What's Killing Vapers? A Conversation with Steve 'The Mad Chemist'

By Josh Bloom — October 8, 2019

Steve, the Mad Chemist, and I go back a long way. We were postdocs together (about 200 years ago) and later worked for the same pharmaceutical company for a decade. We are both deranged (See Blowing Up Your Lab Mate Is A Bad Idea, But It Sure Is Fun [1]). He is also the best organic chemist I have ever known.

So when a tricky chemistry problem comes up, I'll often shoot him an email to pick his warped brain. There sure is a tricky chemistry problem in the news now. As recently as mid-September the lung damage that people who were vaping (mostly) marijuana chemicals was attributed to oily additives (vitamin E acetate was the prime candidate) collecting in the lungs (See Can Chemistry Explain 'Vaping Lung?' [2]).

Not anymore. Researchers at the Mayo Clinic published a paper [3] in the New England Journal of Medicine in which described the damage as being consistent with inhalation of a reactive toxic chemical. This automatically piques the interest of organic chemists, since “we” are responsible for chemical warfare agents like phosgene and mustard gas. It is highly unlikely that anyone could put mustard gas into an e-cigarette cartridge without killing himself and phosgene decomposes rapidly with water; it would not survive the cartridge solution.
So, what the hell is in there? It has to be toxic to lung cells but stable enough to survive the conditions in the cartridge. The most likely candidate (at this time) is probably a reactive electrophile (1) that survives long enough to get into the lungs where it reacts with (presumably) cellular proteins causing cell death. This would explain the severity of the cell damage seen in the pathology slides.

It was time for Steve.

JB: I’m thinking that a reasonable suspect would be one of the electrophilic aromatic aldehydes (2) used as flavorings, something like cinnamaldehyde or anisaldehyde, probably in a very high dose.

Steve: Yeah, or possibly a change in pH in the area where the mystery molecules land in the highly sensitive tissue of the lungs and airways (3).

JB: That’s pretty lame. Is that the best you’ve got?

Steve: It’s possible that it could be a variety of chemicals, maybe not even reactive ones. In what universe do you think dumping any aldehyde or carboxylic acid or amine or hydrocarbon into your lungs is benign? And that’s the problem. This s### is the new snake oil for what ails you. No quality control, no safety/toxicology testing, no clinical assessment of medicinal value or patient safety. It is pre-1906 all over again (4). No one really knows what is in any particular batch of this s### or if any of it is safe to the users when inhaled and subsequently deposited on the tissues of the airways and lungs at high doses or repeated doses over extended periods of exposure.

JB: I’m glad you woke up. Care to continue this rant?

Steve: Sure. Since when is it OK to say: smoking cigarettes doesn’t kill you within a couple of days, so higher doses of concentrated nicotine must be safe too (5)? The whole thing is born of granola-head logic. You know, it’s not safe to eat polar bear livers because the vitamin A levels are so high they are dangerous. However, of course, everyone knows that chowing down on ever more vitamins is safe and good for you. None of these blockheads would touch something called a chemical but have no problem chucking handfuls of concentrated chemical crap down their throats as long as they are called supplements. I hope it all works out, but on the positive side, we could be culling the heard of morons.

JB: Damn, that’s harsh.

Steve: That is why the FDA mandated that I spend about $10 million on QA/QC (5) work and requires rigorous purity characterization and product release standards, as well as shelf-life stability studies. These charlatans are manufacturing and distributing drugs with zippo FDA oversight and that’s the problem.

JB: So is that.

Steve: Haha. It’s some s### that when inhaled is leading to irritation to the point of blistering. Almost all of the s### we worked with in the lab would qualify. That’s why fume hoods were invented – to protect chemists from breathing in crap that would turn our lungs into Swiss cheese. The stuff people buy on the street could contain anything that when deposited on the fragile tissues of the lungs and airways is very irritating to the mucous membranes. What you are seeing is the equivalent of poisonous bathtub gin of the Prohibition era - quick buck backroom moonshining, nothing more. It’s stupidity at its finest.
JB: Dude, you used to be young and cranky. Now you're just cranky.

Steve: *Take a look in the mirror, old man.*

As usual, Steve is right about a lot of things. Although the serious damage to cells in the lungs suggests that the chemical culprit could be a reactive, toxic chemical, it is also possible that it could be something which is benign in your stomach (like a flavoring agent) but not so in your lungs, or there is just too much of it for your lungs to safely clear. Drugs inhaled into the lungs get all kinds of extra regulatory scrutiny because of the fragile nature of the tissues to be exposed to foreign chemicals of unknown topical irritation properties. This includes safety assessment of even the minor impurities and degradation products, novel or not, routinely found in any drug.

He is also right that the "organic lemmings" who are so convinced that anything related to marijuana is safe, natural and good for you (think: CBD oil) that it's cool to vape just about anything, regardless of what's in the cartridge or who put it in there. Likewise, he is correct that supplements and marijuana are given a free pass while prescription drugs must go through rigorous safety studies and still have side effects.

And his regard for people who are willing to try anything off the street because of flawed (or no) reasoning is not especially high. However, as a Libertarian, he feels people can do as they wish with their bodies so long as they take responsibility for their own actions, and not yet again, demand the government foist evermore freedom constraining laws on the rest of us (his words).

I know a place where he would fit in nicely, but we're not hiring and he's not looking. So, I'll wait a few weeks until more evidence is available and wake him up again.

NOTES:

(1) An electrophile (electron lover) is an organic chemical that reacts atoms like nitrogen, oxygen and sulfur (components of amino acids and proteins). Many are highly chemically reactive, which makes them dangerous. Phosgene is a very powerful electrophile, which is why it is a good chemical weapon.

(2) Aldehydes are moderate to strong electrophiles, depending on their individual chemical structures. Aromatic aldehydes, where the aldehyde group is attached to a benzene ring, are less reactive.

(3) Aldehydes are easily oxidized to form carboxylic acids. As the name suggests, carboxylic acids are acidic. Duh.

(4) The FDA was created in 1906 to combat snake oil.

(5) No, Steve is not saying that electronic cigarettes are dangerous. Billions of them have been smoked without this kind of acute toxicity showing up. He is saying that because cigarettes don’t kill you immediately it is wrong to conclude that any device containing any amount of nicotine, especially impure nicotine, will automatically be safe. But it is highly unlikely that nicotine is what is causing these deaths. There can be little doubt that a properly manufactured electronic cigarette is safer than a cigarette. Just about anything is.
(6) QA/QC means quality assurance/quality control.