The Synergistic Benefit of Sulforaphane & Curcumin Together

Martin (00:00):

Today, we're going to talk about something that I think is incredibly timely and something that has to do with synergy, and I think most of us can appreciate that idea of synergy. If you've ever played video games and you're doing the racing cars and you have that NOx, that nitrogen oxide, and all of a sudden your car shoots ahead, you get a little synergy in the game, or if you've ridden an e-bike recently, you're moving along and you put on some of that horsepower of the e-bike, how amazingly more efficient your riding becomes and how much faster you become. Hopefully, you're wearing your helmet. So I think all of us get that idea of synergy and how important it is and how much better it can make us feel, how much more efficient, stronger, and in this part, I guess we're going to speak about healthier.

Martin (00:49):

So if you're thinking about certain things you've heard in the literature, how much vitamin C improves the absorption of iron, makes it better... And so in the plant world, we see a lot of synergy and that makes sense. The plant kingdom, incredibly intelligent. If you look at where we are, David and John, we talk about this all the time. If you're eating a processed-food diet, if you're eating a fast-food diet, you're getting a monoculture of food. You're getting very basic foods. You may get fortified foods. Whether that is helpful or not is likely being proven not to be the case, but in the plant world, these things seem to work together to really bring us the best health.

Martin (01:38):

And so when you're looking at how to eat and what people are talking about, there's a reason we want you eating in rainbows and eating in variety and eating different foods so that we can absorb each one of those together very efficiently well, and bring us the best health. And here at Mara Labs we're certainly working hard on that, not only to bring each molecule to your cell to be bioavailable, but how those molecules work together to bring us best health. And fortunately, we have a PhD and we have folks who know how to work HPLC, and we're looking at these things to figure it out.

David (02:21):

Last week's podcast was on microbiome, and you're talking about food, Martin, and it just naturally came to me, as you're eating the rainbow, you're creating a much more diverse microbiome. So John, as you jump in, I know you may not have studied this, but maybe share some from your perspective on what, if any, part microbiome has to play in the synergy, but I really want to hear your perspective on the study results you found in the lab.

John (02:55):

Yeah. Synergy is a really super-interesting topic, especially when you're thinking about holistically. I think a lot of people... We were talking about vegetarians, and probably every vegetarian knows of a very classic synergy: you combine foods to make your amino acid pool complete. I think the idea of that is really instrumental in that synergy also has to do with deficiencies as well.

John (03:28):

So in the case of if you just eat beans, you're going to be deficient in an amino acid, and therefore, certain functions in your body aren't going to work as well: immune system, different things. But when you combine beans and lentils, it's a classic combination. I think it's actually leucine and methionine; one

is deficient in one, and the other is deficient in the other. And so in terms of amino acids, there's an amount that you need to perform optimally. So just to stretch that idea out into what we all know is that if you eat enough diverse vegetables, there's a whole set of nutrients, like those amino acids, in that optimally, you have a whole slew of different flavonoids, flavonols, that make up what we would consider a really complete diverse diet.

John (04:28):

And so I think some part of the testing that we're doing is examining something like that, in that we have cells in culture; they don't have flavonoids in the mixture of how you are culturing cells. So you add one and it's filling some holes. You might be decreasing inflammation, you might be slowing down the production of cytokines, or something like that, and then when you add a second one, you're unblocking another possible deficiency, or are those two nutrients just working together to optimally drive another pathway?

John (05:08):

So we've done that in the lab a number of different times, and they've been our favorite nutrients so far as sulforaphane and curcumin. Those two are known to work together, and I think it's a little bit easier to understand those two and why those two really should be used together, is that sulforaphane is the best Nrf2 activator and curcumin is the best NF-kappaB inhibitor. So when you put those two together, that deficiency that you're seeing in sulforaphane is enhanced when you take curcumin at the same time.

John (05:49):

And so in the lab, the most stringent version of synergy is where you take one nutrient, dilute it until you can't see a response in any signaling pathway, and then you take the other one, dilute it until you don't see any effect, and then when you put the two together, you see an effect. So it means that there's no other way that those two things are activating pathway outside of synergy, because zero plus zero should be zero.

