Managing ME/CFS and Post-COVID Symptoms with Oxaloacetate Transcript

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Sponsor Message and Introduction

Are you treating patients with ME backslash CFS or long COVID? Consider oxaloacetate CFs. In multiple clinical trials, oxala acetate has been shown to significantly reduce both physical and cognitive fatigue symptoms in ME slash CF and long-COVID patients, with average improvements ranging from 25% to 46% within 6 to 12 weeks.

Oxalo acetates CF is a high dose medical food recommended by physicians in more than 30 countries worldwide. For access to clinical trial data and wholesale options, visit oxaloacetatecfs.com backslash doctors.

Hey everybody, Dr. Rob here, Proven Health Alternatives. I'm excited to share with you Mr. Alan Cash. He serves as a founder and chief science officer at Terra Biological LLC.

What I like most about Mr Cash, I am going to call you Alan for the rest of the podcast, is that he is an entrepreneur with extensive education and his main goal now is family and helping people through health.

So Alan, how are you doing today? I'm doing really well. Thank you so much for inviting me to be on your podcast. Well, I am happy that you were able to make it.

You know, we caught up at a symposium a couple of weeks ago, Integrative Health Symposium in New York City, my home.

Why Oxaloacetate Research Began

And you captivated my attention by talking about oxaloacetate, a nutritional supplement for the treatment of physical and mental fatigue in ME, CFS patients.

And what really put it over the top was the fact that you can use it in the long COVID. Everybody knows that I wrote a book called Immuniboot in 2022, talking COVID-19.

So if you will be so kind, what inspired you to start researching this particular nutrient? Well, I got sick. I had an artery end up next to a nerve, major nerve bundle in my brain and as my heart beat it was cutting through the myelin sheath and then into the nerve itself.

Incredible pain, incredible. They were able to go into the back of my head and follow the nerve along until they found the crossover and put a piece of Teflon in there.

So now not only am I pain-free, but I don't stick. That's a good thing. But whenever you have You know, any kind of brain issue, it takes a while to recover.

And during the recovery I thought, you know my background, I'm a physicist and I became interested in why I got sick and it was essentially due to aging.

As we grow up, our arteries go everywhere and we don't get any bigger and it just happened. A random fact is a random thing. So anyway, I thought I'd look into aging and what I found is that pretty much nothing works to retard aging.

There are a lot of things that have been tried, you know, pyramids and all sorts of interesting things. The one thing that has worked consistently is calorie restriction.

They've shown it in animals, they've done some clinical trials in humans that've showed reductions in things like atherosclerosis. I can't even say that word.

Yeah, and that's the number one killer in America. I thought, as a physicist, I want to look at the energy pathways and see what's changing in calorie restriction.

And I brought some of these ideas to a friend of mine at UCSD, University of California, San Diego. He was a very high-level biologist, very famous guy, lots of awards.

I think at some point he'll win the Nobel Prize. I'm in his office. I am talking to him about this and all of a sudden he just gets up and leaves. And I just thought, oh my God, I've just embarrassed myself.

Then he pokes his head back in and he says, why are you coming? And so I stand up and I follow him downstairs and he has this big set of keys and goes to a steel door and opens the big door.

There's a huge laboratory behind there. It's his laboratory. And he walks over to one of the benches, takes his arm and just scoots everything out of way and says, this is your spot.

Early Longevity and Worm Studies

I said, what are you talking about? He goes, we'll get some worms, We'll give them oxaloacetate. We see if they live longer. Then we will know if you're right or wrong.

And I was like, I'm not a biologist. I don't know anything about raising worms or flies. He says, well, you can learn. So that's what I did for, you know, six to eight months.

And our first tests showed a 25 to 50 percent increase in population lifespan. We published that in the journal Aging Cell. And then we started getting worms that had part of their genes disabled so that we could follow along and see how they were living longer, what pathways we were activating.

And it turned out to be a very conserved pathway that was very similar to what we see in calorie restriction. So I started thinking, you know, the entrepreneur in me said, You know this might be an interesting nutritional supplement because oxaloacetates in just about every cell of your body.

