Published on *American Council on Science and Health* (https://www.acsh.org)

Addiction is the Mother of Invention

By Josh Bloom — May 8, 2016

One of the biggest hurdles in drug discovery is to take something that was discovered in the lab and make it work in pill form. This is referred to as "oral activity." For this to happen, the potential medicine must be able to endure the harsh conditions of the stomach (low pH and digestive enzymes), and be absorbed somewhere in the gut — usually the stomach or the small intestine.

But, this is only one of numerous requirements. Even if absorption takes place (no small task), for the drug to get into the blood it must survive the liver—the most important metabolic organ in the body. The liver's job is to "destroy" (metabolize) much of what passes through it, and it does not care one bit whether this is a toxic substance, a nutrient, or a medicine.

These two functions—absorption and metabolism—have tortured medicinal chemists and biologists in the pharmaceutical industry forever, and are two of the primary reasons that experimental drugs fail so often.

There are "tricks" that scientists use to fight back, but learning these techniques can take years of experience in the lab.

But now, drug addicts are using these exact same techniques to either get high, or to manage their addiction. And they are doing so in much the same way as a very sharp chemist with an advanced degree.

The anti-diarrheal drug loperamide (Imodium), which can be bought in unlimited quantities over the counter, is a weak opioid. It would take an awful lot of it to get high, and that still wouldn't work. Loperamide isn't absorbed very well.

Our bodies have evolved a number of mechanisms to prevent us from being poisoned. One of these is called the p-glycoprotein (Pgp) efflux pump. These are little detoxifying "machines" that are scattered throughout the digestive tract. The Pgps take potentially toxic substances that have been absorbed into intestinal cells and spit them out back out into the gut, where they pass through and are then excreted.

Imodium is one of many drugs that have a hard time getting absorbed into the blood because of these pumps. But, it is possible to inhibit the action of the Pgps by swamping them with other drugs. This is an excellent example of drug-drug interactions, where the presence of one drug affects the blood levels of another. Drug-drug interactions can cause a safe drug to become deadly.

This is exactly what drug abusers have discovered. The anti-ulcer drug Prilosec—also available OTC—inhibits the Pgps, and this increases the absorption of Imodium to the point where it becomes a "decent" substitute for Vicodin or heroin, as well as a dangerous cardiac toxin.

The toxicity of this mixture has caused a 7-fold increase [1] in the number of loperamide poisonings at the Upstate New York Poison Center at Upstate Medical University between 2011 and 2015.

Will Imodium now become a controlled substance like the original Sudafed, which is used to make methamphetamine? To get the version of Sudafed that contains pseudoephedrine (the only kind that actually works) you need to provide ID to a pharmacist, and will most certainly get yourself on a list.

And, will it matter? When pharmacology with this level of sophistication is used to skirt drug laws, it is only a matter of time until someone comes up with another trick with another readily available drug.

Addicts will go to any length to feed their addiction. It is no wonder that the "war on drugs" has been a dismal failure from day one.

Links
[1] http://www.upstate.edu/news/article.php?title=9528