Introduction to Dr. Walker and Amarasate

Welcome again to the Sleep Deep Summit. I'm your host, Dr. Audrey Wells. And for our next speaker, we have Dr. Edward Walker. He's a scientist and lecturer who believes that developing a healthy relationship with food is key for long term wellness.

Now, he's a Ph. D. scientist who works at the New Zealand Institute for Plant and Food Research. And over the past 13 years, his primary focus has been the investigation of plant based appetite suppressants that may reduce hunger and support healthy food choices.

This work led to the discovery and research into a compound called Amarasate, which is a novel New Zealand hops based appetite suppressant that shares an overlapping mode of action with the new class of effective GLP-1 based anti-obesity drugs.

Now, Amarasate is the active ingredient in calocurb, and that's what we're going to be talking about today. Welcome, Dr. Walker. Thank you for having me.

Yeah, it's great to kind of dove into this topic because it is certainly hot right now. You know, we have a couple of anti-obesity medications that use GLP-1 signaling as an appetite suppressant.

And I wonder if you can give me a little bit of background about Amarasate and how it was discovered. Also, how it sort of mimics a GLP-1 response. Yeah.

So it's it's actually a really interesting science story. So and in 2010, we got a $20 million New Zealand and New Zealand dollar grant, a six year grant to investigate novel ways to develop appetite suppressant plant based for sort of application and weight loss.

And one of the ideas that we we came up with was to use bitterness. So we all know you have bitterness on your tongue and that tells you a food is good to eat or not.

But you put something very bitter on your tongue. You want to spit it out? Well, the theory that we had was that if you got that same bitterness and you put it down past your stomach, into your small intestine, that it would trigger your small intestine to basically do the same thing inside.

The food is no good, but instead of having a conscious signal, have a subconscious signal that sort of goes to the brain and says, stop eating. Now, this this research was was based on ideas that came from from basically historical usage of better foods.

Bitterness in the Gut and Appetite Signaling

So if you look in history, you can you can say that bitterness was used to both increase and decrease appetite. So the Romans would use a bitter infuse the wine to drink before a feast like immediately before or face to increase their appetite.

But then if you were looking at suppression of appetite, that culture's all around the world would use bitterness. A couple of examples are in the Kalahari.

They used that as a cactus to decrease appetite when they going hunting, and they also use bitterness and Scotland in the highlands when they were having times of famine and they eat a bit of Heath Pate too to suppress appetite during basically during those times of famine.

Now, the reason we got interested in business in the gut was because that sort of historical dual usage doesn't really make sense. If it's working on your tongue because it's the business is on your tongue, then surely the effect would be the same.

However, if you then look and you say, okay, maybe it's in the gut, you actually have a series of hormones down your gut, and the first one in your stomach is a pro appetite hormone, so it can stimulate appetite.

So think what the Romans were having something just before a meal, you know, boost that appetite up. But then further down past the stomach, there's a series of an appetite hormones which are very potent one, one of which is GLP-1, and that they used to suppress appetite over a longer period of time.

So we thought maybe the specialness was being used to decrease appetite through the gastrointestinal tract, pass the stomach, and that's where the sort of the science started.

It was a long, a long process. And we did some sort of amazing studies along the way. You know, what I'm what I'm hearing already is kind of the natural effects that you're bringing out with these historical descriptions.

And I'm hearing that you're kind of harnessing that in the development of Amarasate. So how did that come to be identified? Yeah, so we did and we did a few studies.

The the first one, which was was probably the biggest investment of time on my part, was to actually validate that you had these bitter taste systems in the gut.

So when we started the project in 2010, we actually had an international expert on bitter taste come across. And he said, I don't think it works, is it?

I believe there's this bitter taste in the gut. And so we said, okay, well, Peter, he doesn't believe it. I believe it. But but what can we do to prove it?

And so we did a biopsy based study from an hospital. And so so what happened basically was I went into the hospital for two years and I asked people who were having routine guest stops or colonoscopy if they wanted to volunteer biopsies of their own test time.

So we wanted people who were healthy, who'd never had a gut condition before and who weren't diagnosed with any gut conditions. And so that made it really challenging because most people who go in for these procedures obviously have something diagnosed wrong with them or they've already got a condition.

