Transcript of “Alan Cash: Upgraded Aging & Living Longer with Oxaloacetate – #183”

Bulletproof Radio podcast #183
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Dave: Hey, I'm Dave Asprey with Bulletproof Radio. Today's cool fact of the day is that goldfish which are reported to only have a 3-second memory actually can remember things up to five months which is why you might want to take care of your own memory. Today's guest is Alan Cash. Alan's never been on Bulletproof Radio. He's the CEO of Terra Biological and the clinical trial supervisor and medical researcher for Upgraded Aging, which is why I was talking about goldfish memory before because if you can do upgraded aging on your memory, you're going to like what happens as you get older, protecting those neurons is something that I do every single day.

You, if you were at least the Bulletproof conference, would have already heard Alan Cash talking about Oxaloacetic, the active ingredient in Upgrade Aging. At the Bulletproof conference, I asked the Bulletproof team to interview Alan Cash while I was on stage presenting so I could get this content out to you. Alan is an amazing, amazing researcher and I'm really excited with how podcast turned out. Enjoy the interview. I came up with the questions myself. Alan and I have met and talked many, many times. I just couldn't be there in person to get this info out to you on video. This is an amazing podcast.

Speaker: Alan, thank you so much for being here with us today. Can you tell us what you're speaking about at the 2014 Bulletproof Bio Hacking conference?

Alan Cash: Absolutely. Thanks for inviting me. I'm going over some recent research on Oxaloacetic which is part of the Krebs cycle. It's up here in the upper left hand corner. This way goes to citrate, this way goes to malate. When we give Oxaloacetic to animals, we wanted to see what happened to their brain. We saw some really exciting things. One, we saw an increase in mitochondrial density. Those are the little power plants that make your cells work. It gives you energy. By increasing the amount of that mitochondrial mass, we're seeing an improvement in brain functioning.

Second thing we saw is that glucose uptake is improved. Here's a way, as we age, we lose the ability to bring glucose into our cells. It just starts circulating in our bloodstream and the levels go up and up and up. This way, it's being brought into the cells where it can be used by those little mitochondrial power plants. That's exciting too. Then we saw a decrease in brain inflammation which is always a good thing because that's another thing the aging brain tends to do, is be saddled with inflammation problems.

The last thing we saw which is just incredibly exciting is an increase in the number of neurons that are produced by the hippocampus. Now, it used to be thought as we age,
the brain was static. If you lost those brain cells in college, you'll never get them back again. I know you know what I’m talking about. What really is happening is there's a place in the brain called the hippocampus which is constantly producing new cells to replace the cells in our brain. But as we age, that ability declines and declines and declines and declines.

here is a method that we found that's able to turn the body's natural process of producing those cells back on and produce them in a much, much higher rate. We’re replacing those cells that were damaged in the brain. Very exciting stuff.

Speaker: I knew we're going to dive more into that in a minute. Can we start with you just telling us what Terra Biological is?

Alan Cash: Terra Biological started off as a research company. I was doing post graduate work at University of California down in San Diego. My partner was working at UCLA. We looked at aging, specifically why does calorie restriction increase lifespan? I mean, it does this throughout the animal kingdom from the single celled animal all the way up to primates. We have 30-year tests in monkeys now, and possibly in humans. We see a lot of good things in humans with people who calorie restrict. Why does this work though?

It was discovered in the 1930's, in 80 years, you think we'd be able to figure out what's going on. Some of that work in the molecular basis of calorie restriction started mid-1990's and continued on, well, through today. One of the things we found is an increase in the NAD to NADH ratio seems to be the start of the whole process. That then activates this chain of molecules that turn on genes and turn off genes that improve our overall health and condition. Very exciting stuff.

We started off as a research into this back in 2004. It started getting more and more exciting as we gave this one compound, Oxaloacetate, which again, part of the Krebs cycle. It's a human metabolite. It's in every cell of your body. When we gave these to animals in excess to what they normally have in their diet, they started to live longer, by a lot, 25 to 50% longer. We started in very simple animals like worms and then we went to more complex animals, flies and then mice. We kept seeing this increase in lifespan just as we did in calorie restriction.

