

Episode 81: Alexander Shulgin - The Man Who Shaped Modern Psychedelics

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Transcript

Welcome back to the Tox Lab.

I'm Rebecca.

I'm Rob.

This week we're taking a look at some history and this is the story of one of the most controversial figures related to toxicology. We've talked in the past about some controversial stories from toxicology. We've talked about Albert Hoffman and his famous Bicycle Day. We've talked about the infamous cocaine bear that was turned into a movie. This week we're turning our attention to I think perhaps the most controversial of all and that is Alexander Shulgin. Before we dive into today's episode if you want to stay up to date with our content you can find us on Instagram at @the_tox_lab. We also have a page on LinkedIn and we're fairly active on there and for those of you who don't use social media but still want to get in touch with episode suggestions or comments for episodes you can check out our new website at thetoxlab.co.uk. So Alexander Shulgin doesn't already hint at one of the most controversial characters. Why don't we take a look at his life?

Who was he?

Where did he come from? So Alexander Shulgin was born on the 17th of June 1925 in Berkeley California. He studied organic chemistry at Harvard before dropping out to join the US Navy where he served on the USS Pope during World War II. During his time at sea he decided to memorize a chemistry encyclopedia thinking it'd be a neat challenge.

And who does that?

I don't know. Chemistry encyclopedias are not easy books are they?

No they're very dense. Very dense, a lot of formula, a lot of big words.

Who memorizes a chemistry encyclopedia?

Someone very special I would argue. He returned to Harvard after leaving the Navy earning his bachelor degree in 1949 and a doctorate in biochemistry from the University of California. After this he began doing postdoctoral work in psychiatry and pharmacology and then worked as the research director for BioRAD labs for a brief period. So I'm going to interrupt you here. Other than the brief period in World War II, his life so far possibly quite similar to a lot of our listeners.

Yeah. Good upbringing, studied hard at college, university, got his undergrad degree, got a doctorate, went to work in chemistry. He then took a job working at the Dow Chemical Company where he invented the first known biodegradable pesticide which is known as mexicarbate, also known as zectrom. And this pesticide made Dow a huge amount of money and gave Shulgin the free rein to pursue his own interest. And that is the dream of many of us, right?

Yeah, get to kind of mess about with what you want to at work, get paid to do it.

This sounds great, this sounds brilliant. On the 16th of April 1960 Alexander Shulgin tried mescaline for the first time and this was documented in his lab notebooks and these are really interesting and I'd highly recommend going to check those out. They've been scanned and transcribed since 2008 by a team of staff and volunteers at Ereward and alongside members of Team Shulgin. So let's consider what's going on culturally at this point in time.

1960. So the World War II had happened.

Yeah.

We're in this post-war era. LSD had been synthesized many years earlier and Albert Hoffman's famous bicycle day trip had happened and psychedelics were occupying a almost pharmaceutical space where they were considered to be therapeutic agents. We weren't quite in the sort of countercultural drug movement yet but there was increasing sentiment. The situation in Vietnam was going on in the background and that was probably influencing culture a bit as there was this rise in the sort of anti-war, anti-establishment movement. So we're going to dive into his very first trip report and there's quite a few quotes that I've taken directly from his lab notebook. So on the 16th of April 1960 he took 400 milligrams of mescaline sulphate in water and described this as having a slightly bitter taste but this wasn't unpleasant. After half an hour he noted noticeable intoxication and was experiencing some nausea which he treated with 50 milligrams of cyclosine. He noted colour and movement distortion three hours after taking the mescaline with maximal effects being reached at four to five hours and he started having noticeable signs of clarity from the drug's effect at six hours with only a few symptoms remaining at eight hours. A mescaline has a long history prior to shulgin. It's found naturally in a few different cacti. Cacti have long been used for their hallucinogenic properties but in this case this wasn't cactus derived. This was synthetic mescaline that had been made in the lab. He noted that when his eyes were open he experienced visual distortion and he described altered depth perception with distances between objects being incorrectly judged although and I quote on the conservative side so that danger is automatically avoided by an overly large margin. He also talks about a remarkable increase in textural and detail perception and objects seem to be in rapid and continuous motion and people's faces seem to distort and crawl into different shapes. He described colours as being most striking with many subtle hues becoming nearly phosphorescent in intensity and subjective time was also lengthened. And this is consistent with what a lot of people describe with psychedelics isn't it?