John (06:22):

The other response is additive. There's a lot of nutrients. It's easy to see that. It's just, you add this amount, you get 10% increase, you have this other nutrient and it goes up 10%, and then you add them together and it's 20%. That's additive. It's a good response. Those two could still be helpful together, but it's not synergistic.

John (06:49):

So we were doing it in cancer-cell culture models. At least in one of the cases we think we know what it was, was in the case of a cancer stem cell, we were adding sulforaphane to the cells and that's known to block these MDR-phenotype, which is called multiple drug resistance, pathways, where they just pump the drug back out of the cell. And then if you did curcumin at the same time, that curcumin isn't being pumped back out of the cell. So when you put them together, you're not only getting two things that are anti-cancer. In one case, you're getting a blocking of an export pump, and the other one, the amount is accumulating in the cell way higher. So that's an example of synergy.

David (07:39):

Are there pharmaceuticals that turn on Nrf2 and turn off Nf-kappaB better than sulforaphane and curcumin?

John (07:49):

There are anti-inflammatories, and especially in the acute hospital situation where you are getting runaway inflammation, the corticosteroids would fill that bill exactly. But it's not something that is good for you long-term. And then there are monoclonals, the biologics that are very specific for turning off certain pathways. There's biologics for rantise , part of the immune system. There's TNF-alpha inhibitors, both drugs and monoclonals. But yeah, there are ones out there, but not ones that you would want to take for a long time, or else it turns off your immune system and it wouldn't be a good thing.

David (08:32):

Yeah. So the sulforaphane and the curcumin are the best natural molecules at turning on Nrf2, turning off Nf-kb, and they are sustainable. You can take them for long periods of time with only health benefits. So going back to the synergy definition, you talked about in the lab, seeing zero effect on one dose plus zero effect on the other dose should be zero, but what were you seeing?

John (09:04):

Yeah. So in multiple cancer-cell lines, and of course, we're not saying anything about disease processes, but in cell culture, it's very easy to see energy between sulforaphane and curcumin in terms of cell killing compared to a normal cell. There are normal cells that are sensitive to xenobiotics just in general, because they accumulate there. One of the best-studied models is proximal tubules. So it's the first segment in the kidney after it gets filtered through the glomerulus. So for instance, gentamicin is a known antibiotic. It just accumulates in the proximal tubule and causes toxicity. A lot of times, the limit of whatever drug that you're taking is because of its killing of proximal tubule cells. So we always use those cells as a negative control if you want to do a model that somewhat simulates what you would hope would happen for an anti-cancer compound.

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John (10:03):

... What you would hope would happen for an anti-cancer compound is show no effect at all on a normal cell, and show cell killing in the case of one, and then synergistic with a second cell. And then, it's also a very clear with sulforaphane and quercetin, and sulforaphane and berberine. So they have similar synergistic activities, and we haven't made it as far as three at a time yet, but I'm pretty convinced that, at least logically, that there is multiple three-way synergies in our top line up of nutrients we're going to produce.

David (10:40):

And so, the effect you saw in the lab, we said let's not do zero, but maybe one plus one, that equal three, that equal five. What did you see?

John (10:49):

Yeah. You can't quantitate infinite. So you say a dilution until you see nothing, nothing, and then you see like a 40% increase in cell death. There's no fold increase in death there, which is normally how you

quantitate things like that. So can't say an infinite increase in death, but that's what it looks like. It kind of looks magical.

David (11:13):

So the berberine study, looking at synergy with sulforaphane, was that identical to how you set up the curcumin study?

John (11:21):

Yeah.

David (11:21):

Okay. And then you also looked at quercetin.

John (11:25):

Yeah.

David (11:26):

And which had the biggest blip after the zeros, was it curcumin and berberine, or quercetin?

John (11:34):

Curcumin was biggest. And then, depending on the cell line, it was either quercetin or berberine. So it's probably different pathways.

Martin (11:46):

It makes total sense, logical sense as to why that would work, seeing you're dealing with most best natural supplement that deals with oxidative stress. You're dealing with the best natural product that deals with anti-inflammation. Two huge processes that create so much chronic disease, certainly in this country, and unfortunately, we're seeing that in most other countries now, developing countries. So is that the reason, is that we're clearing these two incredibly toxic pathways, if they're out of control?

