Episode 32 – Ryan Shenvi: Ethnomedicine to improve learning, memory and mental health

Drew (00:04):

A warm welcome back listeners. Pleasure to have you with us. This is Science Changing Life, and I'm your host Drew Duglan today. We play with nature's building blocks as I'm joined by chemist Ryan Shenvi, whose lab investigates traditional remedies from the four corners of the world with the hopes of reconstructing them in the lab to develop interesting molecules for learning memory and mental health. First though, let's join Ryan as he considers what it does or doesn't mean to be a scientist and how he first approached the field of chemistry.

Ryan (00:36):

You were probably familiar with this big push for representation in movies and in many different fields. And I think that's also true in science. And I think that's really important, not just for, uh, representation of other people who will like you in that field or on the screen, but also for what you could say, self-representation. So like when I was growing up, I didn't have much of an opinion about myself, I guess, one way or the other, but I definitely didn't think of myself as a, as a scientist or having the sort of scientific streak, but you can think of yourself as an artist and you can still be great in science. You can think of yourself as a theater geek or band nerd or a jock, and you can still be great in science. And I don't think you have to think of yourself as a science to be great in science. You just be yourself and do the best you can. So I, I just think that sometimes, um, when you hear about people's childhoods, other people think, oh, I have to be like that if I wanna be good in science. And you know, I think what inhibits people there for, from going into science is the idea that they don't feel like they belong. I think that's true of a lot of different fields.

Drew (01:40):

Yeah, definitely. And I think, I think that applies to lots of things. I think we often sort of have our identity built on one thing and wanna exclude it from other things. So how did you, once you did kind of get into science, what was it about chemistry that sort of made things tick for you?

Ryan (02:00):

I mean, the funny thing is that I I've sort of learned chemistry more from like a top-down approach as opposed to a bottom-up. So what I mean is that I really never cared for a general chemistry that I had in high school or even early in college, which is nothing to say, you know, nothing against my teachers. It's just, I didn't enjoy it. I found it was very dry and it wasn't actually until I took my second semester of organic chemistry, that it really clicked at the time. I was also taking a course in discreet math and the logic of proofs. And there was something about that way of thinking combined with the visual framework, for understanding chemistry that I found really appealing and kind of drew me into this problem-solving process of synthetic chemistry, uh, synthetic organic chemistry in particular, where we're, we're putting molecules together and developing the logic to do that. And now as I've become, uh, as I've been in the field for a long time and I've appreciated the importance of all of the concepts in general chemistry, I've now had to sort of learn backwards from being a professor of chemistry to learn all the basics the other way around to top-down, I guess you could say.

Drew (03:19):

So you mentioned just then sort of organic chemistry and there's so many different types of chemistry. So what is the difference there between organic and inorganic chemistry? Because I feel like those are two major branches right there.

Ryan (03:32):

I guess, to put it simply organic chemistry mainly involves the chemistry of carbon as not exclusively carbon, most organic molecules contain carbon and hydrogen. And in addition, oxygen and nitrogen, and many of the molecules in biochemistry that additionally contain phosphorus. And to some extent, sulfur, this sulphation can occur. But for the most part, it's just a handful of little elements. Whereas in inorganic chemistry, you really broaden out to the rest of the periodic table.

Drew (04:04):

Got it. So that's where sort of metals come in and things like that.

Ryan (04:08):

Yeah, exactly. And that can be anywhere from alkaline metals. So those things like table salt, sodium chloride, or sodium iodide or magnesium, salt, or calcium all the way to the precious metals like gold or platinum or palladium.

Drew (04:24):

Got it. So within the type of chemistry that you do in your lab, what is sort of a broad overview of what you folks study and what the, the aims and, and the goals are of the lab?

Ryan (04:36):

Uh, yeah, so our research group is focused on chemical synthesis and put simply that's building molecules and in particular building organic molecules and synthesis in many ways, sounds a lot like construction work, which kind of gets a low value in our society, maybe unfairly. But you know, if you think about it about a hundred years ago, there were no skyscrapers. So it's not as though construction work is not without value. Or if you think about it, um, more in technological terms, fabricating a microprocessor is incredibly important and that is a construction process. So what we do is we construct small, mainly carbon containing molecules. And the cool thing about that is it's not following a set of instructions. It's not like assembling furniture from Ikea where the plan is laid out for you. Instead, it's a lot more like a game of chess where every atom you can think of as a chess piece and then every chemical reaction is a move you make or a move by your opponent.