I've heard things described like for example the corridor was longer than normal or the floor was shinier than normal and things like that. When his eyes were closed he described and I quote a world of motion and colour. Generation of ex-centrally evolving clouds in intense colour usually evolving from darker shades of blue and purple through green or red green to lighter shades of pinks and reds. Also geometric patterns either in the form of coloured wedges of light usually passing from left to right or in rectangular symmetrical shapes often with erotic suggestions. I don't know what that means that's a direct quote isn't it?

That is a direct quote. I think there are so many interesting descriptions in his lab notebooks as I was drawing through I went down many rabbit holes for all the different trip reports he's written about and his descriptions are really vivid. Maybe we'll come across some more later. During the initial phase of the intoxication he stated that everything seemed to have humorous interpretation with people's faces in caricature and smaller cars appearing to chase larger cars. He also described having extreme empathy for all small things including stones and flowers and he believed it would be impossible to harm anything while under its effects. His closing comments in this trip report are as follows The overall effect is very pleasant. The desire is strong to repeat the experiment on both small doses to perhaps permit one to be alone in safety and on larger doses. Also to repeat the experiment under a

variety of external stimuli with music available for contemplation at the beach at night. There is complete recall of all experiences and thoughts after the drug has been dissipated. The feeling of comfort, introspection and tranquility that remains afterwards may indeed have an effect days after the treatment. One feels that this feeling may be prolonged and further enjoyed upon repeated usages. Such a change would be most desirable in many personalities and may bespeak a therapeutic value for the drug in cases of anxiety and tension. So clearly he saw a potential therapeutic role for this compound and this is similar to what Albert Hoffman described, isn't it?

Yeah. He said exactly the same thing or words to that effect.

So what happened next? We've got this highly educated scientist working at a chemical company, free access to a lab and a whole host of chemicals, synthesized some mescaline, enjoyed the experience. So this whole experience led him to move into the world of psychedelics and whilst working it down he experimented with synthesizing different drugs based on the structure of mescaline, purifying them and would then take that drug starting with low doses and increasing this until he found the dose that caused an effect and then he meticulously document these in his lab notebooks. He also had trusted friends who would also take part in these experiments or would act as observers and during this time Shulgin came up with a rating scale for the subjective effects of the psychoactive substances at a given dose and at a given time. And he synthesized, I mean in his lifetime, hundreds of compounds but at this point it wasn't just a handful. There were lots and lots of compounds all synthesized, lots of different variants and then he proceeded to write them down in his book as to whether they had an effect or not. So a minus meant that there was no effect observed of that drug. A plus minus was that the level of effectiveness of a drug that indicated a threshold action. A plus meant that the drug is active and chronology can be determined but the nature of the drug's effects are not yet apparent. Two pluses meant that both the chronology and the nature of the drug are unmistakably apparent but you still have the choice as to whether you will accept the adventure or continue with ordinary plans so the effect can be repressible.

And I really like that quote. I do but I also don't understand it. So these are compounds where there's something going on but you can just choose to ignore it?

Yeah I think it meant that at that dose you could kind of go with it or you could repress it.

Okay. But I think that must be very like individual dependent.

And dose dependent.

Yeah all of these are at specific doses.

Oh okay that makes sense. Three pluses meant that the subject is totally engaged in the experience. Four pluses meant that a transcendental state had been reached or so called a peak or religious experience or a divine transformation. And this is not connected to the one to three pluses as a measure of the drug's intensity this was a whole separate rating that Shulgin had.

Okay so one to three was the strength and then four was this is a religious compound.