We thought, "Well, I wonder if anyone's ever given this to human beings." We started looking through the literature, scientific literature. What we found is a clinical trial that was done back in the 1960's in Japan. They were looking at Oxaloacetic for diabetics because a mountain plant traditional Japanese and Chinese herb, [Unomius Salatis Sieb 06:37] was the Latin name, was found to help with diabetics. They looked at all the components of this plant and that Oxaloacetate was the thing of interest. They did a
clinical trial with it. They took 25 people. They all had reductions in their fasting glucose levels without side effects.

I thought, "This is pretty exciting stuff." I mean here, a human metabolite, a natural compound, we're seeing reductions in fasting glucose levels in diabetics on average of 25% which is huge, where's the follow on work? I'm searching through the literature and searching through the literature, I couldn't find any follow on work. I flew to Japan and I interviewed the department where this all took place. The conversation went something like this. I said, "Are you familiar with this paper?" "Yes. We wrote that paper." I said, "Oh great," I said, "Were there any issues with the Oxaloacetate or the test?" "No, it worked quite well."

I said, "Where's the follow on work?" They said, "No follow on work." I said, "Wait, you've got a natural compound, a human compound that reduces fasting glucose levels in diabetics and you're not following up with it? Why not?" They said, "Well, it's a natural compound." I said, "Yes, yes, yes." They said, "No patents." That was the end of the conversation. Although it's not perhaps being able to patent it for diabetic use, for anti-aging, it's certainly very exciting.

Speaker: Well, that brings us to the Bulletproof Upgraded Aging formula. Can you tell us what that is?

Alan Cash: Well, Bulletproof Upgraded Aging is a combination of 100 milligrams of Oxaloacetate and 150 milligrams of vitamin C. We combine the two together because they work a little bit synergistically and they also help to preserve the Oxaloacetate. When we first started working with the Oxaloacetate, it degraded almost daily. We had so much trouble. We had to learn how to synthesize it and stabilize it, thermally stabilize it so that we can have a two-year shelf life so that we could use it as a nutritional supplement which is probably why you don't see it anywhere else in the marketplace.

After we learned how to stabilize it, we found that adding vitamin C to it helped with that stability. That's what it is. It's very simple compound. There aren't any excipients. There aren't any preservatives. It's in a veggie shell of a capsule. We had to actually pay more to take out all that stuff and just have a pure product. I think that's what Bulletproof is all about.

Speaker: What does it taste like?

Alan Cash: It's a cross between an orange and a lemon, excuse me, an orange and a lime. Because it's in the citric acid cycle, it has that characteristic citric taste but it's a little different. I actually liked the taste. I open up some of the capsules and I'll put two or three in a glass of ice water and stir it up and with a little bit of honey and I drink straight.
Speaker: Bio hackers strive to achieve better cognitive function daily. Can you share with us some new research in cognitive functioning and how it can be achieved?

Alan Cash: There was just a paper published in the journal human molecular genetics in July of 2014. I mean, this is hot off the press. Where they took Oxaloacetate and they fed it to mice. They wanted to see what was happening with their brains. The reason they wanted to do this is this was some pre-clinical work. They were looking at perhaps using this compound for Alzheimer's disease. I'm not suggesting that you use this for any disease. It's a nutritional supplement. They looked at giving Oxaloacetate to mice and what they found is an increase in mitochondrial density in the brain, the little power plants that power your brain, that power your thoughts.

They also found the brain was able to uptake glucose at a much higher level. Not only are we building more power plants, we're providing more fuel into the cells to power the brain. Then we saw a decrease in the inflammation in the brain which is always a good thing. The last thing they saw in the paper was an increase in the number of neurons that were produced in the hippocampus. Not just the number but the length of the connecting dendrites, I think that's the word, that connect the neurons. These little fibers are longer to allow them to interact a little bit better. Pretty exciting stuff.

Speaker: You brought up mitochondria. What are mitochondria and how do they feed the brain?

Alan Cash: Mitochondria are, there's debate on what they are. A lot of people feel that they're a foreign organism that were brought into a cell and they got along so good together that they stayed that way. They have their own DNA which is interesting. Not very many genes, I think 13, but they work together with the nucleus. One of the things that the mitochondria do is they provide ATP which is our energy currency, our bitcoin of how to run the cell. It does that through a chemical reaction taking glucose in and breaking it down and producing much more ATP than other processes.

One of the things about mitochondria is they've been tied to many disease states lately. It just seems like every chronic disease that's out there is tied to misfunctioning mitochondria. One of the things we should aim for in any kind of nutritional supplement is keeping your mitochondria healthy.