So we wanted a healthy what we call a healthy phenotype. Most people said no, so I'd ask them and they'd be like, You want pieces of my gut? No way. But eventually we got 28 people to say yes and we got three samples from the stomach.

Three samples from the small intestine and three samples from the colon and one from the rectum, from all from these people. And we were able to show that you had most, but not all of the bitter taste systems in your gut that a prison on your tongue.

So most people, those on the tongue, you have 25. But the taste receptors, so the 25 and they take the whole broad spectrum of bitterness in the gut. Would this be sort of in the taste buds?

I think people kind of are familiar with the idea of taste buds. So you're saying that there's receptors for bitterness on the tongue and then also in the intestine?

Is that what you're. Also also in the intestine? If you think of it like the taste buds on the the tongue, that taste but has 25% taste receptors. So taste all of that, all of the range of bitterness humans can detect.

Now, in the intestine, we have a narrow spectrum. So most people have 17 of the or 17 or 18 of the of the 25

person. So your gut can't detect everything that you think, but it can detect a lot.

And we were able to show those bitter taste receptors or those best the taste buds all the way through the gut, right from the stomach, all the way through to the the the end of the large intestine.

And we were also able to show that they were localized in the same region as these appetite suppressant hormones. So that was sort of the first basic science study we did, which said, yes, bitterness in the gut is there in people.

And yes, if you triggered it, in theory, it should suppress appetite. Wow. Fantastic. So now that you've identified that, I would imagine the next step would be to see what sort of molecule or compound would trigger those receptors.

Yeah, absolutely. And that's exactly what we did. So we we sort of looked at what what Big Pharma does really and what Big Pharma will do in a situation like this is they will say, let's test as much as we can and see what works.

Screening Plant Compounds for Hormone Release

And so what I did was we got we got these cells from the gut that have the bitter taste buds and that have these appetite suppressing hormones in them.

And we grew them in the lab, so grew a whole bunch of them. And we then got we did what's called robot assisted screening. So we got about a thousand different plant extracts and basically compounds pharmaceuticals and we put them on to these cells and we basically looked to see if they would then release the appetite regulating hormones or appetite suppressing hormones.

So these cells we had would release GLP-1 and another appetite suppressant hormone called C, C, K. And so we went through and we just basically tasted a thousand different compounds and we tried to figure out what was the best.

You're looking for the signal above the noise. So which one was giving you the most robust response? Yeah. So this was a this was another interesting result we saw because on the tongue, you know, everything's bizarre.

You put lots of stuff on you when you target specific caffeine's better, you know, like a sort of a grapefruit is better, but only on these cells they really didn't respond to much.

So they're very hard to trigger and that kind of makes sense because of that bitterness in your gut was really highly effective at suppressing appetite.

Then every time someone has a coffee, they just they just wouldn't eat. So what we found out was you had to get something really, really potent. So it had to be really strong.

And we only had a couple of real options that came up positive out of the thousand that we tested, a couple of them were sort of small molecule peptides and they're not really suitable because they're highly unstable.

So to get them to the right part of the gut passed the stomach very difficult, very challenging. And the other option was New Zealand was New Zealand hops.

So hops you think of that, you put in beer. That's very bitter in some cases. And we tested those, all these different cultivars of hops and we found that one which we named tomorrow site was exceedingly good at triggering this anti appetite hormone response.

And so that's what we went forward with and to and to clinical research. Well, that's fantastic. And so serendipitous that this is a hops cultivar that is grown right there in New Zealand where you're working.

Yeah, yeah. It was it was it was really good. I mean, that the company that I work for, Plant and Food Research, is a sort of a government owned research institute and we actually have a hops breeding program.

So in some ways I had a little bit of, I guess, advantage that I had access to a whole variety of different types of hops and also a lot of a lot of chemical characterization.

So, so as part of it, we were able to not only identify the cultivar that was the most active, but we were also able to identify what the bioactive compounds were.

So what the actual specific part of the ingredient was that would make it work and the benefit of that as a means of fuel then taking it forward and you making a product out of it, you can standardize and you can test for that those bioactive compounds.