Yeah. In 1966 Shulgin left his job at Dow and set up a home-based lab known as The Farm. He taught classes at local universities and through his friendship with Bob Sager who was head of the DEA's Western Laboratories at the time began holding pharmacology seminars for DEA agents supplying them with various samples of different compounds and he also served as an expert witness in court. He went on to obtain a DEA scheduled one license for his lab allowing him to synthesize and possess illicit drugs on the farm.

Now other than the obvious synthesizing drugs and testing them on himself. Again this is a life similar to many of our listeners right?

Yeah so now we're going to touch on MDMA. So Shulgin referred to himself as the stepfather of MDMA. MDMA was first synthesized in 1912 by Merck and patented in 1930 as an intermediate of methyl hydrastinin which was being investigated as a hemostatic agent to stop bleeding and it was patented to basically stop competitors from using the same synthesis pathways. Shulgin had first synthesized MDMA whilst researching methylene deoxy compounds at Dow but never tested this on himself and then in 1976 he had heard from a student about the amphetamine-like content of methylated mda which is MDMA and then synthesized it and tested it in September 1976 and reported his findings at a conference in Maryland alongside David E.

Nichols. They described it as an easily controlled altered state of consciousness with emotional and sensual overtones and he introduced this compound to Leo Zeph who was a psychologist who used it in small doses to aid talking therapy and Leo Zeph further introduced this compound to other psychologists including Ann who met Shulgin in 1979 and they married him in 1981. And we could not tell this story without touching on Ann, his wife, could we?

Definitely not. She played a very big role in a lot of the work and was involved in like self-testing a lot of these compounds as well. And let's quickly look back at that MDMA and how he introduced it to a psychologist. He was using it to aid talking therapies. We've only in the last five or ten years started allowing research that uses MDMA to aid talking therapies again and this was in the late 70s. So as I said earlier Ann became very involved with this research and together they wrote a couple of books including Pycal which is Fenthyamines I've Known and Loved which was written in 1991 and Tycal which is Triptamines I've Known and Loved published in 1997. And both of these books are split into two parts with half being a fictionalized autobiography about their lives and the second half describing detailed synthesis instructions, determinations of potency, doses and duration of effects of a huge number of drugs. So Fenthyamines I've Known and Loved contains entries on 179 different psychedelic compounds including MDMA and the synthesis method that he describes to MDMA is the most common clandestine method of synthesis and is still used to this day. It also contained details of the magical half dozen which refers to the most important Fenthyamine compounds in children's opinion and these include 2CB, 2CE, 2CT2, 2CT7, Dom and Mescaline. And Dom was really interesting actually because Dom was one of the compounds that escaped. Shulgin had synthesized it, he had tested it with his friends and in 1967 there was what could be described as the first public health crisis relating to a designer drug. So Dom or DOM stands for 2,5-dimethoxy-4 methyl amphetamine and this is a substituted amphetamine compound and it had another name, a street name, went by the code STP and there's some debate as to what this stood for but the most commonly written down translation of STP is serenity, tranquility and peace. And so this started off as one of the compounds that Shulgin had synthesized, he had tested it on himself and his close friends and in the late 60s again considering the context, Vietnam ticking over in the background LSD had seen its rise, in the late 60s LSD was banned and so some associates of Shulgin considered that this could be the legal replacement for LSD that they had all been looking for in this post-ban era. And so one of Shulgin's friends, Owsley Stanley, really saw this as the drug that they were looking for and it's a little bit unclear as to what actually happened because Shulgin was very careful, he only had his trusted friends, he kept things to himself, he only shared things with people who he really worked closely with but the story goes Shulgin had actually given information about the synthesis and how to make this compound. And so in June 1967 the summer solstice in this neighborhood in San Francisco, the Haight-Ashbury neighborhood, quite a famous neighborhood, there was in true late 60s style a love-in and tablets were distributed free to all these people at this party. It's unclear how much DOM was in these tablets but the suggestion is it was around 10 to 20 milligrams a tablet and DOM's quite active in the low