Speaker: What are the steps to take today to build more mitochondrial mass?

Alan Cash: We've learned a couple of interesting things about how to build more mitochondrial mass. One is calorie restriction, eat less, a lot less, like 25% all your life. Put down that spoon of ice cream and a lot of other things. It's kind of funny, I tried calorie restriction for 30 days because I study it. I know you'll find this amazing but my wife suggested that I was irritable. I know, it's a rumor. But it's hard to calorie restrict that well. I mean,
there are people who do it and my hat’s off to them. I think they're incredible but food is such part of our life and you want to be able to enjoy that part but you also want to be able to increase your mitochondrial mass. How do we do that?

Well, one of the ways is through Oxaloacetate supplementation. Another way you can do it is through chronic exercise, run several marathons every week. But that also takes a toll on your body too. we’re thinking that the Oxaloacetate might be your have your cake and eat it too supplement.

Speaker: How is aging a major threat to cognitive functioning?

Alan Cash: How is aging a major threat to cognitive functioning? Well, there's several issues there. One, we see a decrease in mitochondrial density. That's a little, the power plants that power your brain and your thoughts. As those decrease, the brain fails in its ability to get the job done. Another thing we see is glucose which is circulating through our bodies, from the food we eat, the brain has difficulty in taking that up. If you can't get that glucose into the cells, it doesn't do you much good.

As a matter of fact, it does you a lot of harm because that glucose can then react with other proteins that are floating around and cause these advanced glycation end points or age points which are the acronym says it all. They're age related molecules. Then lastly, we see that the hippocampus which generates new cells in the brain to replace the cells that die off lose its ability to do that as we age. Your ability of your brain to repair itself, for a while, we thought that the brain couldn't repair itself. Now we know that it can. That's very exciting.

How do we stimulate it to not only repair itself but to keep it very top shelf. That's some of the things that we worry about with the aging brain.

Speaker 1: The idea of brain inflammation might scare people but in reality, it actually happens to all of us, right?

Alan Cash: Well, as we age, yes. There's a lot of other causes of inflammation in the brain other than just again. One is like a bacterial infection or a fungal infection, mold, chlorinated pesticides has been shown to increase inflammation in the brain, head injury. There are a lot of different causes for brain inflammation but certainly aging is one of them and hopefully that happens to all of us.

Speaker: What can we do to lessen brain damaging inflammation?

Alan Cash: Well, it’s kind of interesting. Oxaloacetate is being used in Europe now in clinical trial. They're looking at closed head injury for instance in football or car accidents or whatnot.
What they've seen in animal models anyway, is that when you get hit in the head, the actual damage to the brain is only about 20%. 80% of the damage to the brain is caused by something called a glutamate. It's when your neurons excrete all this glutamate and that excites the neurons so much that it kills them. We call it excito-toxicity. It's too much of a good thing.

If they can reduce that glutamate level, they, at least in animal models, they've been able to show 80% less brain damage from closed head injury. That's exciting. That's one of the things that they're looking at very closely in Europe with Oxaloacetate because what happens with the Oxaloacetate is once it goes into the bloodstream, it reacts with the enzyme glutamate oxaloacetate transaminase which is a huge word but you can call it GOT. Through GOT, it combines with the glutamate.

The Oxaloacetate and glutamate combine and together they make something called alpha-Ketoglutarate which is brain protective as opposed to brain excitatory. Because of this, it gives us some chance that we may in the future be able to help with some of these brain inflammation and brain excito-toxicity, that's for sure.

Speaker: With Oxaloacetate, can it help us rebuild brain power as we age or rebuild the brain power that's lost as a result of injury or exposure to some of these toxins that you've talked about?

Alan Cash: Well, we can't really say for any kind of injury that Oxaloacetate will help. This is just a dietary supplement but can it help with the ravages of aging. I've seen it time and time again. My mom's 90 years old. When I give her the Oxaloacetate, when she takes her capsules, she remembers where the keys are. That's not necessarily a good thing because she's 90 but we see this time and time again with, especially with elderly people that they seem to have more cognitive functioning, they seem to have clear thoughts and when I talk to other people about Oxaloacetate, I say, "Why do you take it?" They go, "I take it because I have brain fog."

"What does it do?" , "Well, it helps me when I'm tired. I can write better. I can recall better." This is the comments that I'm getting back as a researcher from people who are actually taking Oxaloacetate products.

