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A Conversation with Stosh Kozimor

Mark Peplow

Actinide chemistry reveals unusual bonds and offers a novel form of cancer treatment.

Credit: Josh Smith, Los Alamos National Laboratory

If the periodic table is an atlas for chemistry, then the actinides should surely be labeled "Here be dragons". All are radioactive, only thorium and uranium are found in appreciable quantities, and most of the rest are produced by the sort of modern-day alchemy that relies on nuclear reactors or particle accelerators.

Stosh Kozimor, a staff scientist at Los Alamos National Laboratory, is one of a hardy band of scientists unafraid of taming these dragons. Mark Peplow spoke to him about the challenges of doing research on the actinides, and their potential application in cancer therapy.

What attracted you to studying the actinides?

I grew up in New Mexico, and with Los Alamos being so close there was always talk about the Cold War, nuclear power, and the Manhattan Project. I was turned off, I guess, by that. But there was also an allure to it. I was curious about the problems and the issues, and I just kept coming back to it.

How difficult is it to work with actinides?

When you have highly radioactive samples, you want to limit your personal exposure to them, and the material is usually very scarce and incredibly valuable. So there's a lot of up-front work using nonradioactive surrogates, to make sure the entire process is well rehearsed and your hands develop muscle memory. It takes an incredible amount of mental focus just to load a cuvette, because you don't want anything to splatter.

A lot of times we'll work in pairs to carry out a delicate manipulation, so you need a second person whom you can get along with, and who wants to work on that project with you. You have to have a healthy respect for the material. If it doesn't make you anxious, you probably shouldn't be handling it.

Tell me about your research.

We're interested in understanding how covalent or ionic the bonds are between actinides and ligands, and how that changes along the actinide series. It's one of the most fundamental questions in actinide science. It's important for a lot of reasons: Covalency is invoked in explaining actinide fate and transport in the environment—how they behave in water or soil, for example—or in trying to build good ligands for them, or in separating them from each other.

Aside from fundamental studies, are you looking into novel applications for actinides?

Isotopes that emit alpha particles have the potential to treat cancers. You have to attach the radionuclide to a chelator, a molecule that binds the metal and holds onto it in someone's body. Then you attach that to a biological targeting vector that takes it to the tumor. Actinide isotopes like actinium-225, thorium-227, and uranium-230 are short-lived, so they're not a long-term toxic threat; and alpha particles only penetrate a short distance in biological tissue, so there could be fewer side effects than nontargeted treatments.

Actinium-225 has a 10-day half-life. It decays to give off an alpha particle, and then its decay products subsequently produce three more alphas. That's four alphas for every actinium atom, so you get a lot of bang for your buck.

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We're trying to develop better chelators for holding on to actinium as we put it in the body. As a baseline, we needed to characterize how actinium coordinates to water molecules, even though other ligands may be more important for controlling the fate and transport of actinium in the body.

We made the first bond distance measurements for actinium coordination complexes, and it's surprising how long those distances are in the actinium and water aquo complex, an average of 2.63 Å. The coordination number was also higher than expected, with 10.9 $\pm$ 0.5 water molecules in each actinium's inner coordination sphere. The error bar on our measurement is quite high, but the general trend is that it's going to take a relatively large ligand to cover all those coordination sites, which is what you need to chelate actinium effectively in the body.

Researchers already have little chelators that are good at binding small lanthanides like gadolinium, but there's no possible way they're the right size for actinium—actinium is the largest +3 oxidation state metal on the periodic table. So our main focus now is to design and build macrocycle compounds, which are larger, to reach around and hug it tighter. We're hoping to get some initial results out soon.

Mark Peplow is a freelance contributor to Chemical & Engineering News, the weekly newsmagazine of the American Chemical Society. Center Stage interviews are edited for length and clarity.

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