milligram range so these were really really really highly dose tablets and it's also got a slower onset of action so people were perhaps taking one not being aware that there was much going on and so taking another one. Common story we sometimes see with MDMA today and there was at this love-in a lot of adverse effects something like 60 people actually sought medical attention after taking these tablets freely distributed. My understanding is that no one came to any serious long-term harm that the worst that happened was people experienced prolonged psychedelic experiences but it was perhaps the first public health crisis relating to an unknown compound and crucially that was being used as a replacement for something that was probably less toxic but had been banned. This was the late 60s if you've been listening to the ToxLab until now you'll know this is a story we see all the time but I do think that this is a fascinating cultural story actually shows how interesting pharmacology can become toxicology if the dose isn't really understood or known you don't quite know what you're distributing to people don't people don't really know what they're taking yeah and that was kind of what happened here. The book Tripped Means I've Known and Loved discussed 55 different tripped means and followed the same sort of theme as the fentanyl means I've known and loved and included reports on Ibogaine DMT and Humala alkaloids among many others. Two years after Fenthilamines I've Known and Loved was published the DEA raided Shulgin's lab and requested that he surrender his DEA license for violating its terms and he was also fined \$25,000 for possession of anonymous samples sent to him for quality testing. Richard Mayer who was the spokesman for the DEA said that and I quote, it is in our opinion that those books are pretty much cookbooks on how to make illegal drugs. Agents tell me that in clandestine labs that they have raided they found copies of those books. And I think he probably had a point.

Yeah probably. They do describe in great detail some of the synthesis pathways. Shulgin passed away on the 2nd of June 2014 aged 88 and is said to have more than 4,000 psychedelic experiences during his life. His favorite psychedelic of his own creation was 2CB although in later life when asked what his absolute favorite mind-altering drug was Shulgin famously joked probably a nice moderately expensive Zinfandel. And I'm going to argue that this was the most controversial thing he ever said.

Because I cannot stand a Zinfandel.

Fair enough each of their own. He had such remarkable life didn't he?

Yeah. I think the reason why his story touches me is I don't make drugs in my lab and test them on myself but there are parts of his life that do intersect with mine. And I think also we just wouldn't be where we are now if he hadn't done what he did.

Yeah for sure. He had such a shape on the compounds that we now know about. The compounds that we now have to keep an eye out for in our case work. All because of the work that he did.

Yeah I really enjoyed reading for this episode and taking a dive into his ad-lib books. I only got through the first two. I think there are like six or seven that are available on Arrowhead. But they're just so fascinating the way he describes his experiences. How meticulously he documents like each dose and the time he took it and whether he felt an effect or anything and different people's experiences on different doses. It's just really fascinating and I think without that we wouldn't have such a good understanding of psychedelics. So was he reckless or was he careful?

A bit both.

I think that's probably fair. You wouldn't get away with the ethics of doing what he did now.

No definitely not.

But I think you're right. I think he was careful when he synthesized a new compound. He always tested a very very small amount first.

He didn't go jump all in. He understood that some of these compounds could have potential dangers. So we said he's controversial and I think it's fair to say he's controversial. Was he controversial because of what he made? Or was he controversial because of what he wrote down?

That's a good question. I think it's a difference of opinion isn't it?

I think so. The line at the end about the DEA saying well look these books are just chemical synthesis pathways and it's completely fair.

That's exactly what they are.

Yeah. As well as all the other bits obviously. But it is basically a how-to guide of how to synthesize MDMA and a load of other psychedelic compounds. But is that knowledge in and of itself something we should censor? I mean the issue is is people having access to it in a completely uncontrolled environment with people who don't know what they're doing and whose main goal is to make money off of it. I think that's where it gets really dangerous is when it gets in those sorts of circles. And the synthesis of compounds like MDMA actually carry with them chemical risks in the process as well and then produce lots of toxic off products that clandestine labs need to get rid of.