It's central in, energy production and So I started looking through the literature and I found a clinical trial that showed that it was safe to give people These were diabetics and they saw about a 30 24 to 30 percent reduction in fasting glucose levels with the addition of oxaloacetate I was like This is incredible.

So we started figuring out how to get oxaloacetate. Turns out, of all the citric acid cycle metabolites, it's in the very lowest amount. Trying to extract it out of a plant or out an animal, very difficult.

We started manufacturing it starting off with the distillation bottoms or fermentation bottoms of the wine industry cream of tartar. and we turned it into oxaloacetate and made the first nutritional supplement with it.

Interesting. So this works in the Krebs cycle then through the mitochondria. Yes, there are a bunch of ways that oxaloacetic works and that's really, you know, as we've gone on and started looking at why this work, some of the things that we have identified are one that It increases a protein called PG1C alpha, PG-1 alpha.

And what that does is it turns on mitochondrial biosynthesis. So we see an increase in density of mitochondria when we give oxaloacetate. So I'm going to interject.

If you're getting an increase in mitochondria, obviously mitochondrial dysfunction is a major issue in America today, and mitochondrion dysfunction falls under the funnel idea of longevity.

Yeah. So even though you were talking about caloric restriction, are you stimulating the mitochondry from the Krebs cycle? Are you stimulate the Mitochondria because of the caloric restriction or both?

You're smiling at me.

How Oxaloacetate Supports Energy Metabolism

We're smileing because oxaloacetate is an endemic molecule and so figuring out why things are happening is kind of like taking a jello mold and pushing it one side and looking at the other side, and trying to figure out There's so many things that happen when you give oxaloacetate.

So one of the things we see in addition to increasing mitochondrial density is this same thing we saw in the diabetics is that it starts pulling in more glucose into the cells.

So a lot of times like in diabetes, you have the glucose available, it's circulating around. What you wanna do is you want to bring it into the cell so that it can be used.

And that's where we see a failure in diabetes. We see it in type one, we it type two and type three, which some people refer to type 3 as Alzheimer's disease.

Yes, yes. we did a clinical trial in Alzheimer patients and we saw that oxaloacetate increased glucose uptake in the neurons of the brain by 10%, which usually in Alzheimer's, it drops 1% a month.

So it's like we reversed them 10 months, which was really cool. I'm going to do a little rapid fire with you. Okay, I am ready. Get ready! Oxalo acetate, does it have a positive effect and why on ME slash CFS?

Yeah, it has a huge effect on ME-CFS. We've seen in clinical, we've done four clinical trials now, and in each of the clinical trails, We see this increase in mental functioning, And we see an increase In physical endurance and the ability to do things.

Interestingly, we also see a reduction in PEM, which is post-exertional malaise. The people who were in the oxaloacetate group after three months, none of them had Pem attacks, whereas the people in The Control Group were still getting it periodically.

So we're looking at it now, you know, extending this to see if we can stop post-exertional malaise with oxaloacetate. So that's kind of where we are headed with this.

So that's one of your big ticket items. That's great. Now everybody knows I'm a big long COVID guy post-COVID. Let's talk a little bit about cost for COVID fatigue.

Obviously the fatigue comes from mitochondrial dysfunctions, but give me the tie-in and some of the cellular pathways that it's using to do so. What we see in fatigue models, and this really doesn't It doesn't matter if it's long COVID or if its MECFS or pneumonia or any kind of insult to the body.

The body does a couple of things right away. They go into a cell danger mode. And Bob Navio at UCSD talks a lot about this, where the cell is damaged and it says, oh, we've got to conserve energy and we have to spread this inflammation pathway, which is usually through NF-kappa-B translocation up to the nucleus.

The nucleus opens up and you get this cytokine storm. And in ME-CFS patients and in long COVID patients, we see this storm going on all the time, and they just can't turn it off.

And that seems to be one of the main things that are happening right now. Oxaloacetate, We've seen this at work out of University of Kansas, it reduces the translocation of NF-kappa-B to the nucleus by 70%. Wow.

So it turns down that ongoing inflammation. It still allows the inflammation if there's an insult, but it turn down inflammation with these chronic cases, so that's a huge energy sink.