Speaker: Do supplements like this help daily or over time?

Alan Cash: People have asked me when is the best time to take Upgraded Aging. Right now, right now. I mean, why wait? Should you take it in the morning, should you take it in the evening, how long should you take it? The most important thing is to take it daily because what you're trying to do is turn on the genes that simulate this calorie restricted metabolic state. The best way to do that is everyday, everyday, everyday,
everyday. In our animal models, we gave it to them their entire lifespan because we wanted to see what would happen over their entire lifespan.

What we saw is a decrease in inflammation. We saw a decrease in chronic conditions such as curvature of the spine. We saw improved energy. We just saw healthier animals and they live longer. It should be taken daily, really timing doesn't matter as long as you take it during the day. Some people if they take it late at night, it causes them a little bit of sleeplessness because they're just so alive. Maybe a morning supplement. Other people need it in the mid-afternoon to just kind of get through the day.

Speaker: The effects of this supplement felt immediately?

Alan Cash: This is a very subtle supplement because you're turning on genes as opposed to a pharmacological effect. In pharmacological effect, you feel the results immediately. It's kind of like you have a hammer, you hit your hand, your hand hurts. With genomic type things, you turn on the genes and then you have to wait because the genes then produce proteins and in order to produce enough proteins to have a measurable effect, it takes time. In the case of Oxaloacetate, most of the effects can be felt within 30 to 45 days. Some effects can be felt immediately but they're very short lived. For instance, an increase in endurance can be measured with Oxaloacetate for two hours after you take it. For that reason, a lot triathletes and bicycle type people take the product before they race.

It's kind of funny. I asked one of them to do a testimonial for me. They said, "What are you, crazy? I don't want to tell people about this. No way." Anyway, the pharmacological effects increase in endurance, that can be felt immediately. A reduction in glutamate, the can be sometimes felt as a feeling of peace and better focus but the real huge effects are after you take it for 30 to 45 days where you get those gene expression changes, where you get the increases in mitochondrial density, where you get increase in glucose uptake to the cells, these are critical fun, fun things for your body.

Speaker: What are your top 3 recommendations for kicking more ass at life and being more Bulletproof?

Alan Cash: That's a great question. Obviously, take Upgraded Aging, that's number one because it puts you in that calorie restricted metabolic state that is so hard to achieve any other way. Another way, another thing I would take is vitamin D. Then the last thing I would do is short term interval exercises. Diet and exercise, it's kind of what you've been told all your life, right?

Speaker: Alan, thank you so much for being here with us today.
Alan Cash: You bet you. My pleasure.

Dave: If you haven't had a chance to check out our Upgraded Aging formula, it's worth a look. It's an amazing molecule you can take that helps you to mimic the effects of caloric restriction. You're probably already practicing Bulletproof intermittent fasting, adding something like Upgraded Aging formula helps your body to get the benefits of reducing calories without actually reducing calories. On top of that, Upgraded Aging formula helps your brain deal with large levels of glutamate which is something that causes toxicity in the brain. It helps a healthy brain stay healthy.

It also has other very positive effects on maintaining healthy blood sugar levels and on other aging risk factors. This was the only supplement I've ever come across that very clearly impacts four different facets of aging, that's why I call it Upgraded Aging formula and it's available on upgradedself.com.

Featured

Terra Biological LLC

Resources

Oxaloacetate

Kreb’s Cycle, or Citric Acid Cycle

Citrate

Malate

Mitochondria

Calorie restriction and aging: review of the literature and implications for studies in humans (American Journal of Clinical Nutrition)

Nicotinamide adenine dinucleotide (NAD)

Oxaloacetate Activates Brain Mitochondrial Biogenesis, Enhances the Insulin Pathway, Reduces Inflammation, and Stimulates Neurogenesis (Human molecular genetics)
Adenosine triphosphate (ATP)

Advanced Glutation End Products in Foods and a Practical Guide to Their Reduction in the Diet (Journal of American Dietetics Association)

The neuroprotective effects of oxaloacetate in closed head injury in rats is mediated by its blood glutamate scavenging activity (Journal of Neurosurgery and Anesthesiology)

Pictorial Review of Glutamate Excitotoxicity (American Journal of Neuroradiology)

Glutamate oxaloacetate transaminase (GOT)

Alpha-ketoglutarate

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