Magnetic Resonance Relaxation Induced by Solid Paramagnetic Substances

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Suspensions of solid paramagnetic substances that had been prepared by impregnation of sulphonated polystyrene ion-exchange resin with paramagnetic ions substantially enhance the spin-lattice relaxation rate of water.

There are numerous intriguing uses for those solid paramagnetic substances which can be tailored in both physical and molecular structure, and also in the intensity of their paramagnetism. We now demonstrate that sulphonated polystyrene beads impregnated with various metal ions can be used to enhance the n.m.r. spin-lattice relaxation rates (R_1-values) of aqueous media.

Samples of sulphonated polystyrene resin (Winthrop Laboratories; mesh size 85—170 μ; pore size 30 Å; C 36.6%; H 4.9%; S 10.9%) were immersed in 0.1 M solutions of the appropriate metal salts for 2.5 days, washed thoroughly with distilled water (to remove excess metal ions) and then vacuum-dried. The amount of sequestered metal ions was determined by atomic absorption and u.v. spectroscopy.

N.m.r. relaxation measurements were made at 26 °C with a Varian VXR-300 spectrometer using the inversion-recovery sequence[1,2] with phase-cycling and a composite 180° pulse,[3—5] and the R_1-values were calculated from an exponential fit of the data using standard Varian software. In every case the ratio of resin to water was 24% w/v and the standard 5 mm n.m.r. tubes were fitted with polytetrafluoroethylene plugs to maintain the sample within the region of the receiver coil.[2]

Two series of comparisons serve to illustrate the effects of these metallated resin beads on the R_1 values of the protons of water. Figure 1 summarises the relative efficacy of different metal ions, both sequestered on the resin beads, and free. In accord with previous studies,[2,6] the diamagnetic ions have little effect whereas the relaxation efficiency of the different paramagnetic species increases with the number of unpaired electrons. Comparison between curves (A) and (B) shows that the relaxation efficiency of 10 mM metal ions in aqueous solution is not significantly influenced by the presence of 2% carboxymethylcellulose gel. The data in curve (C) shows that when the metal ions are bound to the resin they have a lower relaxivity than when free (having allowed for the excess of metal ions present on the resin). Nevertheless, they still cause substantial increases in the spin-lattice relaxation rate of water from its normal value (0.34 s^{-1}); Fe^{II}: 10.0% (440 mM) Fe^{2+}, ×75; Cu^{II}: 10.4% (400 mM) Cu^{2+}, ×85; Mn^{II}: 10.0% (450 mM) Mn^{2+}, ×100; Fe^{III}: 7.5% (330 mM) Fe^{3+}, ×100; Gd^{III}: 7.5% (120 mM) Gd^{3+}, ×110.

In a separate study, the relative amount of resin fully saturated with the respective metal and suspended in 2% carboxymethylcellulose gel, was varied. In the case of Mn^{II}