Ryan (05:42):

And in this case, physics is in many ways, your enemy and it sort of a threat threatens to obliterate the pieces you've set up. So it takes really a lot of careful experimentation and analysis to figure out how you assemble all of your pieces, your atoms in the right positions. But then when you do, you know, you have a chance to explore the function of that small organic molecule. How does that particular constellation of atoms interact with a protein or cell or a tissue or an organism? I think, I think that's, that's both very challenging, but an awful lot of fun and potentially very important

Drew (06:26):

It is, but it's always so difficult for me to wrap my head around like this idea of inventing chemistry, like making new molecules. Like I, I never know. What's that starting point? Like how do you, how do you construct this idea of what it, what it will be like? Or if this will be useful in some way?

Ryan (06:43):

That's a great question. So, so there, there are a couple parts to that question. On the one hand, there are plenty of chemical reactions that are already known, right? So you take vinegar, you take baking soda, you mix them together in a poorly constructed clay volcano and you get bubbling occurring. And that is a known chemical reaction of evolution of carbon dioxide. If you take, let's say mineral acid, that you can buy like a hardware store and you take zinc metal of like pennies and you mix them together, you see hydrogen evolving from that metal, all sorts of reactions that are, that are known. And it turns out that many of these reactions are very selective. So if you take zinc metal and some mineral acid, and you put next to it, your wedding ring, which by the way, you probably shouldn't do. I mean, I'm really putting my money where my mouth is here, but, uh, and you, and you mix, you know, pour the mineral acid, it'll react with the zinc metal.

Ryan (07:39):

It won't react with your gold wedding ring as long as it's, you know, high carat gold. So the same is true of these small organic molecules. A lot of chemical reactions that can occur are actually quite selective for particular groupings of atoms. And so if you plan them correctly, you can sequence this, uh, these order of reactions so that you make exactly what you want each time. It doesn't always work that way. And a lot of times, because these molecules are essentially forced together in a way that they've otherwise never encountered each other before, because the atoms are, uh, held in a different position, different proximity, different constellation, sometimes the reacts you plan don't work out the way you expect. Right? Okay. So there's that side of it. And you have to then analyze what has happened and work around problems to come up with a solution, many times the best solution you can think of doesn't correspond to a chemical reaction that's known. And so then you have to invent a new chemical reaction. A lot of it happens by way of analogy. You say, okay, this chemical reaction is known. It looks a lot like this chemical reaction, maybe we can mix and match the components and they'll react in a new kind of way.

Drew (08:54):

Oh, that's interesting.

Ryan (08:56):

So it'd kind of be like, you know, okay, here you have a model T Ford that sure. Looks like a model T Tesla. Maybe, actually there is no model T, model S let's say, okay, so maybe we can take the guts of the Tesla and just put it into a model T and now we have an electric Ford.

Drew (09:13):

Well, I don't want this podcast breaking up people's marriages with that wedding ring experiment. So…

Ryan (09:19):

Don't try that at home. Yeah.

Drew (09:21):

It's funny. You said, um, you know, nature's construction workers, because I think I've described you guys as, uh, the molecular architects. What about that?

Ryan (09:30):

Yeah, I agree with that, but I would say one major difference. Well, may, maybe it's not a, maybe it's not a difference. Maybe it's just a personal bias. We care a lot about function. Okay. There can be molecules that look nice, but probably aren't worth investigating too heavily because they don't, they don't function in a way that's important to medicine. And in a similar way, there are plenty of buildings that are really idiosyncratic and beautiful or creative, but don't really work the way that a building is supposed to. So a great example of that is the Disney theater in Los Angeles. That's made of all these mirrored panels.

Drew (10:05):

Oh yeah.

Ryan (10:06):

The work of architect. Um, Gehry, Frank Gehry right. I actually, I really like his work, but the problem with of course, uh, mirrored architecture in Los Angeles is that it reflects the sun. And in this case, the Disney theater was positioned towards apparently apartment buildings that at a particular time of day had sunlight focused into them and were super-heated. So they had to buff down the surfaces and remove the reflectivity of the surface. So I mean, architecture is a, is a great analogy. It's true. But similarly, molecules have to have to be functional.

