ABSTRACT

This work is focused on the synthesis of a family of new macrocyclic ligands with exchangeable protons on coordinating groups that could potentially serve (after complexation with suitable paramagnetic lanthanide(III) ions) as responsive contrast agents (CAs) for magnetic resonance imaging (MRI). It is expected that measurement of extracellular pH should bring information for tumorous disease diagnoses and/or for suggesting the most efficient treatment. Therefore, our attention was focused on pH-dependent CAs based on a PARAmagnetic Chemical Exchange Saturation Transfer (PARACEST) mechanism capable of reporting pH changes in tissue.

The PARACEST-related properties of a series of Ln(III) complexes with the CEST effect caused by amino groups coordinated to the central Ln(III) metal ions were investigated. Such a kind of PARACEST CA is new and has had no precedent in the literature. It was shown that these Ln(III) complexes produce a pH-sensitive PARACEST effect in the pH region relevant for living systems. The study brings proof-of-principle for utilization of complexes with a linear diamine pendant arm, *i.e.* complexes with two exchanging proton pools, for ratiometric pH determination by MRI independently on the probe concentration. In addition, to ensure a higher kinetic inertness of the complexes and PARACEST properties suitable for potential pH-sensitive CAs, a novel macrocyclic ligand containing aminophosphonate-coordinating pendant arm was prepared. It was found that its Ln(III) complexes could be used as concentration-independent ratiometric probes for pH determination using PARACEST measurements and also ^{31}P Magnetic Resonance Spectroscopy (MRS) techniques. Thus, these complexes extend the family of pH-sensitive probes for possible utilization *in vivo*.