And that means, you know, you'll maintain an activity over the course of time and you know that, you know, one year's production is the same as the next.

And that's really important for the peace of mind for people who are taking a product you develop. Yeah, definitely. I know that's a concern of many people who like to use supplements for various things.

And so the American eight was going to be stable in its travel to the gut. And it's the it is the active ingredient in calico herb, if I understand correctly, how does it work?

How does MRSA work in the body if a person is is taking it? Yeah, yeah. So so we actually we actually had one more one more step. We have to we have to get to it before to make it work.

And this is and this is sort of the the building of the of the side story, every little steps and. Porter And that was that when you get these hops extracts, they're like a wax.

And so we actually, you know, what you do as a scientist, if you've got something, is you try it yourself. You don't tell anyone, but you try it yourself.

I would never admit to that ever. But it's it's a food grade product, so it's okay. So if it was a medicine, we get in trouble because this is supplements.

Alright. So you put it into a capsule and you try it and so we did that and we didn't really do anything. And then one one day we were doing it for a while.

One day we noticed that it would pass through your entire system, basically undigested. So it's a sort of a wax and it would end up as a wax in the toilet as well.

And so it wasn't able to disperse and the gut and of course it was not able to disperse out, then it's not going to have any effect. So we had to formulate it.

We had to formulate it to make it work. And so what we did was a series of model digestion. So what you what you basically do is you get a solution that's like your stomach acid and you put it on a mixer and you then add the you put the capsule into it and you watch what happens and then you transfer it into a solution that's like a small intestine past your stomach.

And so you model how it will break down in your gut.

Formulating Calocurb for Gut Delivery

And what we found is if you if you put this a capsule with this sweat extract and there's just like when we tried it, it would just go through and just at the bottom of this big club.

So you needed to add a small amount of oil to it just to allow it to disperse a little bit when it was in the intestine. So we formulated with a small amount of oil that basically let it go to the gut and disperse out of that.

Got it. So so that makes it more active, I would think, in a physiologic system. Yeah, absolutely. I mean, I think that if you didn't have that formulation, you would get no activity at all.

Yeah. So you have that that formulation is a key part. And also delivering it to the small intestine rather than to the stomach is also a key part of this slow activity.

Yeah, I happen to have a capsule here of shallow curb. It's a little yellow capsule and it seems that there's maybe the oil inside that I'm seeing as an opaque ingredient.

Yeah. So I can see how, you know, taking this, you would dissolve the capsule as it traveled down and then it would be causing an effect. So what? Where do people experience?

Who are taking this this ingredient? Yeah. So when we so the next thing we did basically was we did our mode of action studies. This is really saying, does that theory with bitterness will trigger those hormones that go to the brain to make you feel full?

Does that does that work? So that's testing it in people and showing what the effect will be for the general public when they take it. And so in that study, what we did was we got the the MRA site and we put it in a capsule that you just showed, which is called a delayed release like cap.

So basically what that means is that it resists digestion in the stomach and then releases in the small intestine where all these appetite suppressing hormones are, where these these hormones that make you feel full.

It's also it's also quite a it's a modified cellulose, so it doesn't contain any nasty ingredients. And that was really important for us. That would be a really safe capsule for people to take the the product.

Then disperses out and interacts with the lining of your stomach. Oh, sorry. Your small intestine, just like something would react with your tongue. And it triggers these cells.

And they called into our endocrine cells and they contain these taste buds and makes them release these appetite regulating hormones that then go either to either to your stomach and basically block it to they don't empty anymore or they go directly to your brain and regulate appetite centers.

So basically say stop eating. What was really interesting about about this, the result we got was that it was much more potent than we expected. So what we were expecting in the study was a small boost and maybe kind.

You'll be one and just for a short period of time. And that's not what we got. What we got was an almost doubling of the response that you get to a meal.

So every time you eat a meal, these hormones come out and tell you you're full. What we saw was a response to a meal, basically got double the K and double the GLP one.

And not only that, but it was also extended by a couple of hours. So instead of getting 2 hours of feeling full after a meal, people were getting 4 hours, sometimes more.

