would you need ethanol to push it through?

Georgi Dinkov:

You won't. I think I was commenting on how can you mimic Listerine at home with a naturally made formula. But you can get simply by doing basically the methylene blue in the same concentrations that they use for sterilizing aquariums and for killing all the fungi and the viruses and the bacteria, for the exact same reason. Think of the aquarium as your mouth, so the exact same concentration. Actually, it's 5 milligrams to 6 milligrams per liter. The water will become, I think, a very kind of vibrantly blue color, but I don't think it's going to change the coloration of your mouth.

Dr. Joseph Mercola:

Yeah. The only thing I would be concerned about, and just caution, having partials myself or even full dentures if you had them, but I would take those partials or dentures out your mouth because those will stain. But your teeth don't. I mean, it'll stain a little bit but not permanently. It disappears because as soon as it's reduced, its color is-

Georgi Dinkov:

Yep. The body uses it. In fact, on the forum, a long time ago we proposed the methylene blue test of health. What is the oral dosage of methylene blue that you can take before your pee starts turning blue? And the lower the dosage at which you start peeing blue, the healthier you are.

Dr. Joseph Mercola:

Yeah. The problem with that is that if you're taking riboflavin, it's not going to be blue.

Georgi Dinkov:

Oh yeah, that can change this.

Dr. Joseph Mercola:

It's going to be green.

Georgi Dinkov:

Green or whatever. Yes, yes, yes. So pure, no other supplements, only methylene blue, and if you pee blue at 5 milligrams, that's good. The higher the amount that it requires – Another way you can do, the skin test, but it's mostly a localized test of health. In fact, they're using it for cancer biopsy for that reason. When they're looking with a camera and a scope somewhere in your internals, and they see a problematic area, they go and inject methylene blue, and they measure how quickly the methylene blue gets discolored. They have a threshold. If it gets discolored quicker than, I don't know, 30 – I'm making up a number. But if it's quicker than a certain number, they're saying this tissue is cancerous, and they're then going to take a biopsy.

Dr. Joseph Mercola:

Wow. Yeah. That's pretty good. So, [for] most of the people I see, it's 30 to 40 milligrams before they start peeing blue, so that's relatively high, I guess. I mean, what's the lowest you've seen where pee turns?

Georgi Dinkov:

Five. 5 [milligrams].

Dr. Joseph Mercola:

5 milligrams?

Georgi Dinkov:

In very young people, yeah. I mean, basically, people in their teens.

Dr. Joseph Mercola:

Wow. That's good to know. That's good to know, which is consistent with your recommendation of such a small dose. It's 10 milligrams [to] 15 milligrams or so. Wow.

Georgi Dinkov:

And because the cancer reduces the methylene blue so quickly, it shows you that extreme reduction is definitely bad, right? Cancer is, by definition, in a reduced state because it's consuming the oxidized methylene blue at such a rate. Diabetes, a state of extreme reduction. And then oxidative stress, a state of another, but less extreme. So, it's just a continuous spectrum from health to cancer. It's just measured by the degree of reduction in the organ.

Dr. Joseph Mercola:

That is an unbelievably beautiful anecdotal confirmation of reductive stress theory. It really isn't a theory because you've got the data to support it, but [a] supposition. It's beautiful. I mean, this

has got to be adopted and understood and applied because it's so powerful. Once you understand it, it just helps you navigate the whole process much easier.

Georgi Dinkov:

I think the only hurdle currently is not that the medicine doesn't know about these things, they're convinced that the structural damages in most diseases come first. And there is always some genetic vulnerability, susceptibility. They still can't get over the fact that a simple metabolic disturbance, if propagated over time for significantly a long period of time, will cause those structural changes. And then it will become a self-propagating cycle.

So first, you have the metabolic disturbance or the functional problem. Over time, it leads to a structural problem. But in the structural problem, now you have deranged tissue, which contributes to even more functional problems. And on and on it goes until something breaks that vicious cycle. You want to hear other benefits of methylene blue? It's a very powerful aromatase inhibitor at an effective concentration of about 500 nanomoles.

Dr. Joseph Mercola:

Oh, it supports estrogen. Geez.

Georgi Dinkov:

Yeah. So, it's a sub-micromolar concentration effective aromatase inhibitor.

Dr. Joseph Mercola:

Wow, did not know that. Did not know that. That's great. So, I guess we're going to talk about niacinamide in a moment, too. But anyway, we'll go to obesity treatment. Obviously, the whole world is pretty much suffering with it. We're talking about more than 80% of the people struggle with their weight. And I think the latest estimate is about 95% are metabolically inflexible, which goes to the point of not being metabolically efficient, which is exactly what we're talking about. So, what are your best strategies for addressing the obesity problem and especially in those who are resistant, really struggle with it. And I want to get into the RU-486 and some of the other strategies, the novel approaches that you've mentioned in the past.

Georgi Dinkov:

So dietarily first, I think we both agree on that a hundred percent, absolute avoidance of PUFA, as much as possible. Without going orthorexic, okay? You shouldn't be killing yourself. I mean, it is not possible practically to completely avoid PUFA into the dietary-

Dr. Joseph Mercola:

No. I got my level down to 1%.

Georgi Dinkov:

Wow. Wow.

Dr. Joseph Mercola:

1%. Not PUFA, but just omega-6.

Georgi Dinkov:

Just omega-6, okay. So yes, avoidance as much as possible and, also, maybe a little bit of coconut oil. Maybe a tablespoon with each meal because it's not only the absolute amount of PUFA, it's also the ratio of saturated fats to PUFA, which determines both the metabolic rate, which the coconut oil raises, and also the reduction of oxidative stress, which is, well, reductive stress really. PUFA raises that while coconut oil has been shown to reduce it.

Dr. Joseph Mercola:

But if you're taking ghee, would you need the coconut oil?

Georgi Dinkov:

No. But I'm mentioning coconut oil because you can carry it around with yourself, and most people are okay with refined coconut oil because it has no taste. Even ghee, which I love the taste of, most people kind of balk at, like, "I don't want to eat a spoon of butter." But if you're cooking with ghee, then you probably don't need the coconut oil to start with.

Dr. Joseph Mercola:

Oh, okay. And one of the best foods out there is those boiled potatoes with ghee and a really good sea salt. Oh.

Georgi Dinkov:

Yep. And some cheese. You can put some Parmigiano Reggiano or Pecorino Romano. Man, the best. Yeah. The Russians, the Soviets actually, did a study after World War II about the – They call it the potato diet. You can not only survive, you can thrive, thrive on a diet of nothing but butter and potatoes and salt and water. That's it.

Dr. Joseph Mercola:

That's because it's got the keto acids for the protein, right?

Georgi Dinkov:

Everything. Exactly, everything. It's got potassium, even higher than oranges. It's got magnesium. It's got all the cofactors. It's got all the vitamins that you need as well, so you can thrive on a diet of potato and butter. I don't know of any other –

Dr. Joseph Mercola:

Just make sure it's well cooked.

Georgi Dinkov:

Yes, yes, yes, yes. Yeah, of course. But if you're in a state of war, I think-

Dr. Joseph Mercola:

Yeah, yeah, yeah. It's a good-

Georgi Dinkov:

-you can eat even raw.

Dr. Joseph Mercola:

Yeah. One of the things I had recommended earlier, and I didn't realize it was spot on because at the time I was carb-phobic, but I told people from their preparations when COVID was going on and food was shortages were impending, to pick up some 20-pound bags of rice, white rice. I mean, it's crazy not to have that. I mean, you can survive on that. I mean, obviously, it's depleted in nutrients, but it will give you helpful calories that aren't going to wreck you up metabolically.

Georgi Dinkov:

Yeah. Well, white sugar, packed sugar, bags of white rice, condensed milk is also probably a pretty good thing to have. It's usually sweetened, but it doesn't have to be. I mean, even the non-sweetened version is pretty good. So yeah, these are things – canned fish, canned food, canned oysters [are] also pretty good.

Dr. Joseph Mercola:

Yeah. The problem with the canned foods, though, is you've got the liners-

Georgi Dinkov:

Yeah, the endocrine disruptors. Yeah.

Dr. Joseph Mercola:

-the endocrine disruptors in there. But I mean, if you're doing these other things like methylene blue, it probably messes with those too.

Georgi Dinkov:

It can block most of – methylene blue – another very interesting study – Studies show that you can oxidatively destroy most of the endocrine disruptors by either keeping your metabolic rate

high or taking oxidizing agents such as methylene blue. Isn't that great? You can actually block most of the endocrine disruptors from bothering us simply by taking methylene blue daily.

Dr. Joseph Mercola:

Who would've known? And the experts – I mean, there are some really good committed individuals out there, where their life's work is just warning and informing people about these endocrine disruptors. But no one is talking about using methylene blue as an antidote because sometimes they're just unavoidable. They're pervasive in our environment. You touch the receipt on your grocery store thing, and you're getting BPA (bisphenol A).

Georgi Dinkov:

The highest amount of BPA than any other thing in your environment.

Dr. Joseph Mercola:

Yeah. So, it's almost unavoidable unless you're living in a bubble. So, we need these types of solutions. So, one of the things you had mentioned in my first podcast with you is DNP (dinitrophenol), and you mentioned earlier on this one too, the dinitrophenol as a mitochondrial uncoupler, which simply means that instead of your electrons flowing through an electron transport trying to generate an ATP (adenosine triphosphate) in cytochrome 5, they're shuttling outwards and creating heat.

Georgi Dinkov:

Exactly, yes.

Dr. Joseph Mercola:

So, it raises your metabolic rate quite a bit. And DNP, dinitrophenol, is actually illegal in the United States because it killed a lot of people, but it was very – It wasn't illegal because it wasn't effective. It worked.

Georgi Dinkov:

By raising their thermogenesis too much, and they died of heat stroke. That really was the key. But you go to Mexico, you go to Thailand, you go to any other medical tourism places, and you say, "I want to lose weight." DNP is one of the first things they offer.