Drew (10:42):

Yeah. I've been to that Disney concert hall and it is brutal in the sunshine. Those are some good analogies. And so something you've told me and something I've seen on your lab website before, is this idea of using chemistry to kind of get medicines from industrial waste. So would that be kind of what you were just talking about using these sort of chemicals, maybe some of them would be unwanted or buy products from other things and sort of using different synthesis route to make some functional products from that?

Ryan (11:12):

Yeah, absolutely. There are many examples in chemistry of using industrial waste, which, which is a very graphic way of putting it. Many people refer to chemical feed stocks, which that themselves can be waste, but using those waste streams productively, and you think about it, this is a great service that chemistry can provide to repurpose waste that otherwise end up hopefully purified, but then sent out into ocean, let's say, or put into landfills instead you can upcycle some of these materials. So a, a great example is artificial vanilla, right? So we all probably eaten this. So the artificial vanilla you buy from the store. Yeah. Right. So this is not so real, real vanilla is extracted from an orchid, which produces a bean and you're extract it into usually ethanol alcohol. Okay. And you get the, the natural vanilla extract and it contains all these interesting aromatic small molecules, but artificial vanilla, which is much cheaper.

Ryan (12:06):

It actually comes from the one of two places, either the paper mill industry and waste from making paper or from, um, petroleum industry and purification of crude petroleum to make gasoline. Of course we don't, you know, the gasoline doesn't go into your vanilla, but instead what they do is they take a byproduct or purification of that thick, black, good crude petroleum, and the light hydrocarbons become gasoline. And then you have oils for lubrication, but there are all sorts of small molecules that can be repurposed and actually used instead of, instead of just being waste, that's burned and they can be repurposed. And in this case, one of those byproducts, it can be converted to vanilla, which is what smells and tastes like vanilla. And it's chemically indistinguishable from the stuff you get from the plant that small molecule. So there's no, there's no danger in it whatsoever.

Ryan (13:01):

As long as the quality control in the, in the food company is good, is gonna be identical to the natural vanilla. And the rational of course, is that the global demand for vanilla seeds, the production capacity of vanilla farms, right? So in many ways it's actually very environmentally-friendly to use this existing waste stream, not have to then plow, you know, many acres of forest to plant more vanilla farms and instead repurpose it to make artificial vanillas. So, so our research is basically based on the same general idea. Sometimes living organisms produce very interesting and useful molecules. There are many examples of potentially very useful molecules for medicine that are just not practical to obtain from the source of organism. Sorry. A great example to poster child in this area is Taxol. Taxol is currently used for non-small cell lung cancer and ovarian cancer, but you can't obtain it economically from the source organism, which is a Pacific yew tree. You have to strip the bark off the tree and it ends up killing the tree and it takes years upon years to reestablish the tree. So chemists developed means that synthesize it from a metabolite of a related plant, which could be, uh, it was found in the leaves. Okay. There's, there's a related small molecule called bactin, which is found in the leaves. You could harvest the leaves, regrow the plant very quickly, subjected to chemical synthesis and get Taxol then to doctors and to patients,

Drew (14:31):

Ryan takes a keen interest in ethnomedicine, which investigates how various indigenous groups developed and used traditional medicines based on bioactive compounds in the surrounding plants and animals harnessing this native wisdom. His lab is trying to explore their therapeutic value for modern medicine, particularly in the areas of cognitive and psychological health.

Ryan (14:54):

Yeah. So there are a few ongoing projects in the lab that overlap with we call disorders of central nervous system. So that includes not only mental health, but also, uh, memory and learning. There's a, there's a really interesting molecule that maybe we'll have time to talk about. That is a dissociative hallucinogen. And that also can be very useful for things like PTSD and depression. One of these is one of a number of small molecules from trees that grow in Papua New Guinea and Northern Australia. So, so this is, this is actually a fascinating story and it it's very much related to something you alluded to, which is that people kind of appreciate a lot of the medicines we have come from nature and actually in some ways more and more that's that's, um, I wanna say no longer true, but there are fewer, fewer examples of this.