John (12:19):

I think it's different theoretical framework as what I was talking about earlier, the deficiency model. Toxins cause deficiencies. There's a set of nutrients that are called conditional, essential nutrients that, under stressful situations, you use more of, like ...

Martin (12:37):

Magnesium certainly.

John (12:38):

Yeah. Magnesium is a really good example of it. Another one would be, like in the exercising communities, if you overexercise, you can get L-glutamine decrease, and maybe you know or don't know, L-glutamine deficiency makes your gut lining mess up. And so then, you're not absorbing a whole bunch of other things. So that one deficiency can lead to all kinds of other deficiencies. So that's like what we were talking about with synergies, but in the negative. And I think that is happening in our

environment right now, and is why we want that more complete set of phytonutrients, that they're competing with our introduction of toxins into our environment.

Martin (13:27):

Yeah, it's interesting. I mean, as far as a negative synergy goes, I see it all the time in my practice. Folks who are stressing themselves, maybe with too much exercise, they're not getting the nutrient base, not enough sleep, getting too much stress. I mean, you look at each one of these compound on each other, we even just take two of them, which almost everybody I know deals with. If you're not unbelievably intentional about your health, you're getting a synergistic effect with regard to the microbiome, your immune system, inflammation, again, oxidative stress. And even if it's not happening over a month period or two month period, it's certainly happening over a year or two years or three years or 10 years. And people are coming to me just incredibly sick, going, "Why did this happen to me today? I don't remember doing anything in the last year that would've done it." But it's that cumulative, negative synergistic effect where you're again, eating monoculture, you're just adding one stress upon another. And it's incredibly important that we understand the end effect of that is going to be chronic disease.

John (14:29):

Yeah. That's a great example of it. And I didn't answer before the connection to microbiome, probably because I was trying to simplify, and that's for sure complicating, but in the case of the microbiome, you can think of just what you were talking about, there's like a perfect bad synergy of, if you have inflammation, and then you have either excess sugar, or your lack of sleep, and that synergy that's happening there can be so clearly seen in simple pathways, like eating too much sugar. You're getting a whole different set of microbiome growing. If you're stressed out, it's known that ... Really nice studies showing, if you just tell somebody that they're going to have to stand up and give a lecture, you get an epinephrine surge that disrupts your enterocyte layer, your tight junction layer in your intestines, and you get leaky gut.

John (15:49):

And you can imagine all kinds of interactors there. Inflammation directly affecting the actual bugs that are growing in your large intestine, whether they're making your butyrate or not, that's feeding back again onto your stress pathways, and whether the enterocytes are happy, they grow and love butyrate.

John (16:18):

And so, you're not eating those fibrous vegetables, and you're not making as much butyrate, you've already knocked the whole system down a little bit. Then you eat a pizza, get your gluten, and then you have a bad weekend, then you're back to work stressed, and then you're at a different level.

John (16:44):

Yeah. We really think that you have to do both things. You have to be mindful about avoiding the things that make things worse, and be mindful about doing the things that you have to do, like exercise. Things that are just blatantly, obviously good for you. Sleep, exercise, eat your rainbow, all those things. That whole synergy idea there is essential, especially if you're fighting some disease state.

Martin (17:18):

Yeah. And I think here, at Mara Labs, we sort of realized people's deficiencies, in some ways, and we're trying to, again, bridge people towards health. Do I think that people can do it on their own? Absolutely.

If you're intentional, you're well-read, you're listening to the literature and seeing what's out there, certainly I think you can do it on your own, but here, we're trying to look at the science, look at how things work best, get you some high-leverage products that, again, may bridge your approach to health a little quicker, or get you to healthy a little bit more quickly. So again, we can increase, what we talked about, health span, keep you disease-free for longer, which for us is incredibly important for ourselves, for our families. And now, for the wonderful people who support our products.

David (18:11):

And going back to the microbiome, the podcast, or actually the blog article last week was on a paper, John, that you, I think, pulled for me, maybe, looking at young mice versus old mice, so six to eight weeks versus 21 to 22 months, and giving them sulforaphane. And so, they did old and young controls, old and young with sulforaphane, and the old mice taking sulforaphane had their microbiome just transformed to that of the younger mice, which actually had the bacteria that produces the short-chain fatty acids. And that's linked to better tight junction function, good gut health, that sort of thing. And of course, the gut, 70% of your immune system is in your gut. So having a good microbiome is important for that, as well.