Dr. Joseph Mercola:

So, the other metabolic uncoupler is aspirin, which is another – There are a few things that I think seem to be universal. Methylene blue would qualify if it wasn't for serotonin syndrome, but the aspirin [and] niacinamide for sure, and probably vitamin E, maybe even glycine. These are something almost everyone benefits from. And in some ways, it really even shouldn't be

considered a supplement or drug because it's so essential to optimizing survival in this type of 21st century environment.

So, you had mentioned the first time that they were doing – You saw studies where they're doing 9 grams, which is literally 27 full-dose aspirin a day, which probably caused tinnitus in most of the people who took it. But it was a very effective uncoupler, and people lost weight with it. So are there other strategies like that that you'd recommend? I think 9 grams of aspirin is a little bit too extreme, and it might cause problems in a lot of people.

Georgi Dinkov:

Caffeine, also metabolic uncoupler. A very old study-

Dr. Joseph Mercola:

Really?

Georgi Dinkov:

Yeah, yeah. In 2014, when I first joined that infamous Ray Peat forum, one of the first studies I posted in it, because I found it and I thought it was interesting, is that caffeine, depending on how high of a concentration you do, works the exact same way as dinitrophenol. It's widely acknowledged that caffeine raises your basal metabolic rate. But most of the dosages that are used are within the 50 milligrams to 100 milligrams per study, right? And even that low dosage raises your basal metabolic rate by 4% to 5%. And this increase stays for about 12 hours.

So just two coffees a day will be raising your basal metabolic rate by a couple of percentage points. And that effect will probably stay throughout the entire 24-hour period until you start drinking the coffee again, but at higher doses, but still lower than the aspirin. So, the equivalent of a human dose is about a gram a day, which is kind of a hit on the high side, but I know people who are consuming it. At about a gram day caffeine had almost the exact same uncoupling effect as dinitrophenol. And multiple animal studies actually compared them head to head, the exact same weight loss achieved by the caffeine as the dinitrophenol. Oh, that's-

Dr. Joseph Mercola:

Wow. The only thing at that dose, of course, is you want to be really, really careful about taking it too late, especially if you're caffeine sensitive and you don't metabolize it well, because you won't sleep.

Georgi Dinkov:

Also, caffeine inhibits your synthesis of urea from ammonia. You can get a buildup of ammonia especially if you're on a high-protein diet. So, you want to be careful with caffeine, but not as dangerous as DNP. And of course, it's widely available, so you don't have to break the law to get it.

Dr. Joseph Mercola:

If people aren't drinking coffee, could they just take a caffeine tablet?

Georgi Dinkov:

Sure, a caffeine tablet is great. And if you get the jitters from it, usually it means you don't have enough glycogen stored in the liver because the way the body processes the caffeine, and because it also raises the metabolic rate, it says, "Let me throw more food at it." So caffeine's like the spark. It's the catalyst, right? But without the fuel, you'll be running on empty. So, make sure you take it with a sufficient amount of fuel. And if it still gives you the jitters, usually combining it with the glycine, which is an inhibitor amino acid, or theanine, which is more popular now. In fact, there are even products on the market combining the theanine amino acid, found mostly in tea, with caffeine because it completely eliminates that unpleasant stimulating effect.

Dr. Joseph Mercola:

Oh, I didn't know that. What about adding theanine with GABA (gamma-aminobutyric acid) too?

Georgi Dinkov:

Fine. Taurine is another GABA agonist, another inhibitor amino acid. Unsurprisingly, taurine is in Red Bull precisely for that reason. They found out exactly how much taurine you need to block the jittery effects of a specific amount of caffeine.

Dr. Joseph Mercola:

How much is it typically, a few hundred milligrams?

Georgi Dinkov:

Oh, I think it's like 1 gram per can. So, 1 gram per can neutralize-

Dr. Joseph Mercola:

Oh, it's 1 gram of taurine per can?

Georgi Dinkov:

Yeah, a gram of taurine per can. Yeah.

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

Yeah. But I think it's there also for another reason. They consume a lot of monosodium glutamate in East Asian countries and taurine – the formula was originally invented in Thailand. So, taurine is a known antidote to monosodium glutamate because glutamate is an excitotoxic amino acid. So, they eat a lot of monosodium glutamate because it's got this – It's a flavor enhancer that they add to many soy products and different meats. So, the way you prevent the jitteriness and the excitotoxicity is you eat inhibitory amino acids, either taurine or glycine, right? Or theanine, which is in tea.

So taurine was – This formula, the Red Bull formula, was invented to kind of offset some of the damage that the monosodium glutamate does. So, the dosage is a little bit high. I think one can of Red Bull has about 80 milligrams of caffeine. For that, it may be about 250 milligrams of taurine is enough to negate the jitteriness. The extra taurine on top of that, I think, is because the drink was meant to combat monosodium glutamate toxicity.

Dr. Joseph Mercola:

Yeah. But glycine would be helpful too?

Georgi Dinkov:

Perfectly fine. Glycine, taurine and theanine are all GABA agonists. So even though they – I mean they basically act like GABA, or you can take GABA if you want.

Dr. Joseph Mercola:

Yeah, yeah. Because there's some of the – I think we're coming up with a supplement that's GABA and theanine.

Georgi Dinkov:

Yeah. Beta-alanine, also a GABA agonist. For a long time, medicine was saying-

Dr. Joseph Mercola:

I love beta-alanine.

Georgi Dinkov:

They're very good.

Dr. Joseph Mercola:

The precursor for –

Georgi Dinkov:

Carnosine, yes.

Dr. Joseph Mercola:

Most people don't know, but you would know. AGEs (advanced glycation end products) are terrible, but ALEs (advanced lipoxidation end products) are even worse, and carnosine is a really effective sacrificial sink for it. It just binds to it, so before it hurts you.

Georgi Dinkov:

Yep. And the medicine for a long time has claimed that oral GABA is not bioavailable, and it doesn't cross the blood-brain barrier. Recently, all of this has been falsified, I mean, debunked, just as we are debunking the oxidative stress and, oh, cortisol being an anti-inflammatory. I don't know if you want to go into that next.

Dr. Joseph Mercola:

Oh yeah, yeah. Yeah. Well, let's finish up on the obesity thing.

Georgi Dinkov:

Okay.

Dr. Joseph Mercola:

And we'll talk about proteins too. For resistant obesity, you gave us some ideas of the uncouplers. But clearly, cortisol is the primary contributor, and you get into this vicious cycle, right? The cortisol makes it worse, and you get heavier, and the increase in weight increases the cortisol. So, you talked about RU-486, or mifepristone as the abortion pill, as it was initially developed as a cortisol blocker, and then subsequently found to also block progesterone so that it could be used as an abortion pill. But the primary purpose was to block cortisol.

So, does it block anything else other than progesterone? Does it block testosterone? Because we had talked earlier at the beginning how the anabolic steroids are actually useful because they're anti-cortisol, and limiting the cortisol impact on your catabolism is their primary mechanism of action. So, could you use RU-486 in treatment of obesity, assuming you supplement with pregnenolone or progesterone to counteract the impact on those receptors? Or is it just not a wise idea?

Georgi Dinkov:

I don't know if it's a wise idea, but would it be effective? Absolutely. I mean, if you go to the body building forums, that's actually one of the accepted ways to lose weight without dieting.

Dr. Joseph Mercola:

Really?

Georgi Dinkov:

Oh yeah, DNP or RU-486 or upping your dosage of testosterone, whatever anabolic hormone you're taking because you will block cortisol that much more, right? And then basically you'll lose the weight. So if you're a competitive bodybuilder, they're saying, "You're already taking the anti-cortisol hormones. You don't need to take anymore." But if you're kind of into the healthy bodybuilding stance, you don't want to become a huge hulk, they're saying, "Look, if you just want to keep the weight off and be shredded and have decent muscle mass and not have a big belly, just take RU-486." It's basically less risky than the anabolic steroids that [inaudible 00:52:56].

Dr. Joseph Mercola:

But you'd want to take it with at least pregnenolone, right?

Georgi Dinkov:

Definitely, yeah. Because like any other steroid, it's probably going to disrupt one or more of the steps of the downstream cascade. And usually, even for the anabolic steroids, there's the infamous roid rage. And they found out that the reason the roid rage occurs is that most anabolic steroids block the synthesis of progesterone and, subsequently, of a metabolite of progesterone known as allopregnanolone, which has a very potent, calming and antidepressant effect. FDA recently approved allopregnanolone as a rapidly acting antidepressant.

So clearly, if you're interfering with its production, you expect people to get either depressed or angry, which is a very common sign of depression as well, so these anabolic steroids were disrupting one or more of these steps. So taking pregnenolone or progesterone was found in animal studies to prevent the aggression associated with anabolic steroids. So RU-486, also a steroidal molecule, [is] likely to disrupt probably the initial steps of the steroidogenesis. So yes, pregnenolone, or progesterone, or progesterone and DHEA (dehydroepiandrosterone), but I think pregnenolone is probably the easiest thing, just one thing for people to remember to take together with the RU-486.

Dr. Joseph Mercola:

When you take oral pregnenolone with a saturated fat, more than 14 carbons, which you'd mentioned in our first podcast, does it convert to allopregnanolone?

Georgi Dinkov:

So, what you want is as much of the pregnenolone to get absorbed through the lymphatic system, right, to avoid the first pass metabolism through the liver. And once it gets it released into your bloodstream through the thoracic duct, then basically it gets converted into whatever the body needs. High doses of oral pregnenolone in humans, multiple clinical studies with schizophrenia and other mental disorders showed it – or high doses of oral pregnenolone in humans raise predominantly three hormones. Of course, pregnenolone, DHEA – because pregnenolone is a precursor – and allopregnanolone, so these are the preferred pathways for converting pregnenolone into. And of course, further down, androgens and estrogens and corticoids are

needed, but it turns out that the precursor mostly goes into these beneficial pathways that we know about, allopregnanolone being one of them.