And we think that's because the way the way the the product interacts with the gut, it's quite persistent. So if you to for example, if you were to take that capsule and you were to split it open and put it on your tongue, no, I don't recommend you do this.

But if you were to, what you would find is the bitterness would build up over time, over about the 30 seconds, 60 seconds, and then you wouldn't be able to get rid of it for hours.

It would just sit there on your tongue and trigger and trigger and trigger. Now we think the same thing is happening in the guts. So it's getting to those those bitter taste buds in your gut and it's triggering them and triggering them.

And that's why you're getting that release of the appetite suppressing hormone for much longer than we expected for several hours. And that's really important for, you know, extending your what they call satiation after a meal.

So extending that period of fullness and suppression of hunger you get. That's really interesting. And the experiment of breaking it open onto my tongue does not sound like a fun one.

So thanks for explaining that. But I want to I want to really highlight a couple of things that you said for the folks who are watching and possibly taking notes, because what you're saying, it has appetite, suppressing effects.

And I want to clarify, does that mean that MRSA is clinically proven to reduce hunger? Is it clinically, clinically proven to reduce appetite and even calorie intake?

Yeah. So what we did in the studies, we've done a series of clinical studies looking at that. And again in that first study when we were looking at the mode of action of all of these hormones that go to the brain, making you feel full when people were given an eight to their full meal.

So they basically presented with two big bowls that are just filled with food and a plate. And you say just mixed those, mixed those together. In this case, it was like a pastor in a sauce and eat that until you feel full when they are on the placebo treatment.

So the the capsule which just contain no our site thank you so much food and when you gave them the MRSA capsule, they were about 18% less food.

Clinical Results on Hunger and Food Intake

So, you know, they were shown to eat a reduction of food after taking MRSA. So that was the first study and that's at 18%. So big decrease in food intake.

The next studies we where we did two for follow up studies which were based on fasting and so it was a 24 hour water only fast. And the reason for doing that is because we had this mode of action study and it's really beautiful, it's wonderful science, but it is a science study.

It's not people don't go and have those pills at these exact times and then have these blood tests done and so so it's a little bit artificial. So we wanted to say, okay, let's do a study where we're putting people through a real diet strategy and a diet strategy where you get hungry, you get food cravings and you feel empty.

So we chose 24 hour water only fasting because it's a challenge. You have like an acid test. And we measured these participants for the last 8 hours. So from 16 hours through to 24 hours where their hunger is the greatest, giving them or so capsules at 16 hours and 20 hours.

And so basically seeing if we could reduce the hunger that we're feeling during a 24 hour fast at the time when it's really challenging, what we were able to show there is in the study with men, we were able to decrease their hunger by an excess of 20%.

Now, what that means from a I guess, a behavioral point of view is that anything over about a 10% decrease in hunger is what you call biologically important, but that's likely to invoke a behavioral response.

So if you hunger is reduced by more than 10%, you're likely to be able to make better food choices and you're likely to eat less food. So we were able to show that in the men.

We then did a trial in females. And this is a lot more challenging because you have to think not only what day people are fasting on because people have different sort of hunger profiles based on whether it's the weekend or

all the weekdays.

But you also have to think time of menstrual cycle because you get a lot of menstrual cycle changes. So that's sort of one of the reasons why people do a lot of studies in men rather particularly appetite work rather than in females, because it's way easier to do than men.

It took like three weeks to get the guys through and it took us, well, getting close to nine months to get the females through, to get all of the all of everything lined up.

What I will say, though, is that the female participants are much better at filling in the questionnaires. The Timberwolves say you get all this noise because they'll be they'll be reading through the questionnaire.

I call you a tick, tick, tick, tick, tick, tick, tick. And it's done. Whereas the female recipients actually read all of the questions. So the data is beautiful.

It takes a long time, you get great data. And what we could show on the females is that they were getting almost a 30% decrease in hunger over that last 8 hours.

And when you really look at it, what you see is you see that. But how hungry that were, 16 hours is how hungry they are, 24 hours. So so it was a 30% decrease relative to the placebo, but it was also a flattening.