That's one place where it helps with a long COVID patient and with the ME-CFS patient.

ME/CFS and Long COVID Clinical Benefits

I want to interject, you know, so the listeners understand that NF Kappa B is without question a signal transducer of inflammation in the body and there are not that many things that quell that particular pathway.

So if you're able to affect it and down regulate it, it's a good thing. I mean, when we control inflammation, we have control of our health. And what you are speaking to with these post COVID patients that cytokine storm, that's one of the biggest problems because I believe that most patients are pre inflamed, They get too inflamed in America, and they're not able to control their inflammation.

So this is sort of like turning the switch off or turning volume down on the fire. Turning it way down. You don't want to turn it off, because if you get a cold, you want be able fight the cold.

Sure. But you don' t want t be inflame all the time. And that also ties to aging. If you're inflames all time, your going to be aging faster than you should.

Yeah, they call that inflammation time magazine talked about inflammation cover 21. Yeah. Now that now we talk about information. So taking it to the next step post COVID fatigue.

What about patients with post viral fatigue? We've seen the same thing in pneumonia cases, people coming out of the hospital with pneumonia have tremendous problems with energy production.

And we see the same things with ME-CFS in Epstein-Barr, other places where it could possibly be a viral attack to start the cascade of what's going on.

Interestingly, not only is it inflammation, so that's one major issue with both long COVID and ME-CFS. Other things that are affected is the energy production itself.

So What Oxaloacetate does is it does three things for energy production. It brings more glucose in, which we talked about, so you're getting more fuel.

it makes more mitochondria, So you have more Mitochondria to burn that fuel, and then there's a third thing that we've just discovered in the last five years.

And it's really mind-blowing. we reverse the Warburg effect. Wow. If you're familiar with the warburg affect where glucose comes into the cell and instead of going to the mitochondria to be burned with oxygen to make 32 or 36 ATP, the energy currency, instead it ferments in the cytosol and makes two ATP.

So let's see, which would I rather have, two ATP or thirty-six ATP? That's an easy question. Oxaloacetate has been shown to reverse the Warburg effect and push the components of glucose down into the mitochondria and burn them.

So all of a sudden we have all this extra energy that we're now producing that, you know, the body does this because it needs quick energy to fight whatever it means to find, but the fight is already over with long COVID.

The fight already is over already with MECFS. the Fight is all ready over many of these chronic diseases, But the inflammation continues. So now we're turning off the Inflammation aspect of it.

We're saving a lot of energy for other things and we are making more energy we're making it the smart way. We're bringing their metabolism back to the way it was.

The efficient way, so that really begs the question, are there other metabolites or pathways that may work synergistically? with oxaloacetate? We do know that you have to have enough NAD and NAH in your system to work.

Oxalo acetate, one of the way it works is increasing that NAd to NAh ratio and The first person who actually measured that was a guy named Krebs of the Kreb cycle.

He showed a 900% increase in the NAD to NAH ratio by just adding oxaloacetate to the cell. I mean, we've known that for a long time. And turning on that NAD to NAH ratio activates AMP protein-activated kinase, which then acts like the drug metformin to bring in more glucose.

It's just An amazing coincidence. So in order to treat these chronic diseases, like long COVID and MECFS, we have to do a couple of things. One, We have To bring down the inflammation.

Right. And we Have to adjust the energy production. and it turns out oxaloacetate does both of those things, which is just amazing. Fabulous. I mean, that's outstanding.

You know, like I said, I didn't know to be transparent. They didn' know about oxalacetate until we met and we talked about it. And that is what spurred me on to want to have you come on and talk about this very unique supplement product.

But how long has your company been around? People always ask, is this, you know, are you open for a week? Are you opened for 90 years? How long have you been round?

We started our research on oxaloacetate 20 years ago and we've been Primarily, I ran the company as a family business so that I could do my research. I'm a scientist and I was able to fund all my studies and we've done amazing number of studies to try to figure out what's going on here, why is this working, and now how can we help people.

And it's been a great ride. Well, that's why we had some synergy because that was something that we both concurred on. So do you have any case studies you want to share, anecdotal reports to truly illustrate patient improvements?