Dr. Joseph Mercola:

So in my view, I consider for almost all adults, a daily pregnenolone DHEA supplement would be a really good idea because they're so helpful for combating excessive estrogen, which is pervasive. And almost a factor in almost all the chronic diseases is excess estrogen.

Georgi Dinkov:

Oh yeah. I mean, estrogen is probably the primary death differentiating hormone we have. Unsurprisingly, it increases the oxidation of fat. It decreases the oxidation of glucose. It increases the symptoms of cortisol. In other words, [it] activates the stress response because that's what estrogen is. Many people think of it as [a] female hormone. No. Men can produce as much as females do.

And in fact, older males – Basically, if you look at menopausal females and older males, males can produce much more than females do. And I don't know if you've noticed that the very old people phenotype, the males get kind of feminized, and the females get masculinized. They really kind of merge into a unisex kind of looking organism. And it's now known that the estrogen is one of the primary determinants of that. Excess estrogen feminizes males and masculinizes females.

Dr. Joseph Mercola:

All right. Well, let's get back to – We started on niacinamide, but we kind of escaped it. And in both of our views, you are almost out of your mind and irrational if you're not taking niacinamide. It's almost free. It's a few dollars a year if you buy the powder, and you only need 50 milligrams a few times a day, even up to four times a day. I try to take mine in equal spaces. 50 milligrams of a powder is 1/64 of a teaspoon. Pretty easy to do, and it has no taste at all. You could even swallow it directly, but it's so much easier to put it in water. And we talked about the PDH, the pyruvate dehydrogenase, as the throttle for the Randle's switch, but what activates that PDH, the pyruvate dehydrogenase, is niacinamide or actually the conversion to NAD, the NAD that activates it. Yeah.

Georgi Dinkov:

So if we have an excessive NADH and deficiency of NAD causing all of these metabolic problems, whether it's reactive oxygen species, oxygen/reductive stress, or actually if you have too high of an NADH to NAD, you won't even be synthesizing a sufficient amount of ATP. If you look at the studies, they show that ATP levels have an almost perfect correlation with NAD+. So, the higher your NAD+, the higher the ATP synthesis is, and the better your metabolism works.

Dr. Joseph Mercola:

That's huge. That's a pearl that – I didn't even realize it, and I'm a huge niacinamide fan and NAD+. I never knew that there's a direct correlation between ATP and NAD.

Georgi Dinkov:

80% of your ATP production comes from NAD+. The other 20% from FAD.

Dr. Joseph Mercola:

And you need the magnesium too, right? Because it's always magnesium [and] ATP. You've got-

Georgi Dinkov:

Yes, because if you take magnesium – So here's why a lot of people that are taking magnesium may not be feeling the benefit of it, is because they don't have enough ATP synthesized. If you don't have enough ATP synthesized, the magnesium cannot bind to the ATP, and it's in the body. It's always bound to the ATP as a complex. So magnesium will be floating around in its free ionic form and very quickly excreted as well, which means that people who are the most needy of magnesium are the ones who are least capable of absorbing it and making use of it, which means that if you'll be taking magnesium, make sure you take it with some niacinamide because niacinamide will raise the NAD, which will raise the ATP, and then you'll be able to utilize the magnesium instead of just giving you loose stools or intestinal irritation.

Dr. Joseph Mercola:

Do you think the timing of those should be similar? Like taking the niacinamide with the magnesium?

Georgi Dinkov:

First, I think, first [is] niacinamide to give it some time to raise the NAD.

Dr. Joseph Mercola:

Oh, okay.

Georgi Dinkov:

It takes about half an hour, and then you can take the magnesium a little bit later.

Dr. Joseph Mercola:

Okay. And then because it's a B vitamin, it has a relatively short half[-life], like a matter of hours. So you'd want to take it multiple times a day. You just don't take one dose for the day and that's it, right?

Georgi Dinkov:

Exactly. Yeah, so the smaller doses, because the NAMPT (nicotinamide phosphoribosyltransferase) enzyme, which synthesizes NAD, is easily saturated. So, if you take too high of a dose, you're going to block that enzyme. And in fact, most of the niacinamide dose will float around and get converted to something called 6-methylnicotinamide, which is a metabolite [and] helps the body excrete excess niacinamide, nicotinamide, right? But again, you'll be mostly wasting it.

Now some studies have shown some interesting beneficial properties of even 6-methylnicotinamide being an anti-inflammatory, anti-estrogenic, basically lifespan-extending substance. But it's not as beneficial as letting niacinamide get converted to NAD+. So, you have to take a dosage that does not block the NAMPT enzyme, and that dosage in humans seems to be, for most people, less than 100 milligrams per pop, which means 50 milligrams, as you said. Right. So, 50 milligrams several times daily, you're going to be converting mostly to NAD without creating any excess that can block any of the other pathways.

Dr. Joseph Mercola:

Beautiful things. And you talked about the 6-methylnicotinamide, and you probably know this, but it took me a long time to figure this out when I was studying NAD, that nicotinamide and niacinamide are two different names for the same damn molecule.

Georgi Dinkov:

Exactly.

Dr. Joseph Mercola:

Yeah. So, most people don't know that. They hear or see it, "What is nicotinamide?" That's the scientific term, and then they realize most laypeople [are] confused with nicotine. So, they decided to make it less onerous and named it niacinamide. That's why I like to use niacinamide. Just decreases the confusion. But one of the other things that made me nervous about taking high doses of niacinamide – because when I was studying it, the literature was really clear. High doses. They never specified what a high dose was. But high doses have [a] negative impact on the sirtuins.

Georgi Dinkov:

Yes.

Dr. Joseph Mercola:

And lo and behold, I read one of your blog posts, and the whole thing was upside-down. The sirtuins are not as helpful as with the longevity proteins.

Georgi Dinkov:

You don't want to mess with it too much. Yes. Like autophagy, right? It's there for a reason. You may modulate a little bit, but too much, it's a mechanism that – sirtuins, just like autophagy, are implicated in promoting already established cancers. They can prevent the cancers to start with, if you're activating them. But once tumor is already present, you probably don't want to be messing with the sirtuins.

Dr. Joseph Mercola:

Yeah, it's interesting. David Sinclair is the scientist who catalyzed my interest in NAD in about 2014 to 2015. He had some very compelling research, and of course he's the guy responsible for maybe doing the initial research on resveratrol, which you are not a big fan of, for sure.

Georgi Dinkov:

No, no, no. Actually, a functional antagonist, resveratrol and niacinamide. So if you like one, you probably don't like the other.

Dr. Joseph Mercola:

Yeah. And as he does not talk a lick about niacinamide, never does. He talks about NMN (nicotinamide mononucleotide) as a derivative of it that one of his companies, I think Metro or something, put out. Actually, it was his research, his company's research that did the work on this NMN that got NMN off the market. I don't know if you know it was Sinclair-

Georgi Dinkov:

Oh, the FDA said [to] no longer sell it over-the-counter because it's a new drug, a novel drug, or whatever they call it.

Dr. Joseph Mercola:

Yeah, yeah, yeah. I think it was Metro Pharmaceuticals. It was Sinclair's-

Georgi Dinkov:

Yeah, in Boston. I just saw it in Boston. It's his company? I didn't know it's his company.

Dr. Joseph Mercola:

Yeah, it is. Yeah. It is definitely his company, or he's connected with it in some way. I don't know if he owns it, but he's definitely connected. But anyway, the reason I was sharing that story is that I thank him for waking up my interest to this because we've known about NAD+ since 1905, I think. It's been over a century because it's an essential part of the Krebs cycle. And so I was fascinated about it because of its impact on the sirtuins and PARP (Poly ADP-ribose polymerase) and CD38. But then afterwards, studying your work and Ray's, I realized, damn, it's still all about the basics, the Krebs cycle. That's why it really works, is because it's ramping up the ATP production. It has nothing to do with the sirtuins.

Georgi Dinkov:

Yep. It improves your metabolic rate, no buildup of electrons, or at least tolerable buildup of electrons. No reactive oxygen species. And then basically you stay healthy for longer.

Dr. Joseph Mercola:

And this is another mind-blowing pearl that I don't hear you often mention, but I did hear it on one podcast. It actually is the required cofactor to take cortisol, which we've talked all about its dangers, and convert it to the inactive form of cortisone.

Georgi Dinkov:

And also, to take the active form of estrogen called estradiol and convert it into the less active form. Still active, but less dangerous called estrone. So, estradiol fully reduced. Yeah.

Dr. Joseph Mercola:

Dang, another good thing. You've got to be irrationally out of your mind if you're not taking niacinamide. There was just simply no reason not to. None. Zero. Nada.

Georgi Dinkov:

Yep. I take it every day.

Dr. Joseph Mercola:

Yeah, and actually, I could announce here, because as we're shooting this, we're about six weeks out from actually producing what I believe is the only 50 milligram niacinamide tablet on the market. So-

Georgi Dinkov:

The only one. I've searched for a long time.

Dr. Joseph Mercola:

Yeah. So, I realized for a long time, because I've been taking niacinamide at that dose for a few years now, but it takes us a long time to make these supplements. It's just a lot of – Well, you know. You have a supplement company, so you're familiar-

Georgi Dinkov:

Legalities and trying to somewhere-

Dr. Joseph Mercola:

Yeah, raw materials and labeling and getting all that stuff out. But the other thing is how common would you say liver disease is? Like NAFLD (non-alcoholic fatty liver disease) and then the alcoholic fatty liver disease, too? I've heard you say 70%, 80%. And the reason I mention that is because it's helpful for this, too.

Georgi Dinkov:

Yep. Some form of liver disease. So, you have NAFLD, right? Then you have the more severe form, which is NASH, non-alcoholic static hepatitis. Then you get basically the fibrotic stage, such as cirrhosis, and ultimately, liver cancer, which is the final progression. Then you also have the fatty liver from alcohol, and I don't know why they're separating non-alcoholic fatty liver disease from alcoholic fatty liver disease, considering that they basically cause the exact same condition.