David (19:12):

As an aside, you can't say this definitively, because we don't know, but when we were doing my son's science fair project, we did do three days on the standard American diet, eating McDonald's and Chick-fil-A, and we did get COVID after that.

Martin (19:32):

I didn't realize there was an association there.

David (19:37):

We've had a few people emailing and asking, and the answer is we don't know.

Martin (19:44):

But I mean, again, it makes sense. It's hard not to be stressed in this day and age, and you look at some of Robert Sapolsky's stuff, and what happens to the gut. When you're stressed, you're not getting blood supply to the gut. And so that, as John was saying, that enterocyte layer diminishes in its ...

Martin (20:03):

Enterocyte layer diminishes in its health, and the mucosal barrier decreases what bacteria you're having then, being supported goes down. So, that's just stress. Right now, you add a monoculture of food and what that does to the microbiome, decreases that dramatically. What that does then, to the tight junction, which is now a leaky gut. You're having things go across, your immune system's not doing as well. It's got too many things that it has to fight. It's overwhelmed, could a bacteria, or virus that we know is quite contagious, get in a little bit more easily? You bet.

John (20:42):

Yeah.

Martin (20:43):

And then, there's sleep. And then, there's exercise. We know that exercise is fantastic, but it is a stress. So, if you're over-exercising and not getting enough nutrition, that's a careful balance that all athletes have to undergo. And you look at some of the premier leagues, some of the professional sports, they're are now understanding that and hiring nutritionists to help their players stay healthy longer. So, almost a no brainer.

John (21:17):

Yeah. The microbiome interaction there, it's like, when people are talking about the microbiome and say something to the effect of, what are we doing when we're eating, is you're feeding your microbiome. There's a lot to that.

Martin (21:36):

Or, not. Depending on what you're eating.

John (21:38):

Yeah, for sure. You're starving your microbiome. And then, you're trying to figure out what can I get away with? Yeah. That's so different from, so many studies where you have a mouse model of some chronic disease, where you induce that disease state, and then you can transfer the disease state by transferring the microbiome. It's so clear that it's in the middle of all... Yeah, especially chronic disease states. And I wish there were more follow up studies where they would say, "What's the durability of that maneuver?" If you don't then, start feeding that microbiome that you just transferred, my guess is that, that would drift right back to where it was before. But you'd get into that mindset of trying to do as many things that, you know are, without a doubt, good for you and try to avoid those things as best as you can that, you know are dragging you down.

John (22:45):

Most of the times you probe somebody, they know what they are, they know which stuff they are lacking in their attempt at correcting. I'm not sure how you do that best with your doctor, with some friend, get together with a group, family, of course. Yeah, whatever you can do to move that needle is going to be pretty helpful.

Martin (23:13):

Yeah. I mean, if we just take a step back and say, "Hey, I want to be healthy. So, what does that take?" It takes having healthy nerves, having healthy bones, having a healthy gut microbiome, having healthy blood vessels and blood cells that get oxygen obviously, to the cell, if that's not happening, that's a humongous problem. Having enough blood to carry that around. So, just saying those things, what do we need? We need certainly, vitamin C, we need iron, we need the B vitamins. We need vitamin K2, we need calcium, we need vitamin D. You're not going to get that in a monoculture. You're not going to get that, by not eating a good amount of fiber nutrients and nutrients that support each other and get these things to happen. And so, with that being said, we absolutely understand that these things work together and are synergistic in bringing us better health. And so, again, please understand that this is not nebulous, that this is not important. We need these things working together to have our systems working optimally, as we understand it.

David (24:20):

Martin, you came in pretty confident on microbiome shift in what we ate, impacting our getting COVID. What part of the synergy that John saw in the study, do you think, has to do with the microbiome? So, if you're taking curcumin, clearly would impact the microbiome. What does your gut say about that?