Yeah no of course there are a lot of issues with clandestine synthesis of some of these compounds. I guess it's a whole question around what should be kept hidden. Could you imagine if you worked at a university today? Oh he'd never been able to do any of the stuff that he did. How long before the ethics department shut him down? More general then, can self-experimentation ever be considered good science? I think it has its place in history like without Shorgan synthesizing these compounds testing them on himself working out at what doses you're seeing different effects. We'd never have that information today if it hadn't already been done. I just think it also carries with it so much risk. Obviously people have different ideas of what is risky and what is not. Some people may think the benefit outweighs the risk of trying new compounds that might have like a desirable effect but you've got to be pretty sure you know what you're doing and what you've made is what you think you've made.

That is fair I mean it does still happen occasionally. There was a very famous paper on flubromazolam a few years ago where a volunteer took a flubromazolam sample and the paper documented the experiences of the individual. That was done in a controlled setting with a medical person on standby. Somehow they got that through the ethics department.

Yeah and also for the general publisher I feel like it's also quite a big thing as well.

Absolutely. So let's quickly look at MDMA because I think that is perhaps his most famous legacy.

Yes I think it's also the one that's most misunderstood because I think a lot of people think he was the first person to synthesize MDMA.

Yeah that's fair yes that's true although it sounds like it probably wasn't used as MDMA.

Oh no.

Up until shulgin. I think this is probably the compound that has seen the biggest explosion into culture and again I think it probably really was a continuation of the previous culture waves.

Yeah. The LSD culture and then eventually MDMA becoming peak 90s rave culture. I mean people don't call 90s rave culture counter-cultural in the way we talk about the 60s.

Yeah. But it was essentially the same wasn't it? People having these illegal raves in warehouses taking MDMA. History seems to go in circles in that regard.

Oh for sure yeah. So some of the compounds that shulgin's famous for synthesizing like TCP we see on the recreational drug market do you think there's a chance that some of his lesser known drugs that he synthesized will make their way into mainstream?

That's a good question. So there was a little run of the DOX compounds of which DOM was a member that they very briefly came onto the psychedelic scene being sold as a fake LSD. I think in order for a compound to break into the illicit drug market two things need to occur. Firstly it needs to be something that people will want to take. Secondly synthesis needs to be able to be done at reasonable scale. I don't know how many compounds within shulgin's work fit into those two buckets but I think it's always a possibility. I am going to put it to you that these books have been published a long time and the pathways are there. I suspect if any of these were going to emerge they probably would have done so.

That's a fair point. But I think they probably have shaped what has emerged. Certainly reading these books gives you an idea about some of the group substitutions things that we've seen with other classes of drugs. So is shulgin a hero or a villain? I think it depends on who you ask.

Yeah that was an unfair question because I think it's not a binary thing at all. In my view I've got a lot of respect for him. I think he changed the understanding of drugs as we know them and he did so at a time where particularly in his early work he wasn't breaking the law.

Yeah. Later on perhaps but the DEA eventually shut him down. I think that that really is an unfair question and his legacy is both revered and vilified by different groups of people and I think probably actually the truth sits somewhere in the middle. He was a man who did some incredible work scientifically.

Yes it was controversial and yes it perhaps shaped for example the rise of MDMA that occurred much later but that doesn't mean at the time he was a bad person doing bad things. I think he also opened the door of using psychedelics in a controlled way to help with a variety of mental health conditions and a lot of that work stopped as these substances have become controlled but it's now starting back up again and so I think that time and that sort of experimentation has had value.

I think that's completely fair.

Yeah I think that's completely fair. We discussed this didn't we when we talked about Albert Hoffman but exactly that that following the ban any therapeutic research stopped and it's only recently in the last 10-15 years started to pick back up and we are starting to see positive trials using some of these compounds in a therapeutic context and actually in some ways we're 20 years behind where we could have been in terms of that research. I think we're going to wrap it up here. I hope you've enjoyed this week listening to us talk about as I say easily one of the most controversial figures in toxicology history, drug development history, psychedelic history. If you've enjoyed listening do give us a like, give us a follow, follow us on your podcast platform like Spotify or Apple podcast or go and follow us on YouTube. And if you want us to do a deeper dive into any of the compounds that you're going to send us forward do let us know in the comments or you can send us a message on our website. Hope you all have an amazing week and we'll see you next time.

Bye!