Dr. Joseph Mercola:

Yeah, identical. There's no difference.

Georgi Dinkov:

But if you're taking niacinamide, basically, by improving the metabolic rate, you're preventing a lot of the buildup of these reactor species, which are attacking the polyunsaturated fats that are in the liver, and it's been shown that it's this peroxidative process that is responsible for most of the damage that occurs in the liver. The other portion is increased lipolysis, which supplies those fats to the liver. And guess what? Niacinamide, by converting it into NAD, restricts excessive lipolysis. I emphasize excessive. It does not inhibit baseline lipolysis. Insulin does, but not niacinamide, not NAD. If you're too much lipolytic, you'll lower them. I don't know if I sent you the article where [a] single low-dose niacinamide, I think it was 100 milligrams, dropped triglyceride levels by 75% in humans.

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

So that means it's rapidly – because most of the triglycerides are coming from the fat, right? Either you ingest it, but these people were fasted, which means most of the fatty acids were coming from the fatty tissue. And if you're decreasing the triglycerides by that amount, which means you're probably inhibiting lipolysis by about 75%.

Dr. Joseph Mercola:

I know aspirin inhibits lipolysis, too, but does it inhibit baseline lipolysis?

Georgi Dinkov:

I don't know if it's been studied. It's possible because it's known that aspirin in very large doses starts to mimic insulin, and that's one of the reasons why they're using it back in the day when they didn't have insulin isolated. If somebody shows up in the hospital with diabetic ketoacidosis, one of the treatments they had was very high-dose intravenous infusions of sodium salicylate, which is just an analog of aspirin.

So, they were using it in lieu of insulin. And since insulin can suppress baseline lipolysis, chances are that very, very high doses, not something that I will try, and by the way, it was by IV, it wasn't oral. So, I think they were giving the equivalent of the 9 grams that we discussed over a period of a few hours through IV, and that was acting like insulin. But in the regular doses, I think the one that we are discussing here, no more than a couple of grams daily or just a few tablets daily, I think it's still related to excessive lipolysis. You don't want to inhibit baseline lipolysis too much because, remember, at rest-

Dr. Joseph Mercola:

Your muscles.

Georgi Dinkov:

-your muscles rely on it. Yeah, so you don't want to starve the muscles.

Dr. Joseph Mercola:

And what's the primary heal source for the heart? Is it fatty acids?

Georgi Dinkov:

At rest. But then once you start exerting yourself, because the beta-oxidation process is too slow to basically meet the requirements, when you're exerting yourself, the heart starts to demand glucose. And one of the most successful ergogenic products on the market is the drug, meldonium, Mildronate. And the way meldonium works is it restricts the oxidation of fat and allows the heart to use more glucose. But it only works as an ergogenic aid when you actually need it. If you are at rest and you take meldonium, it's not going to give you more energy.

But if you are running, let's say, if you're running a marathon or you're doing a tennis match – unsurprisingly, tennis players used to abuse meldonium before it got banned by the World Anti-Doping Association, WADA. Tennis player Maria Sharapova, meldonium being a former Soviet drug, was using it. And basically, when you are under exertion, it increases your threshold to failure, so to speak, by about 30% to 40%, which is huge. So, if you're playing a several-hour long tennis match, being 40% more resilient or quicker or more energetic, of course, can mean the difference between winning and losing.

Dr. Joseph Mercola:

Okay, great. This is phenomenal stuff. So, I want to progress to the hormone of darkness, supposedly, which is melatonin. It's a bit intriguing because it's gotten a lot of publicity and it

seems to be really good. But here's an interesting thing. It's an antioxidant, and foundationally, it could contribute to the reductive stress that we talked about earlier.

Georgi Dinkov:

Absolutely.

Dr. Joseph Mercola:

So yes, independent of its role in augmenting sleep – because there are two roles. I mean, actually, it's connected because the pineal gland secretes it at night when you're in darkness. If you had bright light exposure in the daytime and you didn't see blue light before you went to bed, then you're going to get it. But still, that's only 5% of the melatonin your body secretes. 95% of it is made in the mitochondria, subsided mitochondria, or subsided melatonin. And in response to near infrared light, which is just an amazing, amazing, powerful nutrient. I think it should be a nutrient. We talk about all these supplements and nutrients, but sunshine has got to be part of it. I mean, there's just no way around it. I look at the vitamin D level as a biomarker, assuming that you're not swallowing vitamin D, it's a biomarker for sun exposure.

Georgi Dinkov:

And for longevity and for many other things.

Dr. Joseph Mercola:

Oh, yeah.

Georgi Dinkov:

The most reliable predictor or future development of something like multiple sclerosis is for how long you are vitamin D deficient. There's an almost perfect inverse correlation between latitude and rates of multiple sclerosis, with the rates being the highest in the Scandinavian countries and going down to virtually zero around the equator.

Dr. Joseph Mercola:

Yeah, but that's correlation. That's not causation-

Georgi Dinkov:

Right.

Dr. Joseph Mercola:

-of course. And I think the correlation is there because it's sun exposure.

Georgi Dinkov:

Sunlight, yes. Yes.

Dr. Joseph Mercola:

I don't think you're going to get the same benefits, autoimmune benefits, if you're swallowing it. You may get something similar, and a lot of the vitamin D researchers believe that. I suspect there's some truth to it, but it's going to be far in excess if you get it from the sun. I haven't swallowed vitamin D in over 15 years, and I just had my blood test back from vitamin D last week. It was 99 nanomoles per liter. So-

Georgi Dinkov:

But you live in Florida, right?

Dr. Joseph Mercola:

I live in Florida and I am obsessive about getting out at solar noon every day to get into sunshine. It is absolutely crucial, from my perspective. You've got to have that. You don't have to, but it really – 70% of the solar radiation is near-infrared. Did you know that? 70%.

Georgi Dinkov:

Yeah. Some people said – I mean, it's been known in the industry that produces electricity from the sun, they're saying, "Look, if we're only using the photons to produce the electricity, we've actually wasted most of the sun's energy because it's mostly in the infrared spectrum. So, we're going to get more energy by trying to heat things up with the sun instead of converting the photons into electric energy." So yeah, most of it that we get is heat and the invisible infrared spectrum.

Dr. Joseph Mercola:

Yeah. Yeah, well, the near-infrared doesn't heat as much as the far infrared does. So, I think most of it's in the near[-infrared]. I mean, definitely you can get – I had one, I actually still do in my house, I have a solar water heater. So, I don't use an electric heater to heat the water, I use that. But I don't know if it's as efficient. That's the issue. But anyway, it's a tangent.

So, I'm wondering what your thoughts are on melatonin because for those who aren't familiar with melatonin metabolism, we talked about the negative impacts of tryptophan. It's not a good amino acid that you want to have large amounts of, but tryptophan gets inverted to 5-hydroxytryptophan, which is also called serotonin, and serotonin is a direct precursor for melatonin.

So, I don't think anyone's in disagreement that we need melatonin. There's no dispute there. But the concern and the difficulty to reconcile between those is that we want to minimize tryptophan and serotonin. Not good things, and we'll have a serotonin discussion, not this time, but in a future interview. But how do you reconcile that with melatonin? Is it the conversion that's the

issue? Is there some crucial enzyme that's responsible for converting it? Because if you have low serotonin, you're not going to make melatonin.

Georgi Dinkov:

Exactly. But here's the thing, healthy people are known to have higher levels of melatonin, but the production of melatonin from serotonin depends on ATP. So once again-

Dr. Joseph Mercola:

It's ATP!

Georgi Dinkov:

Yes.

Dr. Joseph Mercola:

It's not the enzyme. It's just simply ATP.

Georgi Dinkov:

Well, no, it's a cofactor. But if your metabolic rate is not good, if you're not taking niacinamide-

Dr. Joseph Mercola:

But the [inaudible 01:13:15] is ATP?

Georgi Dinkov:

Yeah. So healthy people can convert – And actually, since serotonin is not good for you, there is a theory out there, a hypothesis that melatonin is like the protective version of serotonin that puts you to sleep because serotonin puts you into torpor, in a very non-restorative, shallow sleep. Hibernating animals have it. They're half awake, right? They're neither asleep nor awake. So, if you don't have the melatonin, you're going to build up serotonin, and that's really bad for your sleep and bad for your overall general health. Now, however, taking more melatonin, depending on – I will be really careful with the dosage because I'm seeing supplements on the market selling 5 milligrams and 10 milligrams, even 15 milligrams, where you're producing about 500 micrograms per 24-hour period.

Dr. Joseph Mercola:

There are people recommending 100, 300, 400 milligrams of melatonin.

Georgi Dinkov:

Wow.

Dr. Joseph Mercola:

Yeah. I'm telling you-

Georgi Dinkov:

I think that's obscene. So here's what happens if you take that excess, by the negative feedback pathway, you're going to be basically inhibiting the enzyme that converts the serotonin into melatonin because the body says, "Oh, I have plenty of melatonin. Don't give me more," and now serotonin starts to build up.

Dr. Joseph Mercola:

Oh, then-

Georgi Dinkov:

If your monoamine oxidase enzymes are not working properly, and even if they are, if you build up a sufficient amount of serotonin, you're going to get terrible nightmares, which are the identical to the nightmares that people with post-traumatic stress syndrome have. And they're known to be treatable by serotonin antagonists. So if you take too much melatonin, you will build up serotonin, and that's not a good thing. But if you're deficient in melatonin and you take a physiological dose to recover it to the point where you sleep well, you'll be in a better position than not addressing it at all.

Dr. Joseph Mercola:

That is magnificent. Exactly what I was looking for. Man, that is great. How-

Georgi Dinkov:

And by proper dosages, I mean, micrograms. Basically, 5 milligrams to 1 milligram before bed is usually all you need to restore melatonin to the levels that basically a healthy person has. The multi-milligram dose is like 100-

Dr. Joseph Mercola:

So wait, wait, you said 5 milligrams. You meant 500 micrograms?

