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# Speciation of actinides in biological media - impact on the organs targeting

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## Résumé

In the context of organ targeting, whether from the point of view of nuclear toxicology or nuclear medicine, the concept of chemical speciation appears essential. The chemical form of radionuclides (influenced by the oxidation state of the radionuclide but also by the chemical composition of the biological environment: nature, concentration of the species, pH, etc.) can significantly influence targeting and accumulation in the organs (thus chemical toxicity or the effectiveness of radiological treatments) but also the retention and excretion rate of these radioactive elements after exposure (whether voluntary or involuntary).

Our team (Human and Environmental Radiochemistry) is particularly interested in the impact of the speciation of actinides (An) which are radioactive heavy metals mainly involved in the nuclear fuel cycle and in the military field, on organ targeting and on the expression of their chemical toxicity in the organs. What are the characteristics of the biochemical actors (small molecules, proteins, etc.) involved in these mechanisms? How can the nature of the chemical functions present within these molecules (carboxylic acids, phosphonic acids, amines, etc.) or the conformation of these molecules influence their reactivity to An? How can the biological function(s) of these actors be altered by their interaction with An? Although numerous studies have endeavoured, since the middle of the 20th century, to describe on a macroscopic scale, the nature of the organs targeted by actinides (kidneys, liver, skeleton) according to the mode of exposure (injection, ingestion, inhalation), their impact on their functioning as well as their retention and excretion rates, the understanding of the molecular mechanisms at the origin of these observations is still limited and much less widely explored. This is mainly due to the difficulty of carrying out these studies associated on the one hand with the handling of radioactive elements in the laboratory and on the other hand with the high chemical reactivity of An, which makes it difficult to study them in biological environments, which are always complex from the physico-chemist’s point of view.

To carry out our studies, we use a combination of (i) physico-chemical characterization techniques at the molecular level: Fourier transform infrared (coupled with the use of an ATR device and a micro-fluidic cell) and UV-visible spectroscopies, X-ray absorption spectroscopy performed using synchrotron radiation (SOLEIL, ESRF), (ii) molecular modelling tools (DFT, molecular dynamics), and (iii) analytical chemistry techniques (alpha, gamma and ICP-MS spectrometry). Other techniques such as X-ray or neutron scattering are useful for defining the impact of An interaction on the conformation of larger molecules and thus on their function.

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In parallel with the understanding of the molecular mechanisms involved in the An interaction with living organisms and always in a toxicological framework, our group is working on developing new approaches for the decorporation of An (functionalization of polymers by carboxylate or phosphate functions, etc). I will also present in a few words, the work recently carried out within the group in the framework of this research line.

**Mots-Clés:** speciation, actinides, chemical toxicity