Yeah, sure. People love that. They want, they want hear a story to try to relate to it because you know, here's what they're looking for.

Inflammation, NF-kappa-B, and Post-Viral Fatigue

And I get this all the time at the end of every podcast and people ask, you they love the guests, but they always want know who can they trust, what's right and where can I.

Yeah. So my daughter was telling me about a customer of ours that called in and she was talking to him and wanted to interview their son because he had severe ME-CFS.

And ME CFS can occur from very much just I feel tired all the time to I can't get out of bed. And this was one of the, I can't get out of bed patients, a young man.

And our hearts go out to these parents. So she said, is it OK if I I could talk to him? Because you told me he's doing really well. What does that mean?

How has he changed? And they said well, he is not here right now. He's out body surfing right now. Wow. He goes to school now, he's with his friends now he is body-surfing, He is asymptomatic right know.

And this is a kid that five months ago was confined to his bed. I can give you another example. A young girl, 17 years old, she She got very sick, long COVID.

She was a great student, very popular. All of a sudden she's in her room, it's dark, she is staying there all the time, She's not talking to people, not going to school anymore, and she can't.

she starts Oxaloacetate. in a month's time she's going back to school. Wow. In three months time, she has got all her friends, and she goes on to college.

She is thriving, thriving. Now, it doesn't work in every patient. We have seen in the clinical trial that the cognitive improvements, you know a 10% improvement in brain function, seems to be universal.

We see that in MECFS and we see in Long COVID, which in itself is pretty amazing considering brain fog is a big issue and these people are driving out there, think about that.

But in the physical standpoint, it seems like 70% see an improvement. And of those 70%, about 40 to 45% 25% improvement or more, which is life changing.

Yeah, with which substantial. So if I would ask you for a protocol, You would start with oxaloacetate. Are there other supplements that you would want me to take, other nutrients like a vitamin D for synergy and concert with the oxalocetates?

The nice thing about oxala acetate is it's a human metabolite. So you can add it with anything else you're doing. We have no negative interactions with other drugs reported at this point in time.

And we've been selling an oxaloacetate supplement for 20 years. What we do see rarely is if someone is allergic to vitamin C, they may have a problem with oxaloo acetate because structurally they're very similar.

We also oxaloacetate can relax the upper sphincter muscle in the stomach so you can get some acid reflux if you take this on an empty stomach. So we suggest taking it with food.

and even with food you can have some acid reflux. We had about a two to three percent increase in that in the clinical trials. It seemed to be helped with any kind of antacid or if you take the oxaloacetate out of the capsule and make a smoothie with it.

Energy Pathways, NAD, and the Warburg Effect

Interesting. Well, curious, how's your research evolved since when you first started to study this particular nutrient? Wow. First of all, we started off with animal models to see if we were actually mimicking the calorie-restricted metabolic state, and we did a lot of gene sequencing or metabolomic sequencing.

and saw really a pretty good overlap. The other thing we started doing is safety studies because you don't want to just put a new dietary ingredient on the market without having substantial safety study and we did that.

worked with the FDA in doing the safety studies. We then started working with groups that we thought, you know, what type of diseases can this be helped with?

And so Basically, after we started selling this as an anti-aging compound, we start listening to our customers who kept coming to us and saying, you know, oh, this has been good for me for this, and you hear something like, I'm doing much better and I had chronic fatigue syndrome for 20 years.

All of a sudden, I am doing better, and this is the first time. You think, okay, maybe I should listen to them. After you hear it four, five, six times, that's where we started doing the clinical trials.

So far, we've done four clinical trial in ME-CFS and long COVID. Outstanding. So let's talk about dosage. Is it a standard dosing or is there an acute?

Is there a subacute, a chronic, is their a performance? No, that's really good as we're classified right now as a medical food. Which so you have nutritional supplements which keep healthy people healthy.

You have drugs that are a, you know, monopoly for treating a disease. And Congress back in 1986 made this very small classification called medical foods, and we fit into that medical food place.

So as a medical food, we rely on the physicians to suggest dosage to the customers, to their patients. And a lot of

that's because ME-CFS is a spectrum.