Georgi Dinkov:

500 micrograms, which is half a milligram, so basically 1 milligram is usually what is the healthy way to restore melatonin to the level of a 10-year-old, 12-year-old child. So you sleep well through the night. And, of course, hypometabolic people will have less melatonin, more serotonin. But if a hypometabolic person takes too much of a melatonin, they're going to raise the serotonin even more, and they're going to end up in a situation where they don't sleep well.

I've taken higher dose melatonin and the dreams are just absurd. And really, you wake up shaken up.

Dr. Joseph Mercola:

Well, that's interesting because I heard you say on another podcast that a common source of nightmares is high cortisol levels.

Georgi Dinkov:

Which activates tryptophan hydroxylase.

Dr. Joseph Mercola:

Oh. Is that the reason? Because it increases the serotonin? I didn't know that was a mechanism.

Georgi Dinkov:

They all go together. It's basically part of the stress field, which helps you survive at the expense of your functioning as a human.

Dr. Joseph Mercola:

Oh. I knew this would be an unbelievable compilation of material and knowledge that you're transferring.

Georgi Dinkov:

Estrogen activates 225-hydroxylase while simultaneously suppressing tyrosine hydroxylase. So when you're under stress, you're going to have more serotonin, less dopamine. Conversely, when you're in a good health, happy and gregarious, more dopamine, and dopamine is an inhibitor of tryptophan hydroxylase, so you're going to have even less serotonin. It's really like a feedback cycle. Once the good times start and you maintain it for a while, they become self-propelling. Once the bad times start and they continue for a while, they also become self-propelling.

Dr. Joseph Mercola:

Well, perpetuating.

Georgi Dinkov:

Yeah, perpetuating. Yes.

Dr. Joseph Mercola:

Yeah. Sorry to correct you, but I'm always impressed how literally 15 years ago, you probably didn't even know English, and you're so articulate and able to communicate these complex

scientific concepts into material that we can digest and understand. It's just amazing. You're just an incredible human being.

Georgi Dinkov:

Thank you.

Dr. Joseph Mercola:

So, one of the things we skipped over, and I think we have some time for it now, is protein, because you're really cautious about certain amino acids, and I think rightly so. The protein levels down that you quoted earlier are really pretty small, and actually, those are much lower than is recommended to build muscle mass. I mean, typically, it's twice that level. But you still want to keep the total dose down for most people below 120 grams a day. But I personally shoot for 120 grams, but you were advocating 80 grams or so, and that's interesting to know that people could do well with that level of protein.

But anyway, the specifics of the protein are – methionine is well – I want you to talk about the methionine, how it's well correlated with a decrease in longevity because it has some negative impacts. And then there are other amino masses, like the tryptophan and cysteine, that are problematic also. So, one of the ways that you can address the methionine – because certain healthy foods like eggs and beef, at least the muscle meats, are high in methionine. So, I personally add 7 grams to 8 grams of glycine to my eggs and my beef to mitigate that methionine and balance it out. And I didn't realize glycine was an inhibitory amino acid. That's nice to know. And then you also mentioned the branched-chain amino acids, which is a really good anabolic because it activates mTOR, leucine and isoleucine and the valine, but the branched-chain acids can actually inhibit absorption of tryptophan, I believe you said.

Georgi Dinkov:

And methionine.

Dr. Joseph Mercola:

Oh, methionine. Okay, didn't know that.

Georgi Dinkov:

And aspirin. Another reason [to] take aspirin, it inhibits the absorption of methionine, cysteine and tryptophan from the food.

Dr. Joseph Mercola:

Really?

Georgi Dinkov:

Yeah.

Dr. Joseph Mercola:

And what type of dosages would it do that at? Is it like-

Georgi Dinkov:

Oh, probably just a single tablet, because the reason I found the study is that they were studying different types of phenolic molecules, which aspirin is a type of a molecule like that, and they found that they're widely distributed in nature, virtually a lot of food, especially grapes. Speaking of grapes again.

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

They're in oranges, pears [and] apples, right? But they're usually in the skin, which a lot of people peel and throw out, but that's where actually most of the benefits are. So anyway, if you eat phenolics, a significant amount of them, and they're saying that the average daily consumption is in the several hundreds of milligrams daily, which tells me that about the same amount of aspirin should probably have similar effects, except that it's taken as a single tablet versus spread out throughout the day, which is what the phenolics in the diet would be. So maybe take a baby aspirin with each meal, which would come down to slightly over 200 milligrams, and then you'll be inhibiting a significant amount of the absorption, a significant amount of these inflammatory amino acids from the food.

Dr. Joseph Mercola:

Wow. So, you think a dose as low as 80 milligrams to 100 milligrams of the aspirin with the meal itself would be enough to inhibit the absorption?

Georgi Dinkov:

If you take whatever, let's say eating three or four times a day, that means about 250 milligrams to 300 milligrams of aspirin daily, which is about the same as the amount of phenolics we'll be consuming from the food. And by the way, we're still consuming those phenolics. So, all you're doing is you're augmenting.

Dr. Joseph Mercola:

[inaudible 01:20:30] augmenting.

Georgi Dinkov:

Yeah, yeah, exactly. Yeah.

Dr. Joseph Mercola:

Wow. So, what do you think is the ideal dose of aspirin for most people, and are there specific subsets of individuals who would benefit from a higher dose?

Georgi Dinkov:

So, they call it primary prevention, right? For cardiovascular disease, the baby aspirin is probably enough. For cancer prevention-

Dr. Joseph Mercola:

Wait, let me stop there.

Georgi Dinkov:

Oh, sorry. Shouldn't say that. Yes.

Dr. Joseph Mercola:

Is there a dose of the aspirin that is optimal for blood thinning as opposed to other metabolics?

Georgi Dinkov:

Yes. Lower doses, paradoxically, of aspirin basically prolong – They increase the prothrombin time, which means they thin the blood and make it more prone to bleeding. A lot of research has been published trying to demonize aspirin and how it increases your bleeding risks and whatnot, and a lot of doctors are not recommending [it] because of that. But I have multiple studies showing that aspirin prevents you from dying from severe bleeding events in the gastrointestinal tract and the brain, which is precisely the reason more doctors say, "Don't take aspirin because it can kill you from a bleeding stroke or a bleeding in the gastrointestinal tract."

In a higher dose, which means a regular tablet, 325 milligrams or higher, aspirin actually decreases those risks. So, you can think of it as a bleeding modulator. At a lower dose it will thin the blood and maybe prevent a heart attack, but at a higher dose, basically, it still prevents the heart attack, but not so much through the coagulation mechanism, but because, probably, of the prostaglandin inhibition and reduction of inflammation in general, which is well known to be the primary cause of these plaques that are causing the heart attacks to start with.

Dr. Joseph Mercola:

Ah. So, it blocks it at a more fundamental level.

Georgi Dinkov:

Exactly. It prevents them from happening versus you already have the plaque, right? You are concerned the plaque will rupture and plug a vessel, right? Then the small amount of aspirin, the baby tablet is probably the best way. But to prevent those plaques from forming, I think the higher doses of aspirin, which is a regular tablet, and by the way, not every day. For cancer prevention, the studies show that if you take aspirin three times a month is enough.

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

Yeah. Three times, and one tablet, 325 milligrams, two, three times a month, I think, was enough.

Dr. Joseph Mercola:

But I don't think that's optimal. I think-

Georgi Dinkov:

Yeah, it's not optimal. No.

Dr. Joseph Mercola:

No. But it will provide some benefits. So that's [a] relief in case for those who tend to forget your supplements. But for someone who's really interested and can really be compliant with any regimen, what do you think, for someone who's healthy, the dose of aspirin should be?

Georgi Dinkov:

I will take a regular tablet of aspirin daily, and if you skip a few days because you forgot, which comes down to, let's say, five days out of the week, it's probably enough.

Dr. Joseph Mercola:

Just one a day. Okay.

Georgi Dinkov:

Yeah. One a day. Exactly.

Dr. Joseph Mercola:

And potentially divide that up. I like the powdered aspirin that comes with a little scooper and each scooper is 100 milligrams. So, you could take that with each meal.

Georgi Dinkov:

You could take it with each meal or make yourself a nice solution of, let's say, orange juice and aspirin dissolved in it, maybe heat it up a little bit. It'll be a little tangy, even more, and drink it throughout the day.

Dr. Joseph Mercola:

Do you think there's any benefit to taking it at night before you go to bed, because you said it inhibits lipolysis, and I'm wondering [if] you're fasting essentially at night. Hopefully, you're sleeping for eight hours, so it's an eight-hour fast and the tendency is for your glycogen stores to become depleted. But my guess is if you're healthy, you've got enough glycogen in your liver where that's not going to be an issue.

Georgi Dinkov:

But if 70% to 80% have liver disease, their glycogen level stores are terrible. So aspirin is great for improving sleep.

Dr. Joseph Mercola:

Would that be better – So, here's my proposal for most people, is to take maybe 100 milligrams of baby aspirin with each meal that has a lot of protein. And then before you go to bed, take one aspirin [to] inhibit the lipolysis.

Georgi Dinkov:

So basically, if you're taking it throughout the day, you probably don't need to take it at night because aspirin metabolizes into salicylic acid.

Dr. Joseph Mercola:

Oh, and it's a three-hour half-life.

Georgi Dinkov:

Salicylic acid's half-life is like a three – some odd hours of half-life.

Dr. Joseph Mercola:

Oh, yeah. Okay. So that's-

Georgi Dinkov:

So you'll be okay.

Dr. Joseph Mercola:

So, it doesn't matter. Okay. See, this is a refinement. So, you also posted a study on your blog about – It was from the New England Journal in January of this year where I think that the dosage was a baby aspirin twice a day was equivalent to subcutaneous heparin for clot prevention.