So they had no increase in hunger over that last 8 hours. And so that's a real potent change. So just like over hunger that we're at 16 hours into that 24 hour fast, that's the same hunger, though, but are able to maintain that hunger with no increase.

We also showed changes in craving food and these were really big changes. So the craving for food was actually lower 24 hours into the fast, but it wasn't 16 hours into the fast.

So the Inmarsat was able to reduce the craving from food and the placebo treatment obviously went up by about 20%. So again, really, really great changes.

We then gave them an eight a full meal. So this was again the acid test to say, Alright, you're feeling less hungry, here's a meal at the end of your 24 hour fast.

How much food do you actually going to eat? And we're using about 14% less food and that eat to your full meal. So in line with what we saw in the guys that were reduced by 18% in the first study, we were getting a reduction of 14% in the females when they're breaking the fast.

So reduced hunger during fasting and also reduced basically reduced behavioral response to that. So they're eating less as a result. So so really great results from that.

Yeah. And you know, you said something that I think is meaningful to repeat, which is that when research studies are conducted, there is such a thing as statistical significance, which may not be clinically meaningful.

But in this case, the MRSA was resulting in clinically meaningful reductions in appetite and even craving. Yeah, absolute and and very, very biologically important.

So very clinically significant. So we're talking ten, 10% changes what you call what you call clinically significant. And we're looking at changes between 20 and even up to 40%.

So you know. Well, really, really potent changes. Yeah, I would imagine that Calico Herb, which is containing the MRSA, is used to regulate appetite for people who are wanting to lose weight.

And this is a really important application, especially as these weight loss drugs are becoming available and yet very expensive or not covered by American health insurance.

Is there anything that you can say to kind of compare and contrast Carla Curb with the GLP one medications like Wegovy or Zap bound? Yeah. So so it's really interesting.

And of course, when we, when we started this work in 2010, those, those drugs didn't exist. So it's sort of almost, again, serendipitous that we developed a natural product that, you know, could boost up GLP one a release. So the drugs are synthetic versions for the most part of GLP one.

So when you when you eat your food, food goes to your small intestine and then your small intestine releases GLP one as part of making you feel full and also to reduce your glucose levels.

The challenge with GLP one from a pharmaceutical point of view is that it's not very stable. So your body has to be constantly releasing it or it stops working.

So technically the half life is what they call 2 minutes. So you can't really ingest GLP one by itself because it goes up and then goes down really quickly.

So what they did was they they basically changed the structure and they made it so it was more stable. So now it lasts for well, in the case of the Semaglutide.

So it will go by, it lasts for about two weeks, sorry, a week as a half lives. Now that makes it very potent for suppression of appetite, but it also makes it very unnatural as far as what your body's rhythms are.

So if you look at GLP one during the day, it will go up when you have a meal c breakfast it goes down again, then it goes up when you have lunch, then it goes down again.

It goes up for dinner down again. Then it's relatively flat during the night time. If you look at what happens to Semaglutide, so it will go by when you inject them.

The same would lose high level as high in the morning. It's high at lunchtime. It's high in between your meals, it's high in the evening, it's high all the time.

When you're asleep, it's high the next morning again. So it's not a biological rhythm at all. So it's it's really a block with them. And that's completely in contrast to how our site works.

So our site takes that natural response you have and boosts it up a bit higher and then extends it so glass a bit longer. So we're just boosting up that natural cycle.

And I think that that's really powerful for people because what it means is that they're not if they do happen to get a side effect from something like Wegovy, then those side effects can be relatively long lasting because that level is high for a long time.

But something like our side, the side effect levels are much lower. But if they do occur, they're very transient. So very short term because your levels go up and then back down again.

So you don't have to worry about those those long term gastrointestinal upsets. I think I think it's also it's also reassuring for people who are who are maybe not ready for a pharmaceutical, who want to do something that's a little bit more in sync with your body's natural rhythms.

How Calocurb Compares to GLP-1 Drugs

But they want to try something that's biologically active. You know, you're singing my tune because I as a sleep medicine physician, I am very concerned with biological rhythms and how that sort of lays over a 24 hour period.

So I'm constantly beating my drum for people about the importance of regulating your meal timing. I'm a big proponent of intermittent fasting. I love it when people regulate their sleep timing, not just getting enough sleep and

high quality sleep, but also making sure that their sleep period is fixed and as consistent as can be.