Martin (24:51):

Good one. So, I mean, I'm a professional. I have the ability to provide my patients with a product that we have here, it's a professional product called Broccoli With Curcumin, likely one of my favorite products, just looking at what sulforaphane does to the health of the gut, the health of the gut microbiome, and then looking at what curcumin does for inflammation. Those two things, working synergistically, to provide you with a healthier gut microbiome and a healthier intact gut. So, a gut that is not leaky. And then, helping your gut calm down inflammation with the curcumin, is a synergy that I see as being tremendously beneficial to one of the more important aspects of our health. If you've missed the importance, if you haven't been reading about the importance of the microbiome and importance of intact gut membrane, certainly, hopefully this is a good introduction to it, because it is Uber, Uber important to ongoing health and, or attaining health.

David (26:00):

John, I'll ask you the same question. And I know you don't know the answer definitively. What's your suspicion, as far as the part of the microbiome shift that occurs when you take both sulforaphane and curcumin, or these other products, what part does the microbiome play in the synergy?

John (26:23):

I think, a clear example might be helpful. I really like this study that was done, where they were looking at people that got COVID. This was in Israel, after they were given the vaccine. And I hope this isn't controversial, but the clear outcome of that study was that I think, it was something like 380 patients, or so, that they found got COVID after they were vaccinated. Pretty much, every one of them was immune-compromised in some way. So, for me, that has to be at least one aspect of a clear connection between your microbiome and your susceptibility, is it's known that your immune system and your state of inflammation, is essentially regulated by your gut, your enteric immune system. And if that's off, you're fighting other invaders that aren't real invaders and COVID getting in is almost makes sense, is you're thinking everything that you eat is a foreign entity. Well, one little virus, how are you ever going to fight that?

John (27:59):

So, age has a lot to do with it. There's a bunch of connections with disease states, but it's literally, all the disease states that are chronic disease states, that are increasing in numbers now. Hypertension, metabolic syndrome, diabetes, those are all connected with these viral states. And they're also connected with the microbiome and they're also connected with immune function. So, I think they're all linked together. It's almost a perfect example of, there's a symptom, you get COVID, and then what is it? It's a whole-body health issue.

David (28:45):

Awesome.

Martin (28:46):

And at some point I'd love to talk about that further, because in our whole discussion about COVID, we talk about, vaccination, no vaccination, masks, no mask. And I certainly don't want get into that whole discussion and political quagmire for sure. But, what I do want to talk about at some point, is what can we, as individuals be doing outside of the government, outside of our doctors, to ensure that our health is better. So, what is the gut microbiome? What does it do to help protect us? Eating what? Exercising what? Sleeping how? This is for me, a unbelievably important part of the discussion that, for the most part, is being left out. And so, hopefully we can get to that at some point. And I think we've touched on a little bit here, but get into a little bit more detail at some point.

David (29:46):

So, John, your synergy study was on cells in a Petri dish. And so, when we're taking curcumin combined with sulforaphane, we're taking CurcElite, let's say, and broccoli. BrocElite.

Martin (30:01):

BrocElite, those two. What, if any, what's your sense, as far as, and you see a synergy. That, what, if any part, would the microbiome play in that synergy?

John (30:25):

So I think we touched on it earlier was the most obvious would be how intact your enterocyte layer is. There's some really nice feedback systems in there that we could talk about, like how intact your microvilli on your cells, in your enterocytes, and how tall the villus, the actual slightly larger structure that increases the surface area. The height of those and feedback with your pancreas in producing enough of the digestive enzymes.

John (31:12):

I think that whole system gets degraded over time with a 1000 knife cuts. When you eat out once in a while, you get that whole system smacked down. Most people I think can feel, like when they go out and they know that they've eaten improperly, they feel cruddy for a little while. That's a symptom that you should pay attention to. And if you don't, maybe you are feeling cruddy all the time. So you would probably benefit from getting onto a really structured diet where you're making sure you're getting your macros and micros close to correct.

John (32:07):

But I think all of those things are feeding onto the microbiome. The microbiome is producing nutrients that feed the enterocytes. Those enterocytes are secreting mucins and that biofilm layer that is protective, further protective, and the growth in the correct place. Water reabsorption, correct. Whether you have diarrhea or constipation and can throw off like crazy that balance.

John (32:49):

I just think that the microbiome is in the middle of everything and that to get it in balance with your enterocytes and then your enterocytes interacting with your immune system and your pancreas, your liver. That whole system down there that you think about what you do with nutrients is so essential.