Georgi Dinkov:

Yes.

Dr. Joseph Mercola:

In a surgical-

Georgi Dinkov:

They call it non-inferior. I love the start.

Dr. Joseph Mercola:

Yeah, yeah. And you know what that is? Because I went to medical school. You know what that is? That's a double negative.

Georgi Dinkov:

Yeah, exactly. So, the confusion is like, "What do you mean by non-inferior?"

Dr. Joseph Mercola:

That's totally fucking confusing, yeah.

Georgi Dinkov:

Yeah, but people remember the inferior, so they say, "Oh, aspirin and inferior in the same sentence? I'm going to go heparin." Right?

Dr. Joseph Mercola:

Yeah. They love doing – They think that makes them look smarter, you know?

Georgi Dinkov:

Yeah.

Dr. Joseph Mercola:

It's classic-

Georgi Dinkov:

But I think it's a thinly veiled attack towards aspirin by trying to put into people's minds the idea that, "Look, aspirin is for grandmas. It's an obsolete drug. We have the modern nice stuff now," which, by the way, did I send you this article that the Xarelto trials were fully fraudulent? Not wrong. Fraudulent.

Dr. Joseph Mercola:

Which trials?

Georgi Dinkov:

Xarelto, which is the flaxseed blood thinner that they use now for afib (atrial fibrillation) and for preventing strokes. It's X-A-R-

Dr. Joseph Mercola:

What's the brand name of it? Is that-

Georgi Dinkov:

Xarelto. Rivaroxaban is the name.

Dr. Joseph Mercola:

Oh, geez. I've never heard of it.

Georgi Dinkov:

Xarelto is that-

Dr. Joseph Mercola:

I've never heard of it. I don't prescribe these drugs. I don't know.

Georgi Dinkov:

So, they moved away from heparin into the Xarelto type of drugs, but then there was an article in Slate, slate.com, which is a, really, an investigative journalism magazine. It used to be much better than this now, but anyways-

Dr. Joseph Mercola:

Oh, yeah, yeah.

Georgi Dinkov:

So, they said [the] FDA – most of the clinical trials were done in Mexico and other places. The FDA knew that the trials were fraudulent. They weren't simply substandard. It was based on

made up data. It still approved the drug. And when the journalist started questioning the FDA, "Why did you approve it?" The FDA said, "If you don't stop questioning us, we're going to throw [you] in jail." I don't know how that works. But anyways, aspirin is non-inferior to any of these blood drugs.

Dr. Joseph Mercola:

Not inferior.

Georgi Dinkov:

I don't want to say superior because the FDA will come up to me and say, "Who are you to make health claims?"

Dr. Joseph Mercola:

Yes. So, it's not irrational if your doctor – because this is a common, common scenario, as I'm sure you're aware of, people who have a stroke are put on prophylaxis or have a stent for a coronary bypass, or they're going to surgery like the study did, that they're going to be put on this DVT (deep venous thrombosis) prophylaxis. And they usually use heparin or these other – Eloqua, I think is the other one that's-

Georgi Dinkov:

Eliquis.

Dr. Joseph Mercola:

Eliquis, yeah, Eliquis. So, which seems to be the more common one now. And then, Plavix?

Georgi Dinkov:

Yeah. Plavix.

Dr. Joseph Mercola:

Plavix, yeah. Which is interesting. There's a woman who is an MD-PhD out of Stanford, Barbara Starfield. And I wrote an article based on her studies she published in JAM in July 2000, 23 years ago now, that I abstracted from it the meme that doctors are the third leading cause of death.

And that was actually my meme that I created. And the irony, and the reason I mentioned here, is that she died 11 years later in 2011 from taking Plavix, which is a –

Georgi Dinkov:

From bleeding? From a bleeding event?

Dr. Joseph Mercola:

Yeah, yeah. It's from Plavix. So, she died from the very article that she helped promote, that doctors were the leading cause of death. So anyway, the point here is that there's a lot of options on there, but Plavix being one of them. So, you think that it's reasonable and relatively safe to consider a baby aspirin once or twice a day?

Georgi Dinkov:

I don't know of a single person who died of taking aspirin. I mean, I've looked at the case studies-

Dr. Joseph Mercola:

Well, but I mean-

Georgi Dinkov:

I've scoured PubMed-

Dr. Joseph Mercola:

But it's not the "die of the aspirin." The concern is, was that going to be enough of a prophylaxis to prevent dying from the stroke or a clot somewhere?

Georgi Dinkov:

Absolutely. Yeah, basically. I mean, to this day, I don't know of anything that provides the same benefit as baby aspirin for primary prophylaxis while having equal or fewer side effects. Nothing comes close to aspirin, except possibly vitamin E, which is very similar in its effects.

Dr. Joseph Mercola:

So, another supplement that should be taken pretty much by everyone every day is vitamin E. We talked about this on our first podcast, actually, our first interview, is that there are some specifics you got to be careful of. The dose isn't really high. You want to get the right stereoisomers, which is the dextro, not the levo.

So, you don't want [inaudible 01:29:10] version. And you want primarily alpha, because there's alpha, beta, gamma [and] delta. You want primarily alpha. So, you want all isomers. And you want that. And you want some tocotrienols, but not as much, mostly d-alpha-tocopherol, and small doses, too. I mean, not 400 units. We're looking at 100 and 150 [units], somewhere in that range.

And then, I remember that you did a lot of work on this, I think you actually came up with a vitamin E supplement because based on Ray Peat's work – because Ray Peat was doing his work on – He was a big proponent of vitamin E, but it was a very specific vitamin E, one that was

extracted from wheat germ, which doesn't exist anymore. And wheat germ has some problems. I think it's really-

Georgi Dinkov:

62% linoleic acid.

Dr. Joseph Mercola:

Yeah, I was going to say it's really high in linoleic acid. So, you don't want to take wheat germ oil. That's for darn sure. But in small dose – That's a confusion, too, because our vitamin E supplement is from sunflower, and sunflower is really high in linoleic acid too. But people say, "Oh, you can't – That linoleic acid is wow." It might have a few milligrams. It doesn't have 20 grams. A few milligrams is not going to hurt you. It's probably less than 1% of linoleic acid you've taken a day. So anyway, that's a diversion. But a lot of people have questions about some of the supplements and if they have a seed oil in there.

You've got to get the vitamin E from somewhere. It's typically from a seed oil, that's where they're at, because you don't want synthetic, you want it derived naturally. So, are there any other pearls on vitamin E, generalizations that you can make on how people need to consider taking that as a supplement? Because I think almost everyone benefits, largely because it's going to limit the oxidation of the PUFAs to the dangerous metabolites like malondialdehyde [and] 4-hydroxynonenal, the things that really cause the damage. So, it's not that the omega-6 linoleic acid is dangerous by itself. It's the metabolic byproducts, the degradation products that are so toxic. That's what kills you.

Georgi Dinkov:

And linoleic acid, by the way, even its non-peroxidized form, acts very similarly to estrogen because of its unsaturation.

Dr. Joseph Mercola:

Oh, I did not know. Leave it to you to leave another pearl. I did not know that.

Georgi Dinkov:

It increases the fluidity of the bilayer lipid membrane. And all six cells, especially cancer cells, are known to have drastically increased membrane fluidity. So, very easy to permeate in and out. So, that's not a sign of-

Dr. Joseph Mercola:

And then, we talked about earlier, cardiolipin. It's one of those fatty acids in the tail that's going to increase the likelihood of susceptibility. And my guess is, once it's in the mitochondria, it's going to contribute to that reverse electron flow –

Georgi Dinkov:

Precisely.

Dr. Joseph Mercola:

-which is going to shut down metabolism and increase reductive stress.

Georgi Dinkov:

Precisely. Yes. So, if you damage the cardiolipin, because it's got a lot of PUFA, it gets peroxidized. Cardiolipin cannot bind with the complex IV. So, that complex is now dysfunctional, even if all the others are working. Then you start getting a buildup of electrons. And eventually, the mechanism says, "Okay, they can flow in only one direction now, backwards." Right? Because forwards is blocked.

Dr. Joseph Mercola:

All right. So, you revised yet another concept they had about linoleic acid, that it is toxic in and of itself. It's not just the metabolites which are – What do you say is worse? Just the linoleic acid by itself or the metabolites?

Georgi Dinkov:

The metabolites are worse, definitely, because they're directly mutagenic and carcinogenic.

Dr. Joseph Mercola:

Okay.

Georgi Dinkov:

However, linoleic acid itself is dangerous in a very pernicious way. By itself, it doesn't directly immediately cause problems. Even though it can get metabolized into the arachidonic acid and the prostaglandins and leukotrienes, this process takes a little time. But linoleic acid by itself, because of its structure and the multiple double bonds, synergizes greatly with estrogen. So, it can actually cause, in animal models, cancer by injecting a physiological dose of estrogen that normally would be even healthy.

However, if they're combined with a sufficient amount of unsaturated fats – I think they tried linoleic acid mostly, but other saturated fats did the same thing. Linolenic was also not as pro-carcinogenic as linoleic, but still similar. And the EPA (eicosapentaenoic acid) and the DHEA-

Dr. Joseph Mercola:

Is that the omega-3, 18 carbon-

Georgi Dinkov:

Yeah, omega-3 were actually the most carcinogenic, but they had the “side benefit” that they peroxidized so quickly they couldn't exert their cancer potential quickly enough. But their peroxidative byproducts we're also carcinogenic, so we're still getting the benefit. So yeah. So, ideally-

Dr. Joseph Mercola:

Vitamin E will protect that.

Georgi Dinkov:

Exactly. Vitamin E will protect that. And also, vitamin E has been shown to also have an antagonistic relationship with estrogen. One of the first – the reason – The name of vitamin E, one of the common names, is tocopherol, which means pro-fertility, right? In Greek. So, they knew back in the early 20th century, even before that, that giving people – at the time, it was wheat germ oil, but it's very rich in vitamin E, that it can actually improve fertility in both males and females. Subsequently, it was found that vitamin E is the main factor for that. And it's capable of binding and blocking and acting as an antagonist at the estrogen receptor alpha. And it's also a moderately strong aromatase inhibitor, all of the tocopherol isomers, not so much the tocotrienols.