So that really resonates with me because what you're describing is a biological rhythm or even a biological processing of the empiricist, which is more mirroring what's happening in your own body versus the injectable medications that are GLP one agonist.

That's very interesting. Yeah. And I think that some it's more than just that it's mimicking your natural cycles. I like to think of it like it's, it's restoring your response.

I would say more about that. Yeah, because I think when we look at the sort of foods people have and the modern lifestyles, you get, you get your guts are not the same as they used to be.

But I believe personally that there's a big reduction in modern people about how their guts and their brains communicate and the Amarasate at a and at one level it's an appetite suppressant that might be able to help people with weight loss.

But at another level, it's also boosting up will restoring the ability of your gut to talk to your brain and then sort of modulate those signals? And although I'm not the sleep expert, you do get disruption and signals such as GLP-1, etc.

All these gut signals in general when people are doing shift work. And so there's definitely an interaction between your how your gut talking to your brain and some of these, you know, metrics related to sleep.

Well, you know, I my brain is going a little bit crazy right now, but I want to keep an eye on the time and really deliver what I think people are probably wondering at this point, which is if you want to try Calocurb, how does that go?

What side effects might you see? Who is it good for? What sort of results could one expect? Yeah, so I mean, the product has been commercialized so there is a it is available on Amazon.

I get I get nothing from sales. So I'm purely a scientist. I sign away all my rights are working for the New Zealand government. So what you'd expect.

So the side effect profile is, is quite, is quite low so we don't get a lot. What we do tend to say is in a few people they'll get what's called an acute bluestone response.

And so this is as you get used to taking it and it's essentially a pill with a flushing response. So usually not with any associated nausea and very rare cases.

We do get some people who get, again, acute nausea, but it's quite mild. So we're not seeing any large amounts of gastrointestinal side effects, just the occasional ones.

And again, transient in nature. So short term in nature, the way the way it's typically used is you take it an hour or slightly more if you want to before a meal, and it then reduces the amount of hunger and then reduces the amount of food you'll you take your own meal.

Or if you're fasting, you could take it an hour or so before your normal meal time. So, for example, if you normally have lunch at 12:00 and you're skipping lunch, if you took it at 11 or 10, you know, an hour or two beforehand, it would be fully active by the time your normal lunch hunger comes up and it would suppress that. Now.

Who Should Use Calocurb and Final Takeaways

Fantastic. I'm wondering, is there anyone who should not take calocurb? So, I mean, I'm I'm a scientist, not a medical doctor, but from a science point of view, if you have some major issues or something that's really like inflammatory bowel disease, Crohn's or ultralight of colitis, that's probably not a good idea.

Also, if someone had IBS, that was diarrhea predominant now. So if they're suffering from a lot of diarrhea because the most likely side effect, if you're going to get one, the most likely one will be low stool, then you would make your condition worse.

So if you had a bypass surgery as well, so if you had already had a bypass surgery or a stomach reduction, I'd talk to your doctor about that because that might alter how it works.

And we don't really have any data on efficacy. When you've had altered gastrointestinal structure. That makes a lot of sense. You know, the inflammatory, inflammatory disorders of the gut, chronic conditions of the gut, surgical manipulation of the gut.

I think anyone who's gone through that is generally sensitized to the way different medications and supplements can interact. So I want to say again, the the Calocurb Supplement is available on Amazon, which is how I shop mostly lately.

And you have a website as well, which is calocurb.com, is that right? Yeah. So the commercial partner who sells it has has that website. We also plant and food has a website which is just being refreshed, which is a motorcycle engine which will contain, I guess, more, more details about some of the scientific work that we have going forward.

That's really fantastic. you know, I think this presents a very interesting and viable option for people who are interested in reducing their appetite, even losing weight.

And again, from a sleep medicine perspective, this is the interplay between weight and sleep or food consumption. And sleep is something that I deal with a lot.

So I really appreciate you having this great information today. It's been a fantastic discussion. Dr. Ed Walker, very nice to see you. So thank you very much, everyone.

Have a good day.