Ryan (15:44):

Okay. But I think it's really important to remember that Western prescription medicine all the way from, you know, including aspirin, which is discovered by the Greeks, not aspirin itself, but salicylic acid, which is found in the, the bark of Willow trees. So all of Western prescription medicine comes from the apothecary. So the traditional apothecary prescribed mainly herbal remedies. And this is what we associated in apothecary was this practice evolved pretty quickly, even though it was in existence for thousands of years from the 19th and 20th centuries, this became the modern pharmaceutical industry. So our story, in some ways, the story related to Papua New Guinea begins also with this idea of ethnomedicine, which is another way of saying a study of traditional medicine from the perspective of modern science ethnomedicine is kind of fascinating, cause it combines anthropology and botany and chemistry and pharmacology.

Ryan (16:42):

Essentially you are investigating the traditional medicine or ritual of a people group that's different than yours to figure out how, how do they handle with, how do they handle maladies that you normally encounter. So in this case, this story comes from work of these, um, anthropologists named Hamilton and Glick, and they reported in the 1940s through sixties, the use of certain plants in the medicine, the ceremony of people from Papa new Guinea. And what was really interesting is that they discovered a connection between the bark that was being used in Papa New Guinea and a collection of related trees in Northern Australia, which had been studied for a collection of molecules. Um, a certain kind called alkaloids that are, were found in their bark, but people really didn't know what these alkaloids did. So what we're really interested in is leveraging our skills in chemistry to access these molecules more economically in a more environmentally friendly way that doesn't require stripping the bark from these trees and trying to figure out what receptors in the, in the human brain are actually being targeted by these compounds. And we're really interested in figuring out what causes the hallucination that's observed in the ritual.

Drew (17:53):

Wow. I mean this space in the hallucinogens I think is really, really growing and I mean you're on the inside. So do you see a lot of compounds that are gonna be useful? Do you think for sort of mental health and PTSD and all these other applications?

Ryan (18:07):

Yeah, there's a, there's a great question. I don't know that I'm qualified to give an answer on the utility of some of these compounds, but the science behind it is actually pretty fascinating. Some of the compounds we're working in are dissociative hallucinogens, and those have generated a lot of excitement because to put it in layman's terms, which are really the terms that I understand some of these concepts and what they do is they dissociate one sense of personality, one sense of person, one sense of localization. And it does. So by inhibiting, what's called the default mode of the brain. So it's really interesting. I mean, I'm, I'm not that well versed in FMRI. So this is using MRI to study areas of activity in the brain, but basically when you are alone, when you're alone with your thoughts, you're accessing, what's called the default modes, particular area of the brain and a particular connectivity in the brain. And what many of these dissociative hallucinogens do is they shut down that connection. And so you lose your sense of self.

Drew ([19:10](#)):

Right

Ryan ([19:11](#)):

And as I understand it, this is actually potentially very important for things like depression or anxiety, where you may feel that something is tragic. You may feel the feeling of tragedy, even though circumstantially, you may not be surrounded by tragedy. So if you can break that connection where your sensation of what is real and what is true has become disconnected, it can actually give you yourself some great insight into the reality of your circumstances. And so some, uh, patients with resistant depression that have been on antidepressants and has been little to no help have found great relief in some of these dissociative hallucinogens being repurposed, um, not for recreation, but for therapeutics.

Drew ([20:01](#)):

Another ongoing project in Ryan's lab involves an ominous sounding compound called picrotoxin. This molecule has shown promise for memory and learning disorders, but as its name suggests, if it acts on the wrong areas of the brain, it's potentially harmful. So Ryan's team is busy tweaking its molecular makeup, turning this age old compound into a longer acting drug that would have no toxic side effects.

Ryan ([20:27](#)):

This is a substance that was isolated from a plant and it was found to be the poisonous principle. So kind of like morphine was the principle of the opium, poppy that caused sleep or analgesia. So, I mean, this is so old that you'll find reference to it in Charles Dickens' work.

Drew ([20:48](#)):

Oh no way.

Ryan ([20:49](#)):

It was amazing. He, he edited a serial magazine in London that commented on there were, there were short stories and small opinion pieces, and one of them bemoaned the adulterants that were added to the brewing of beer in London. And one of them were the seeds from this plant and make this toxin because if you get a sub lethal dose anyway, it's kind of excitatory. And so then if you mix it in with the hops that are used for brewing of beer, you get the effect of the alcohol, but you also get the excitatory effect of this toxin. So it's a little bit scary actually. I mean, so what our lab is interested in in a general way is if you think about this constellation of atoms a little bit like the constellation of pieces on the chessboard, what we'd like to do is make a single change, like pulling that piece out of the chessboard that simplifies the problem.