So, basically, by taking vitamin E, whatever estrogenic effects are out there, even from non-peroxidized PUFA, or if you're producing too much estrogen for whatever reason, if you have endocrine disruptors, which are capable of binding and activating the estrogen receptor just like estrogen does, tocopherol will block some of that as well.

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

It's really a versatile molecule that has genomic steroid-like effects, but it mimics progesterone, which is also the main anti-estrogen in the body for females, testosterone and dihydrotestosterone being the main anti-estrogens in the body of males. Tocopherol will have most of these effects. And it's probably much fewer side effects than taking steroids. And the daily needs have been shown to correlate perfectly with your intake and also storage of polyunsaturated fats.

So, the daily need, RDA (recommended dietary allowance), real RDA, of vitamin E is about 2 milligrams of vitamin E for every gram of PUFA consumed-

Dr. Joseph Mercola:

Wow.

Georgi Dinkov:

-which means, if you're taking 50 grams of PUFA, you need 100 milligrams of vitamin E to combat basically its peroxidative potential and also estrogenic potential as well. How much? So, most people are used to measuring the vitamin E in units. And basically, if you take the vitamin E dosage in milligrams and multiply by 1.5, they're going to get the dosage in international units (IUs).

Dr. Joseph Mercola:

So, I only have 5 or 6 grams of PUFA a day. So, I would only need 10 grams?

Georgi Dinkov:

10? What is it, 5 or 6 grams?

Dr. Joseph Mercola:

10 milligrams.

Georgi Dinkov:

Yeah, less than 15 milligrams of vitamin E daily, which is like 20, 30 IUs a day.

Dr. Joseph Mercola:

Is there any danger, taking a higher dose than you need?

Georgi Dinkov:

No. Well, it acts like aspirin. It can thin your blood to the point where it basically could become a problem. But I've never seen a person that – There's these famous researchers in Canada known as the Shute brothers, and they were treating people with vitamin E, massive dose, I think like 7 grams or 8 grams of mixed tocopherols daily. And they were treating them from diabetes, heart disease, various other different conditions.

And I, based on their publications, some of which are peer-reviewed, not all, I don't know of a single case of a person who had a serious negative experience with vitamin E, but it does thin the blood, so it may prolong bleeding time.

Dr. Joseph Mercola:

Okay, perfect. Wow, that's really, really helpful.

Georgi Dinkov:

And since estrogen clots the blood, I think we can actually use that little bit of extra vitamin E.

Dr. Joseph Mercola:

Yeah. The other thing too is that you – Vitamin E is a fat-soluble vitamin, which means it's stored in fat tissue, so you don't have to take it every day, right?

Georgi Dinkov:

Yep. And that's the good thing because most of the PUFA is stored. Right? When you eat a meal that has a lot of fats in it, they're usually a mix of monounsaturated, polyunsaturated, saturated [fats]. Ideally, it should be mostly saturated, but let's say eating a mixed meal. The saturated fats, because they're more easily passed through the process of beta-oxidation, they're preferentially oxidized.

The monounsaturated and especially the polyunsaturated are predominantly stored in the fatty tissue, which means that most of your fat stores are PUFA. That's exactly where you want your vitamin E to go, to protect that PUFA from getting peroxidized.

Dr. Joseph Mercola:

Is that where it does go when it's absorbed? It goes into the adipose cell and next to the PUFAs?

Georgi Dinkov:

Yes. I mean, it goes precisely into the – It actually can build up in the lipid bilayer of the cell, which is basically going to be made mostly of fats. So, that's where it needs to be in order to prevent the reactive oxygen species from damaging it. Yeah.

Dr. Joseph Mercola:

Wow. All right. So, that's good because you won't have the dangerous metabolic byproducts, but you still don't want PUFA, primarily because of the reductive stress.

Georgi Dinkov:

The reductive stress, and also the PUFA itself being estrogenic and antimetabolic in general, and pro-inflammatory.

Dr. Joseph Mercola:

Do you think the reductive stress from the PUFA is the primary reason for obesity?

Georgi Dinkov:

Yes. They're the primary anti-metabolic factor in our diet that changed dramatically over the last hundred years.

Dr. Joseph Mercola:

That's what I thought. Yeah. Okay.

Georgi Dinkov:

Plus, the endocrine disruptors, which act remarkably similar.

Dr. Joseph Mercola:

Yeah, it doesn't help. It doesn't help.

Georgi Dinkov:

So, let's go this way. PUFA is an endocrine disruptor of natural origin. We have other ones.

Dr. Joseph Mercola:

Beautiful. Beautiful. Absolutely beautiful. So, would you include glycine as an essential supplement to a nutrient like vitamin E and the niacinamide and aspirin?

Georgi Dinkov:

Glycine, together with methylene blue, are the only two ingredients that I've seen showing full reversal of the aging phenotype in human cells, but it was in vitro studies.

Dr. Joseph Mercola:

What type of dose – Because clinically, it seems like you need grams. I'm talking five-

Georgi Dinkov:

Millimoles, yes.

Dr. Joseph Mercola:

10 grams, 15 grams per day.

Georgi Dinkov:

The study that I showed in vitro, I think, showed 3 millimoles per liter concentration, which in humans is achievable by about 10 to 12 grams of glycine daily, which means 2 tablespoons of gelatin will probably do it.

Dr. Joseph Mercola:

Okay, perfect. Yeah, because I mean, gelatin's like one-third glycine, I think, because the rest is probably a hydroxyproline. So, that's another good point. Thank you. A good segue. I didn't have that on my list, but I think this is another one of the essential supplements people should be on that we're pretty much all in agreement. Niacinamide, no question. Aspirin, at the dose we just discussed.

Georgi Dinkov:

Methylene blue.

Dr. Joseph Mercola:

And methylene blue, with the cautions if they're taking SSRIs, methylene blue for sure. I think it – It's not that one's better than the other. You need them both. Methylene blue and niacinamide is a one-two punch, unless you're taking SSRI, no methylene blue. Or get off the SSRIs and you can with the strategies that we talked [about] because it's – Well, when you're coming back, we're probably going to talk about serotonin and cancers and stuff. But serotonin, it's easy to control it once you implement these strategies. Maybe not easy, but the strategies that are there, and they work, they're effective. And you don't need drugs to modulate your serotonin, although you have some really interesting-

I have not gotten into the supplements you sell on your site now, but it's like it's a wizard's apothecary. You've got these – that don't exist anywhere else in the world, that you create in your lab, that you need a drop or two of these things. And it's just like, oh my gosh, I just got the five – talking about serotonin, it's the five – ten-

Georgi Dinkov:

10-methoxyharmalan.

Dr. Joseph Mercola:

10-methoxyharmalan, which is essentially an analog of LSD (lysergic acid diethylamide) that, which worked on serotonin. Right?

Georgi Dinkov:

It's a metabolite of melatonin. We produce it internally.

Dr. Joseph Mercola:

Really?

Georgi Dinkov:

Yeah. It's a direct metabolite of melatonin.

Dr. Joseph Mercola:

I did not know that, but it seems to be fairly effective. It's like one to three drops a day for someone who's on an SSRI and they get off the SSRIs.

Georgi Dinkov:

So, if you look at the molecule, serotonin, melatonin and 10-methoxyharmalan are almost identical. Basically, the melatonin molecule with an extra molecule of hydrogen becomes 10-methoxyharmalan. And because they're so structurally similar, they can bind to each other's receptors, serotonin having seven receptors or more that we know of. melatonin, I think, having three — M1, M2, M3.

Oh, another reason I forgot to mention, the reason I'm a little bit wary of taking more melatonin is that some of the newer, very successful antidepressant drugs that are still in animal research are melatonin receptor antagonists.

Dr. Joseph Mercola:

No.

Georgi Dinkov:

So, there's something about melatonin at higher dose, which I think is expected, it puts you to sleep, but a really deep sleep. And the way it does that, it lowers the oxidative phosphorylation in the brain, which can be helpful at night when you're not active. You want to be asleep. You want to recover. You want to be careful, and you want to spare as many resources as possible. It's not good during the day.

And people that are basically depressed, they're known to be sleepy. They're known to be tired all the time and they're fatigued and whatnot. A lot of it is from serotonin. But if you have high serotonin, this means that, by extension probably, they're going to have an elevated melatonin as well. So the-

Dr. Joseph Mercola:

It's antimetabolic.

Georgi Dinkov:

Yeah, antimetabolic. Exactly. And they found out these drugs also, which we kind of expected, they relieve depression, but they also increased the metabolic rate, which to us is one and the same. Right?

Dr. Joseph Mercola:

Yeah.

Georgi Dinkov:

So, depression is a sign of low ATP production. A study with insects – I know a lot of people say, "Well, insects are not humans." But it was replicated in rodents, and various other animal models demonstrated that basically there's a spectrum, continuous spectrum, between very good health and really violent homicidal aggression at the other end of the spectrum. And it's all

controlled by ATP levels. A 20% drop of ATP levels in the brain will make you depressed. Another 20% will make you almost comatose. And then, another 20% will get you to a really violent aggressive phenotype which, by the way, the SSRI drugs have been shown to cause.

And what do they do in the brain? They lower the levels of ATP. So yeah, there's some revelations that are going to come out soon about SSRIs. I think people know about them. But I mean, in the legal system. People are going to start suing. Some of the mass shooters are – The victims of the mass shootings have banded up together and said "Every single mass shooting in the United States has been on a psychotropic drug. 90% of those cases have been one or more SSRI drugs. It cannot be a coincidence."

Dr. Joseph Mercola:

Yeah. Then, I think you have mentioned several times. I think it's still in phase 3 clinical trials. Pfizer's coming out with a new drug that's a serotonin antagonist?

