

## **COSI SIMILI, COSI DIVERSE**

### **4. EPHEDRINE AND PRIMO LEVI**

In February 2003, Steve Bechler, a promising 23-year old baseball player for the Baltimore Orioles team, reported to spring training 10 pounds overweight. Under pressure, he took one morning three pills of an over-the-counter so-called natural food supplement, Xenadrine. Its active ingredient is ephedra, a natural product containing in turn the compound ephedrine. Ephedrine, a stimulant, once was widely used as a bronchiodilator. And it is suspected of leading to strokes, heart problems, and psychotic episodes. Xenadrine advertised itself as a “rapid fat loss catalyst.” That afternoon, Bechler collapsed and died. The medical examiner said it was heatstroke, and that ephedra contributed to his death.

There are many lessons in this. One is the continued use of drugs or treatments, natural and unnatural, by athletes under pressure. The recent banning of many of the Tour de France favorites is just one example. Another story is of the athletes’ own resistance to the control by society of such drugs. Still another, of the role of natural food supplements, the fascinating advertising for them, both scientific and anti-science at the same time. But here I just want to look at that molecule of ephedrine, and two of its cousins.

Ephedrine is a pretty simple molecule. At its core is a chain of two carbons and a nitrogen. To the end carbon is attached a ubiquitous  $C_6H_5$  ring called a phenyl group, and another typical “substituent”, as they are called, a hydroxyl group, OH. A hydroxyl group is what makes an alcohol an alcohol – it is there in methanol and ethanol and propanol. And there lots of them in sugars. At the second carbon of ephedrine there is attached another popular group, a methyl or  $CH_3$ . The third atom in the chain, a nitrogen also has a methyl group attached to it. Methyl, phenyl and hydroxyl are all the rage in the biochemical world, the enzymes we have attach them to all kinds of carbon groupings.

Now the first cousin, actually a molecule that is the mirror image of ephedrine. It’s called pseudoephedrine, which finds a use in a number of over the counter medical combinations, cold drugs. It has fewer bad side effects than its mirror image, ephedrine. There is nothing bad about pseudoephedrine by itself, only what human beings do with it. Pseudoephedrine is easily transformed into “meth,” or methamphetamine.

Relative to pseudoephedrine, methamphetamine just has the OH attached to the first carbon of the chain of three removed, and replaced by hydrogen. Meth is also known as ice, crank, crystal, by many other names. And is an addictive drug. The difference between pseudoephedrine and methamphetamine is one little oxygen atom.

Easily removed means just that, for it can be done in a small laboratory, using phosphorus and iodine, or lithium or sodium and ammonia. The processes are as dangerous as they are easy, and there are many reports of injuries in the manufacture. There are thousands of meth labs discovered each year in the US.

If the drug were not such a problem, the following story would be funnier than it is. A man was at work in his home lab on meth when some people knocked. So he put the phosphorus and iodine into a film canister and stuffed it in his pocket. The man began to look uncomfortable to his visitors, as the reagents did their thing, their reaction releasing heat. Eventually flames shot out, and the drug chemist suffered second and third degree burns to his sensitive parts.

The biological world is full of molecule as that are small variations on each other. Some have been co-opted by evolution to serve us. Others cause trouble, one way or another. Probably the reason they cause trouble is closely tied to the reason their "good" analogues are of use -- they bind to some of the same receptors in our bodies, or serve related functions. Yet it is the differences that tell. Remember that one oxygen atom difference between the anticongestant and meth?

Primo Levi, in his wonderful autobiography/history "The Periodic Table", tells the story of an explosion he had while doing some research at the university. He needed sodium to dry an organic solvent, but he used potassium, another alkali metal, right under sodium in the periodic table instead. He writes of what the experience meant to him:

*...I thought of another moral...and I believe that every militant chemist can confirm it: that one must distrust the almost-the-same (sodium is almost the same as potassium, but with sodium nothing would have happened), the practically identical, the approximate, the or-even, all surrogates, and all patchwork. The differences can be small, but they can lead to radically different consequences, like a railroad's switch points; the*

*chemist's trade consists in good part in being aware of these differences, knowing them close up, and foreseeing their effects. And not only the chemist's trade.*