

Abstract

In this Thesis, structure and dynamics of paramagnetic complexes for medical application are studied by Nuclear Magnetic Resonance (NMR). It focuses mainly on development of contrast agents (CA) for Magnetic Resonance Imaging (MRI) which is one of the most effective radiodiagnostic method nowadays. Most of the MRI CAs contains paramagnetic complexes of *d*- and *f*-metal ions.

The presence of unpaired electron in proximity of NMR active nuclei has two main effects: paramagnetically induced shift and paramagnetically induced relaxation. Both processes can dramatically change the NMR spectrum and often make it unobservable at all. Nevertheless, in many cases, acquisition of such spectra is possible and sometimes even less time-consuming than observation of diamagnetic molecules. Enhanced T_1 relaxation allows faster pulse sequence repetition and increased chemical shift dispersion may lead to resolution of originally overlapped signals. Moreover, the analysis of paramagnetic effects can provide useful information about the structure and dynamics of the studied system. Theoretical background of these effects is described in the Introduction of the Thesis.

In the first part of Discussion in the Thesis, a new class of contrast agents for ^{19}F -MRI based on nickel(II) and cobalt(II/III) ions is introduced and discussed. Structure and dynamics of their complexes with fluorinated ligands is discussed together with formation, dissociation and isomerism of these complexes. A huge difference in the kinetic inertness of nickel(II) complexes was observed. The complex of the ligand with acetate pendant arms withstand days in 12 M aqueous HCl at 80 °C, while its analogue with 2-aminoethyl pendant arms dissociates after a few hours in neutral water at room temperature.

Strong relaxation enhancement of ^{19}F nucleus in proximity of nickel(II) was observed and it is associated with dipole-dipole interaction between ^{19}F and slowly relaxing unpaired electrons of nickel(II). Smaller, but still reasonable relaxation enhancement was observed in cobalt(II) complexes as well. Analysis of the ^{19}F -NMRD profile for one of the nickel(II) complexes showed that relaxation of the

nickel(II) electrons is magnetic field-dependent and it is modulated by transient zero-field-splitting mechanism.

Significant increase of ^{19}F -MRI CA efficiency was described for these compounds when the complexes are detected by fast MRI pulse sequences.

Internal (TSAP \leftrightarrow SAP) dynamics of Ln^{3+} complexes with $\text{H}_4\mathbf{dota}$ and $\text{H}_5\mathbf{do3ap}$ ligands is the subject of the second part of the Thesis Discussion. The NMR pulse sequence and data analysis were optimised to determine precise exchange rates and activation parameters of both the arm rotation and the macrocyclic ethylene ring inversion. The results were compared with detailed DFT calculations which were done in order to reveal mechanism of the exchange. Unexpected intermediate with bidentate phosphonate group was shown to be involved in the arm rotation process of $[\text{Eu}(\mathbf{do3ap})(\text{H}_2\text{O})]^{2-}$ complex.

Beside the description of the important process in widely studied complexes with DOTA-like ligands, the developed methodology can be generally applied in many dynamic paramagnetic systems such as proteins with open-shell ions or in battery materials.