

Multinuclear and multifrequency NMR study of the interactions between Ln^{III} ions complexes and fluoride anions

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Contrast-enhanced Magnetic Resonance Imaging (MRI) has revolutionized the modern radiodiagnostic field, as it significantly improves the accuracy of diseases diagnosis. Most of MRI contrast agents (CAs) in clinical use are octadentate macrocyclic Gd(III) chelates with one metal-bound water molecule (q) in fast chemical exchange with the bulk. Such coordination cage grants the high stability and inertia properties required for *in vivo* applications, making Gd-based CAs among the safest drugs on the market. Recently, a new MRI CA has been approved, GadopiclenolTM[1], that is a heptadentate Gd(III)-complex with $q = 2$ and double efficiency compared to conventional CAs, which allows to decreasing the administered dose with equal efficacy. However, many bis-hydrate chelates form ternary complexes with anions (carbonate, phosphate, citrate etc..) following the displacement of one or both water molecules [2]. Here, we investigate the interaction between the fluoride anion and two negatively charged Ln(III)-complexes with similar structure but different hydration states (see *Figure 1*), with the aim of determining how the nature of the ligand affects the water substitution. For this purpose, a combination of high- and low-resolution NMR techniques in the frequency and time domains has been employed, which allows an in-depth characterization of the kinetics and thermodynamics of the fluoride binding event. In particular, fast-field cycling relaxometry (¹H longitudinal relaxation rates vs B_0), ¹⁷O transverse relaxation rates vs temperature and high-resolution NMR measurements (¹⁹F NMR) were performed on the paramagnetic Gd(III) and diamagnetic Y(III) complexes, respectively. This approach allowed us to gain insights into the binding affinity, thermodynamics and kinetics associated with the chemical exchange of water molecules with fluoride anions.

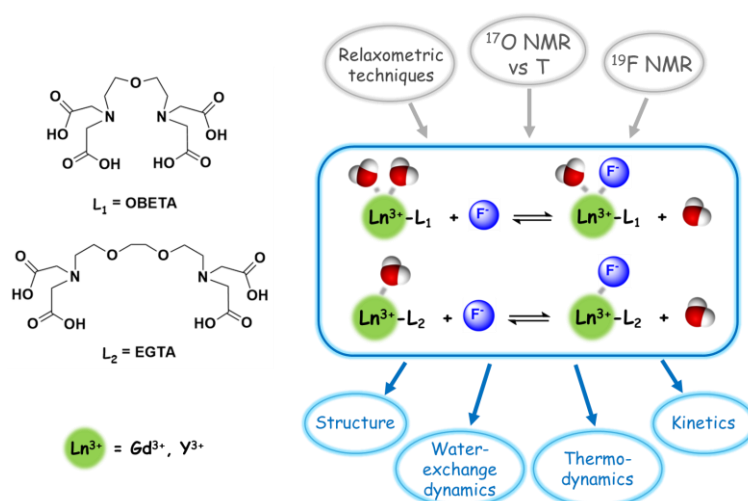


Figure 1: Low-field and high-field NMR techniques used to study the interactions between Ln(III)-OBETA/EGTA complexes and fluoride anions.

[1] C. Gendron, P. Bourrinet, A. Dencausse, N. Fretellier. *Investigative Radiology* **2024**, 59(2),108-123.

[2] F. Travagin, M.L. Macchia, T. Grell, J. Bodnár, Z. Baranyai, F. Artizzu, M. Botta, G.B. Giovenzana. *Dalton Trans.* **2024**, 53, 1779–1793.