Toward High Relaxivity and High Stability in Gd MRI Agents

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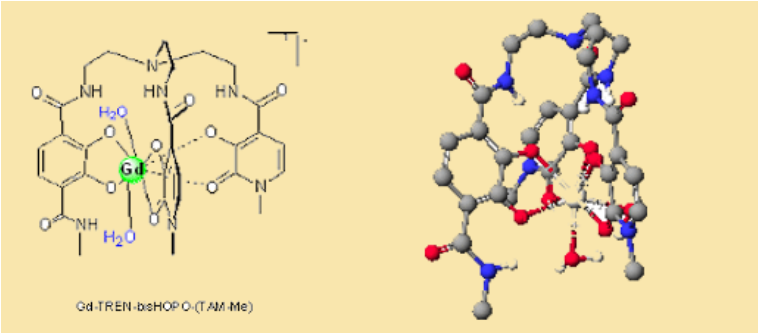
Most commercial MRI contrast agents utilize gadolinium because of its long electronic relaxation time and $4f^7$ electronic configuration. To attain maximum water proton relaxivity one wants as many coordinated water molecules as possible and yet complex stability must be maintained to minimize in vivo toxicity. In addition, one must optimize the water exchange rate and rotational correlation time. These parameters limit relaxivity in current commercial poly(amino-carboxylate) complexes. These requirements present some interesting problems of fundamental coordination chemistry. A series of Gd^{III} complexes based on hydroxypyridinone and terephthalamide has been prepared and will be described in terms of the complexes' water exchange rates and thermodynamic properties. These complexes are stable and have substantially higher relaxivity than most clinically used agents due to their near optimal water exchange rates as determined by ^{17}O NMR spectroscopy. The mechanism of water exchange has been probed by high pressure NMR and single crystal X-ray diffraction studies. Furthermore, the relative stabilities of the eight and nine coordinate states have been modulated by charged substituents. The fast water exchange rate and relaxivity at several field strengths have been studied and structural modifications of the ligand have been made.[1]



1. Raymond, K. N.; Pierre, V. C. *Bioconjugate Chem.* **2005**, *16*, 3-8.