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Editorial

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The Perils of Pursuing the Single Molecule in Forensic Toxicology

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Throughout the Middle Ages, doctors are frequently depicted holding a glass filled with urine, the most readily available biological sample. They were able to detect diabetes by dipping their finger into the liquid and then licking it to taste sugar, if any was present. When mothers kissed their children with cystic fibrosis, they tasted their saltiness and realized that something was seriously wrong. Patients in diabetic coma would be alerted to their impending death by the delicious scent of ketones.

We have advanced significantly since our first, rudimentary use of our senses to distinguish between sweet, salty, or fragrant substances (and diagnose illnesses). The study of biological materials for the presence of poisons, including pharmaceuticals, is known as forensic toxicology, and it is now an established and acknowledged field.

In the field of forensic toxicology, technological advancements have been incredibly impressive, pushing the boundaries of detection ever further. In fact, the ability to detect the existence of individual molecules in a sample is not far off. Although the results of such solid-technology-based analytical miracles are reliable and repeatable (albeit they might not be if a sample contains only one molecule), the interpretation of the data is far from straightforward. I had the chance to visit exotic, distant kingdoms at one point in my life; but, I had to fill out immigration documents with the warning, "Death penalty for drug possession," inscribed in huge red letters before I could enter the foreign countries. Although I never used opiates, I was well aware that some of our possible intestinal parasites could manufacture traces of morphine to make it harder for us to eliminate them through bowel movements (thus causing constipation).1, 2 Now picture the following situation: a biological sample taken from your body is examined and, for whatever reason, it turns out to have traces of morphine. "I didn't do it, your honor; it was my intestinal parasites," is your defense when you are taken before a judge. To make matters worse, the nematode Ascaris suum, the big roundworm of pigs (and humans), appears to be the most effective morphine generator.

Not likely to make the aforementioned judge feel sorry for you. Begin writing your obituary. Naturally, I chose to take mebendazole as a preventative measure, so I could never experience such a thing. However, there are plenty additional ways to get into trouble.

Although I'm not a vegetarian, I could theoretically eat a lot of nutritious meals without being aware of the risks. Benzodiazepine sedative-hypnotics are produced by and found in a variety of cereals and vegetables.3, 4 Now picture the following situation: a biological sample taken following an automobile accident in which you were a party turns out to contain diazepam. If you live in a culture that is obsessed with lawsuits and dominated by lawyers, saying "I ate too many potatoes" won't help you keep your driver's license or your wealth.

However, that was merely a benign scenario; let's find a method to get included to Homeland Security's coveted "No fly list," which is updated on a regular basis. What if your luggage included traces of organophosphates (cholinesterase inhibitors, ChE-I)?

Although there are hundreds of non-organophosphate inhibitors of cholinesterase found in nature, it has only recently been discovered that strong pesticides and nerve gas-like inhibitors of cholinesterase are also found in nature and are produced by bacteria, algae, and marine sponges, among many other organisms. The first to note that "Nature made them first" were Rainer Neumann and Heinrich H. Peter, who worked for Ciba-Geigy in Switzerland. They identified two similar furo-dioxa-phosphepin cholinesterase inhibitors from cultures of the soil microbe Streptomyces antibioticus.6. A few years later, a Japanese team announced that Streptomyces lavendulae had produced cyclophostin, a closely related chemical.7. It was also found that green-blue algae produce anatoxin-A(s), a structurally distinct imidazole phosphor ester.8. Lastly, ulosantoin, another imidazole phosphor ester, was isolated and discovered from a marine sponge called Ulosa ruetzleri (Orange Lumpy Encrusting Sponge); it has a low nanomolar range ChE inhibitory potency that is similar to paraoxon's.9.

In conclusion, even while it is astonishing to say the least that we can identify compounds at ever-lower concentrations, practically pursuing the single molecule, results must be read carefully and contextually. Even though they can be quite strange and improbable, potential reasons why banned chemicals might be present in biological samples should be investigated. It is important to remember that truth is, as Lord Byron once said, "stranger than fiction."10.

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