

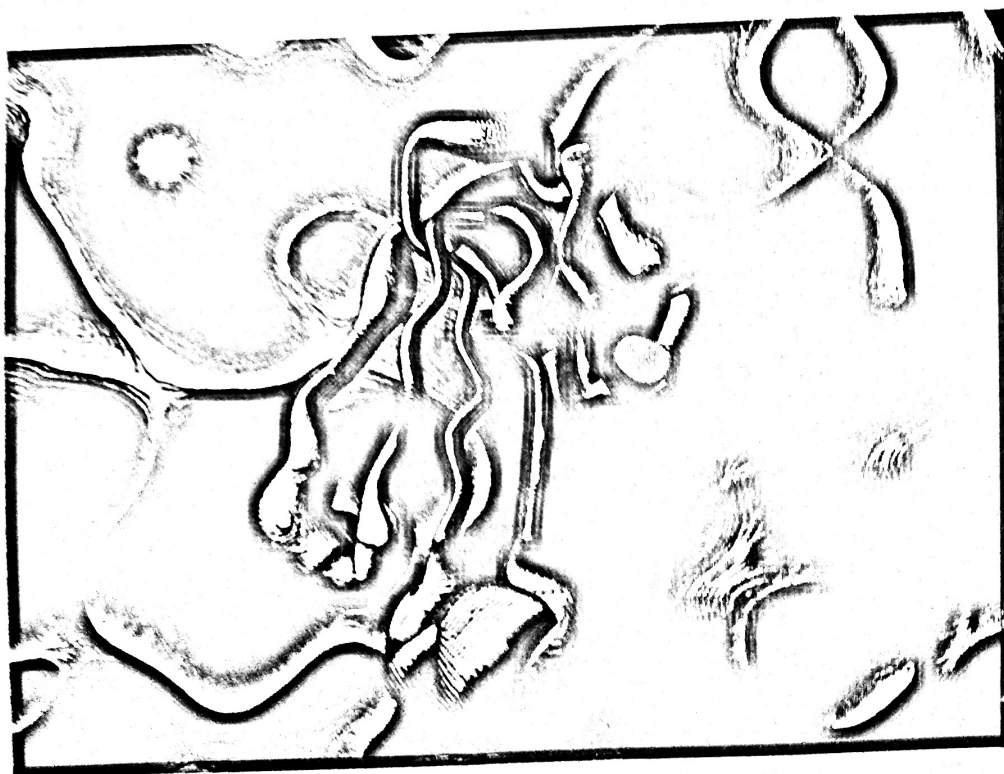
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CONCENTRATION EFFECT ON THE MULTINUCLEAR ANALYSIS OF THE PARAMAGNETIC RELAXIVITY. A CAVEAT.

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Proton relaxivity of paramagnetic substances is defined as the increase of relaxation rate of water proton induced by 1 millimole of the compound per liter of solvent. While proton relaxivities are measured on solutions containing 0.5 to 5 millimoles of paramagnetic agent per liter, higher concentrations are usually needed when heteronuclear NMR techniques (^{13}C , ^{17}O ,...) are used to determine some of the physical parameters defining the proton Nuclear Magnetic Relaxation Dispersion (NMRD) curves. For example, ^{17}O NMR measurements of water are typically carried out on solutions of 50 mM or more to determine the rotational correlation time (τ_R) of the complex and the rate of the chemical exchange ($1/\tau_M$) between bulk water and water molecules of the first coordination sphere (1,2). Values of the rotational correlation time were also derived from ^{13}C NMR analysis of even more concentrated samples (3). Little attention has however been paid to the fact that water concentration and viscosity could be both affected by these high concentrations of the paramagnetic compound.

It seemed therefore important to investigate the influence of concentration on the proton relaxivity and on the rotational correlation time of some linear and macrocyclic gadolinium compounds used as MRI contrast agents.

Proton relaxivities were measured at 4.7 T (MSL-200-15, Bruker, Karlsruhe, Germany) using an IRFT sequence. T_1 were obtained by a three parameters exponential fit. Rotational correlation times (τ_R) were derived from deuterium longitudinal relaxation rate measurements performed on labeled diamagnetic compounds. Concentrations ranged from 1 mM to 500 mM. Three contrast agents were tested: Gd-DTPA dimeglumine salt (Magnevist® Schering, Berlin, Germany), Gd-DOTA meglumine salt (Dotarem® Guerbet, Aulnay-sous-Bois, France), and Gd-DTPABMA (Omniscan® Nycomed, Oslo, Norway).

Results show that proton relaxivity as defined above is not constant over the whole range of concentration even after correction for the actual water concentration. The largest effect is obtained for the dimeglumine salt of GdDTPA. This observation is related to the increase of rotational correlation time at concentration higher than 50 mM as demonstrated by the longitudinal relaxation rate of deuterium.

It is thus evident that care must be taken when values of rotational correlation times are extrapolated from ^{17}O or ^{13}C NMR measurements. Deuterium relaxation rates analysis seems to be more reliable since concentrations less than 50 mM are needed for such measurements.

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