You see people who are just tired who might only need, you know, 100 to 200 milligrams a day to people, who were bedridden that are taking up to 5,000 milligrams today.

We've seen in our studies, we did dose ranging studies at a thousand milligrams of day. So we have 500 milligram capsules, two with breakfast. We've seen, we've done 2,000 milligrams a day, so two with breakfast, two lunch, and then we tried two breakfasts, with lunch and two dinner for up to 3, 000 milligrams per day.

And what we saw is an improvement. We used medium ME-CFS patients, okay? And let me just talk about that for a minute. We didn't use the very severe patients because the scales that we have to test for fatigue go off the scale with these people.

And how do you measure improvement when you start off-the-scale? So we started with mild to moderate people, What we saw was measurable improvements. We used validated fatigue scores.

Safety, Dosing, and Practical Use

Basically, we saw at a thousand milligrams, We saw an effect, so two capsules a day with breakfast, or if we went 2,000 milligrams we, saw more of an affect, So we see the improvement, and 3,00 we seen more improvement but it drops off.

So 2.000 mg is where most people will want to be. That's two capsule with a breakfast and two with lunch. going to tell you to skip the two capsules with dinner, unless you're very severe, because it can give you so much energy.

based on our studies, it can give you so much energy that it makes sleep difficult. You're just ready to go and we want you to sleep. Oh yeah, sleep without question is a huge longevity health hack and it's great that you delineated the dosage because they once said the dose is the poison And I think in supplements, the dose is the secret sauce to outcome.

So if I say take vitamin D and you take 600 IUs, like the RDA says, probably not going to move the needle all that much. Probably need 2,000 to 5, 000 Ius.

I'm happy there was some clarity there for us. Are there any studies or clinical trials that you're particularly excited about that would you like to share?

Well, I'm really excited about the three studies that we just completed. They were just published in Frontiers in Neurology, which is a high-level publication.

Yeah, and so those are available for free now. You can download those studies and take a look at them. Basically, it shows that eliminated post-exertional malaise in the oxaloacetate group which is great for quality of life.

Any physician who has ME-CFS patients, one of the first things they'll want to do is eliminate those crashes. So that's great that we showed that. We showed the increasing in brain function in both ME CFS and long COVID, which brain fog is such a big thing.

Yes. Every time I'm driving on the highway, I think, wow, there are probably a lot of people with long COVID here driving right now, which is kind of scary.

Yeah, scary thought. But if you can get rid of those brain fog issues and allow people to go back to work, if can allow them to have good quality of life, eliminate post-exertional malaise in these patients, this is groundbreaking for these patients.

Do you have any other potential applications beyond fatigue syndromes for oxaloacetate?

Published Trials and Future Applications

Well, the improvement in cognitive function has been shown in cancer-related cognitive impairment in breast cancer patients, so I don't know if you know this but a third of the women who've had breast cancer and are now in remission, so they don't have cancer anymore, have terrible cognition problems.

And we just finished a phase two trial at UCLA showing remarkable improvement in these patients. So that's someplace we're looking at. But we are also continuing our work in ME-CFS and long COVID.

There's certainly a lot of questions still out there. This is all new information. People are still digesting this. combine it with low dose naltrexone or maybe we should combine with other things.

The question is how can we make this even better? We've taken the first huge step for ME-CFS patient. I had someone call me yesterday, she had had ME CFS for 30 years.

She said, this is the first product that has moved the needle on this for me. That's great feedback. And she's had it for thirty years! That is great.

So I want to hit the finish line with this final question. You've been in the business for 20 years, you're looking into your entrepreneurial research designed crystal ball.

Where are we going in healthcare in America today? Exactly. Where I'd like to see us go is to help more people. Is to prevent more. Certainly here we have a molecule that's part of every system in our body for energy production.

If we could get this out here and help with the various forms of fatigue, whether it's mental fatigue or physical fatigue I think that will help a lot of people.

Here, here, indeed, I echo that. So this has been a great little conversation slash interview. I've learned a lot. My listeners have learned. A lot I look forward to round two, Mr.

Alan Cash. It's been exciting and don't go anywhere because prizes await you when we're done. Thanks so much for your time. Rob Silverman, Proven Health Alternatives.