Ryan ([21:39](#)):

Can you change the structure in such a way that you can get check me in just one step, but potentially helps the function. This is what we've done with picrotoxin. So what we did was we took picrotoxin and we actually added something to it. And we said, huh, if we make that change, it's probably not gonna change its function. It's probably still gonna bind the GABA receptor, but it could actually stabilize picrotoxin against degradation. And it sure looks like it's gonna make the synthesis a lot easier. It turns out that, uh, it actually makes it much more selective against invertebrate receptors. And so it doesn't cause toxicity in mammals, but also significantly stabilizes it towards degradation in water or blood, which is pretty amazing.

Drew (22:32):

Wow. That is exciting. Yeah. This idea that you can just make one subtle change and leave a lot of the function intact, but then also make it easier to, to produce as well. And I mean, I'm just shocked at the wrong beer and, and we could have just not had any Dickens.

Ryan (22:48):

Yeah that's true. It's pretty amazing. The people have tried to use this substance for years in medicine. At some point it was recommended as an antidote for barbiturate poisoning, but I guess the therapeutic window for getting therapeutic effect versus killing somebody was just too narrow. So now is not really recommended for any use except as a tool.

Drew (23:10):

When you're not engaged in chemical synthesis. What are some of your hobbies and passions outside of the lab? I think, I think I've seen you with your kiddos before.

Ryan (23:19):

So I have four kids seen us probably at the park. I don't know if I've been with all of them at the time, but for, for a good six-year period, they all had to be with me at all times because my wife was in residency.

Drew (23:32):

Wow.

Ryan (23:32):

So she was just not around, it was not her fault, but you know, she was working 80 hour work weeks and sometimes working overnight. So, so now, now I'm trying to get back into getting into shape a little bit more. I've always, I've always really loved, uh, listening and playing music. So I'm getting back into piano. I'm trying to balance music. I really love with his jazz versus the music I'm actually good at, which is just playing sort of standard classical pieces. Because I'm just not, I'm not a good jazz pianist, but I really love the music of Chopin and Debussy. See, and then just for a little fun, I've thrown in some Scott Joplin rag time

Drew (24:13):

Fun. I feel like there's this fun confluence between science and music. Actually.

Ryan (24:18):

There's a lot that is in many ways, all consuming in so far as it's a large creative endeavor, all these multiple components that you're trying to put together. I've never composed a symphony. But I imagine that, you know, some of the projects we have in lab are a little bit like that, where you have these many different strains that were all trying to put together into a cohesive story.

Drew (24:40):

You're conducting molecular symphony. I would say

Ryan (24:43):

Thanks. I'll I will, I will steal that analogy in the future.

Drew (24:46):

Yeah. You can have that one. That can be one of your, uh, testimonies.

Ryan (24:53):

Yeah.

Drew (24:54):

Cool. All right. Well I'll just end it with this question and you sort of alluded to a bit of this at the start, but it could be even more broad. So if you could give just one piece of advice or your wisdom to anyone in the realm of work, uh, or it could be career progression, life health self-improvement what do you think it would be and why?

Ryan (25:11):

I don't know. Listen, what I almost tell people is if you just do a good, honest job, that'll take you so far, right? You don't have to spin. You don't have to dominate. You just do a good, honest job and be yourself. It's tough because you can't say you can't guarantee success. A lot of success is circumstantial. Even if you fail, you can still look at yourself in the mirror and say, I did a good, honest job,

Drew (25:38):

Right? Yeah. I think hard work and honesty are some of the best currencies.

Ryan (25:43):

Yeah.

Drew (25:44):

Well that brings today's chemistry lesson to a close. And it's amazing to think that with a bit of molecular magic, we could unlock scores of medicinal products that appear all around us in nature, providing the next potential therapeutic for physical or mental disorders. A huge thanks to Ryan today for breaking this down for us with some fun history thrown in and thank you, lovely listeners for tuning in. If you appreciate what we're doing here, please take a second to hit a star rating on Spotify or wherever you listen to podcasts, it will really help us to get these life changing discoveries to as many people as possible.