John (33:23):

Back in the days where I was really interested in autism, there was a saying out there, is don't try and fix anything else until you get your digestion correct. And you won't have any success until you get rid of the dysbiosis, if you get, yeah. That is a central feature. And maybe that's a central feature for all of us, since autistic kids are kind of canaries in the coal mine, that they're more susceptible to the toxic insults that are around us and maybe we're one just step behind them.

David (34:03):

That's a good point.

Martin (34:06):

So just real quick. And do you think that BrocElite and curcumin, that that synergy helps in all those manners?

John (34:15):

Absolutely.

Martin (34:16):

Yeah. That's what I was figuring you were saying. I just wanted to hear it.

John (34:20):

Yeah. Just make it clear. Yeah.

Martin (34:21):

Yeah.

John (34:22):

They're in the middle of all of those processes very clearly.

David (34:25):

Sure. So let's make it personal. What do you guys take? Do you take both BrocElite and CurcElite? Do you take it religiously every day? Do you take it when you need it? Do you not take it? What do you? So Martin, we'll start with you. What do you take daily?

Martin (34:44):

Yeah, there's no question. I take BrocElite with some form of curcumin every day, whether it's BrocElite with curcumin product or BrocElite separately. Curcumin really depends on what I'm looking for. If it's just at the gut level, or if I'm looking for curcumin getting to be bio available at the cellular level, because I've sort of overextended myself athletically or what have you. So, I am getting those two products every day. If it's allergy season, I'm probably a little bit more heavier CurcElite. I absolutely love the idea of [inaudible 00:35:18] and how CurcElite helps.

Martin (35:21):

I am genetically blessed to have some cholesterol issues. And so, BerbElite is also in my armamentarium. But I'd say consistently, I'm doing BrocElite with curriculum most consistently. Those are the things planned, depending on where I am.

David (35:39):

And so do you do that because you know it's good for you or have you felt the difference?

Martin (35:44):

That's a great question, David. Thank you. I don't want to get too specific or TMI out there, but there's no question that I am an IBS kind of guy. I mean, almost everything affects me. John or you saying, "Hey, you need to be out on a podcast" or "You need to be in front of a television." My gut goes nuts. Before a sporting event, before a big test in medical school, you could generally find me somewhere close to a bathroom.

David (36:16):

Okay. Easy.

Martin (36:19):

And so, my bowel movements vacillate and oftentimes will be loose. And with BrocElite with curcumin, I've seen a magnificent difference in the regularity and the health of what my stools look like. Again, maybe too much information, but absolute correlation. And that applies the same with taking the two separately. But BrocElite with curcumin has made a magnificent effect. An impression on me, quite honestly.

David (36:50):

John, what about you, as far as the do you take BrocElite and CurcElite together? Do you take them one or the other? Do you take them both religiously? What's your day to day look like?

John (37:06):

Interestingly, we spent so much emphasis early on in getting therapeutic doses of them and that was kind of single doses of each of them. So we could see an effect from a single just curcumin or just our [inaudible 00:37:28] product. I think taking a full dose of both of them for me is a little too strong. So I take half dose of both.

John (37:38):

And then I think for me, it's a very clear no trope where I get good brain buzz for a good six hours from that. And those are definitely every days. I have some symptoms that appear like long COVID. And so I'm doing specific stuff for that. Without getting into a new topic, like I'm taking some things in that area that look like anti COVID measures, which is helping a lot with ...

John (38:24):

I had blood pressure, went up when I got COVID and got the vaccine. And so it makes it easy to track, is if I'm on target, my blood pressure goes down. And so those are kind of things that you would think. [inaudible 00:38:49], zinc, quercetin.

John (38:53):

Interestingly, I'm trying one right now. It was Tocotrienols that gets into the sort of RANTES immunology world. And that is, it's turning out that that's one of the things that's part of long COVID, is RANTES being high and COVID debris persisting in macrophage and kind of traipsing all over the place, keeping everything inflamed. So that's magnesium and vitamin C. It's pretty much my routine right now.

David (39:33):

Great. Well, gentlemen, thank you so much for sharing about your experience, about your thoughts on synergy, microbiome, and thanks everybody for listening. We will be back next week.

Martin (39:45):

Thank you.

John (39:46):

All right. Bye. Bye.