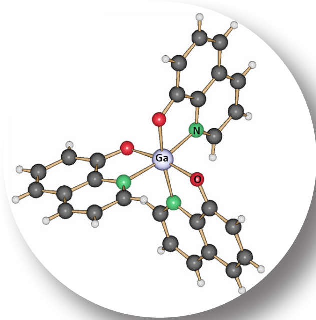
Case Study

Spectroscopic studies on anticancer therapy gallium

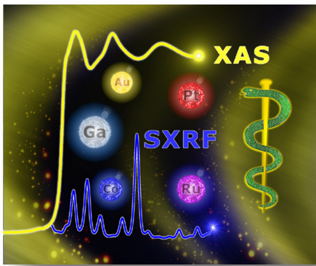
The Problem

Gallium (Ga) based salts show very promising anticancer properties. However, the maindrawbacks of therapy with Ga salts is the need for slow, long-term infusion to avoid the toxicities associated with high plasma levels of Ga, and the poor bioavailability when the drug is dosed via the oral route.



The Challenge

It has been posited that these issues could be circumvented by the application of novel Ga complexes such as tris(8-quinolinolato)gallium(III) that show superior anti-tumour activities.It has been demonstrated that the drug evades unicellular and multicellular resistances and exhibits antiproliferative activity in cell lines expressing multidrug resistance-associated protein (MRP) and lung resistance protein (LRP). However, the structure of the compound in tissue samples and in the presence of potential transport proteins required investigation.



The Solution

Scientists from the University of Vienna and the Hamburg Institute teamed up with researchers from Utrecht University and Diamond to conduct Ga K-edge X-ray Absorption Spectroscopy (XAS). XAS can be used to probe materials with no long-range order and offers the possibility to investigate spectroscopically silent elements. Hence, metals like Au(I), Zn(II), and Ga(III) possessing a full or empty d-shell are ideal candidates for XAS investigations. Microfocus X-ray fluorescence (μ-XRF) can provide information on the distribution and concentration of multiple elements within a sample simultaneously, allowing for the chemical state of several elements within subcellular compartments to be probed. Both techniques taken together allowed the researchers to investigate the oxidation state, the coordination environment of Ga, and probe the elemental distribution of Ga, Zn, Fe, Ca, and Cu in normal and tumour tissue.

The Benefits

XAS has proven to be a valuable tool for the investigation of the anti-cancer metals Pt, Ru, Ga, Au and Co in biological environments. XAS is one of the few methods that allows the monitoring of exchange reactions of atoms at the absorber, such as O/N for Cl/S or vice-versa, and the accompanying possible changes in the oxidation state. This fact was employed in these interaction studies of the metal based Ga drug with possible transport proteins in vivo like human serum albumin (HAS), bovine serum albumin (BSA) and apo transferrin and to test their stability in solutions.

"Synchrotron radiation spectroscopic techniques will play a vital role in medicinal chemistry in the future. The co mbination of μ-XAS and μ-XRF will allow for the simultaneous investigation of the metal distribution and its metabolism."

Prof Annette Rompel, University of Vienna

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