Georgi Dinkov:

Yes. Terguride, for cardiac failure, which they – up until even now, medicine says it's irreversible. It's a progressive condition, which eventually kills you unless you get a heart transplant, or pulmonary fibrosis, which is also terminal and you cannot usually get a transplant for that. So, they're saying that terguride, by blocking the serotonin receptor 2B, is able to not stop [but] reverse the fibrosis.

Dr. Joseph Mercola:

Interesting. Wow. We're going to dive deep into that later. But I've got a question, just a curiosity. I'm sure you know the answer.

Georgi Dinkov:

Sure.

Dr. Joseph Mercola:

With a popular biohacking intervention that I'm not too fond of, I tried it initially, but it's very painful, it's something called cold thermogenesis where you jump into – An ice bath would be sort of the extreme, but certainly you can use lower temperatures, 50 degrees F, 60 degrees F even. Obviously, if you're in an ice bath for too long, you could die.

But the reason that many people encourage it or recommend it is because of an increase in dopamine. And it just seems to me not a wise strategy, but maybe I'm confused. And I'm just really curious as to what your take is from a metabolic perspective and if there's any harm or damage?

Georgi Dinkov:

Definitely harm. And your intuition is always. almost always on the right track. It evolved for 4 billion years. I think, if we listen more to our intuition, of course backed up by data, it's better than simply following some abstract reasoning. So, the reason cold – So, first of all, cold thermogenesis, it raises your thermo – not the baseline [but] the peripheral temperature, by increasing the release [inaudible 01:45:29] of adrenaline. Now, of course, it's going to raise your dopamine first because dopamine is the precursor to adrenaline.

Dr. Joseph Mercola:

Oh, no.

Georgi Dinkov:

But it seems like a rather torturous way to basically – First of all, you're going to raise dopamine, but not much will stay as dopamine because it will quickly get converted to adrenaline. And that's what converts the white fat into the brown fat. And the brown fat is more metabolically active. And the proponents of cold thermogenesis say, "Hey, These fat cells are going to burn more calories. They're going to consume more of their own fat. So, it's great."

Dr. Joseph Mercola:

Yeah.

Georgi Dinkov:

The only-

Dr. Joseph Mercola:

That's what they-

Georgi Dinkov:

That's what they do.

Dr. Joseph Mercola:

Yeah.

Georgi Dinkov:

But guess what other condition has the exact same process? Metastatic cachectic cancer. Patients in cachexia have almost no white fat left. They're almost entirely brown. And first of all, they lost a lot of it. They look gone. Right? But the exact same process, driven by adrenaline, is implicated in the cachexia of cancer, that is in [the] exact same process in cold thermogenesis.

So, it's a stressful response. Why on earth would you want to cause yourself more pain? Now, no pain nor gain, I can kind of agree with it, but it does not mean that more pain is going to give you more gain.

Dr. Joseph Mercola:

So, you don't think it's really good for anyone, with that answer. It might sound good.

Georgi Dinkov:

I would say it would be better if you move to actually a very warm environment high up in the mountains.

Dr. Joseph Mercola:

It's why I live in Florida.

Georgi Dinkov:

Exactly. Florida. And it’s going to be burning more calories without stressing yourself to the same level. Now, extreme heat is also a stressor, but not nearly as dangerous as extreme cold.

Dr. Joseph Mercola:

It's not extreme heat. And then, they've got these AVAs, these arterial vascular anastomoses, in the soles of your feet, and the palms of your hand, on your forehead, so that if you're walking on the beach and your feet are in the ocean, you're dissipating all the heat. So-

Georgi Dinkov:

Exactly.

Dr. Joseph Mercola:

There's no issue with stress.

Georgi Dinkov:

Yep.

Dr. Joseph Mercola:

Zero.

Georgi Dinkov:

It's like elephants. They have big ears for only one reason. That's their dissipating mechanism for heat.

Dr. Joseph Mercola:

Yeah, yeah, for sure. So, yeah. And I live in Florida, but I live in, well, North Central Florida, so it gets too cold here in the winter. You can't go in the water. So, I go south. I go to Central America or Mexico, where we can go in the water.

Georgi Dinkov:

Really? Florida gets so cold that you cannot go into the ocean in the winter?

Dr. Joseph Mercola:

Well, you could if you want to do cold thermogenesis. Yeah. The water goes into-

Georgi Dinkov:

No, no.

Dr. Joseph Mercola:

-low 60, high 50 [degrees F] for sure.

Georgi Dinkov:

Oh wow.

Dr. Joseph Mercola:

Now, South Florida is probably not as bad, but it is up here, so I just don't go in. So, it's like six months out of the year. I mean, it's like in the mid-80s now, which is good. But oh man, that is good stuff. I didn't want to follow up on it.

Georgi Dinkov:

Cortisol? Should we talk about cortisol and it's-

Dr. Joseph Mercola:

No, no, just finish up on cold thermogenesis, so that – The conclusion I had reached prior to your comment on this, which is different now, but was that it was okay for people if you were young, because they could tolerate-

Georgi Dinkov:

Oh, sure. They could tolerate it, of course.

Dr. Joseph Mercola:

They have much more resiliency and reserve than the average person. So, the intuition was spot on. But it really isn't good for anyone, which is interesting because there's so many people – I mean, there's a lot of leaders in the biohacking space. And almost every single one of them are strong advocates of cold thermogenesis, which-

Georgi Dinkov:

One of the established methods for aging animals prematurely is to expose them chronically to extreme cold.

Dr. Joseph Mercola:

And the other thing they don't get is that cortisol elevation is the primary reason. That's where every strategy should be directed, at lowering cortisol. So, what are your thoughts on meditation as an effective way to address lowering cortisol? Because there's a lot of people [who] recommend that. I don't-

Georgi Dinkov:

The expert meditators have been shown – I've seen studies with the monks in Tibet and whatnot. They're really good at controlling their physiological response. But that takes decades of practice. I think, for a lot of people, it's become a fad. And I posted a study showing that, if you are an inexperienced meditator, and basically, you're doing this for several years, and if you have some mental problems that are not addressed, meditation can make them worse. And in fact, apparently, it was well-known among the meditation community. They call this coming to Christ moment, or kind of like you're facing your problems without any bias and somehow working through them.

However, several studies I posted on a blog show that, in some people, meditation actually could generate mental health problems, de novo. They got mentally ill by meditating, especially the more extreme forms of meditation that – the practice like extreme fasting or under extreme temperatures or in extreme environments. But I think meditation in their –

Just like aspirin or methylene blue, if you know what you're doing, and there are not many people that do, or [you're] at least paying attention to what you're doing, it can be helpful, but it's not the cure-all that is being presented, and I'm kind of concerned it's becoming another fad. Everybody that I know around me says, "Oh, you under stress? Meditate."

Well, I mean, if I'm working a toxic job or I'm surrounded by toxic people, meditation is not going to address that. It's just another Band-Aid, right?

Dr. Joseph Mercola:

Yeah.

Georgi Dinkov:

You have to always work for the ultimate cause and try to resolve it. Granted, sometimes it's not easy to resolve, so you kind of have to Band-Aid sometimes. There are things that are – Let's face it, there are things that cannot be directly resolved. But for most things, yeah, go ahead.

Dr. Joseph Mercola:

It would seem to me, you can modulate a lot of the stressors if you focus on increasing your metabolic rate.

Georgi Dinkov:

Precisely, it'll be much more direct the physiological way.

Dr. Joseph Mercola:

Because once your cortisol level goes down, doesn't the stress decrease?

Georgi Dinkov:

Of course, by definition. I mean, the primary feeling of agitation and nervousness and basically the fight or flight response, that's driven by cortisol, that is its primary role, to keep you alive. Whether it's somebody chasing you like a saber tooth tiger a million years ago, or you're in an office with some toxic people and somebody's yelling at you for no reason, [it's] the exact same situation.

Basically, the body perceives this as a threat and says, "Okay, since you're not eating right now, I need the energetic resources to handle this threatening situation." Where are these calories going to come from? From your body.

Dr. Joseph Mercola:

Well, I've exhausted my questions for now, but I'm definitely going to have you back. We have to have a really long-term, long discussion on cancer because you – And I know you've done some original research in animal studies and you've got some really novel approaches that absolutely conflict with my previous understandings and people I've interviewed in the past who are experts. So, I'm really looking forward to that discussion for sure.

But I can't thank you enough for your commitment, your dedication, your knowledge, your willingness to share all the time, and provide such a wealth of knowledge [and] information that's going to radically change people's lives.

Georgi Dinkov:

Thank you.

Dr. Joseph Mercola:

So, you're BA, you're beyond awesome. You took a few months off this year because, I don't know, you were busy or something, but until May-

Georgi Dinkov:

I'm a government contractor, I think I told you.

Dr. Joseph Mercola:

Yeah, yeah.

Georgi Dinkov:

When there's a project, I get sent to the client side of the government agency and I'm basically all day there. When I come back, I have family to deal with, so it's not exactly a – But these articles accumulate. So, I read on a daily basis, but I just can't post on a daily basis.

Dr. Joseph Mercola:

It's a lovely, lovely resource. I'm so glad you compiled it. So, all right, so that's one place for you. And then, we'll keep-

Georgi Dinkov:

That's pretty much it. I'm on Twitter as well.

Dr. Joseph Mercola:

Twitter. Is there anything on Twitter aside from your blog post?

Georgi Dinkov:

I mean, sometimes I interact with people, they send me some interesting studies and I comment on those too. So, it's like a-

Dr. Joseph Mercola:

What's your Twitter handle?

Georgi Dinkov:

Same as the blog, Haidut, H-A-I-D-U-T. So twitter.com/haidut.

Dr. Joseph Mercola:

Okay, perfect. All right. Well, thanks so much, Georgi.

Georgi Dinkov:

Appreciate it. Always a pleasure. Great honor to be on your podcast.