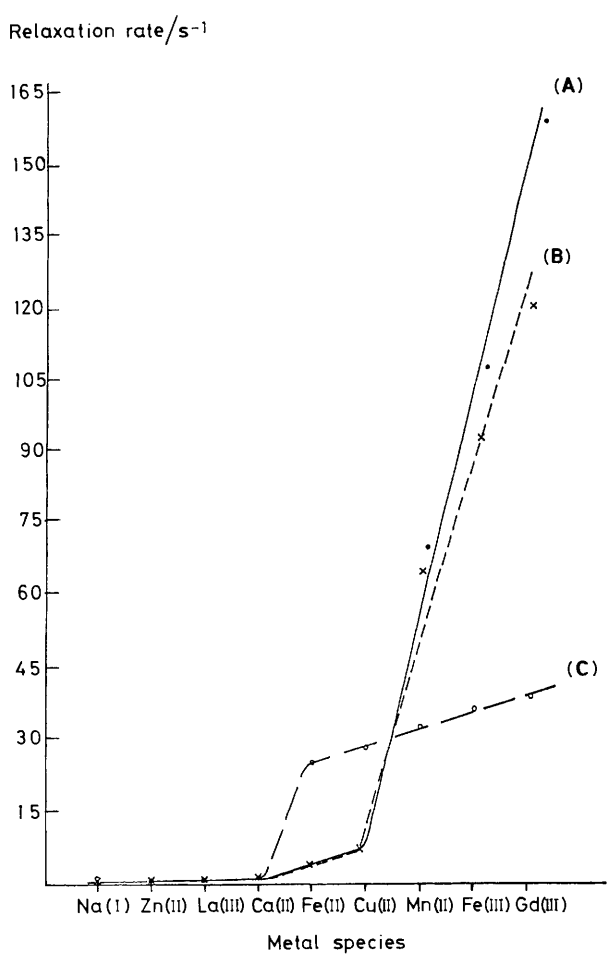

Figure 1. Plot to show variations of the proton spin-lattice relaxation rate of water induced by: (A) 10 mM solutions of the free metal ions, (B) 10 mM solutions of the free metal ions in 2% carboxymethylcellulose, (C) 24% w/v suspensions, in 2% carboxymethylcellulose, of resin that had been fully saturated with metal ions.

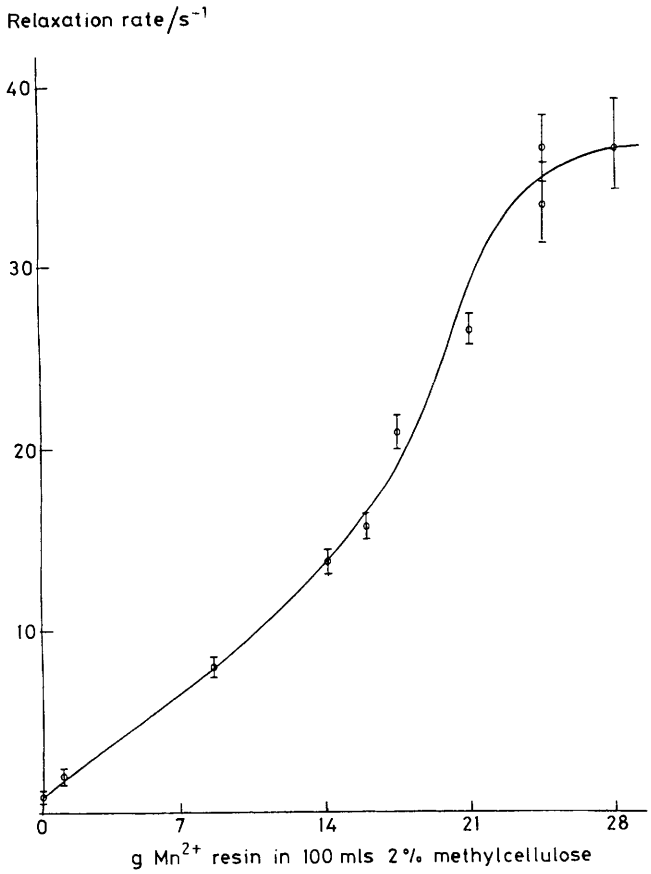

Figure 2. Plot to show the enhancement of the proton spin-lattice relaxation rate of water induced by increasing the concentration of a resin fully saturated with manganese and suspended in 2% carboxymethylcellulose.

suspensions, the R_1-enhancements were linear up to 16% w/v suspension, but thereafter levelled off (Figure 2), in contrast to the linear concentration dependence observed with soluble paramagnetic ions.[7,8] It would be expected that as the concentration of metallated resin increases there would be an increase in the relaxivity values (due to the increased amount of paramagnetic metal ions present). Nevertheless, a point arises when the resin material is present in such quantities that some falls out of suspension. Assuming that the observed relaxivity values are an average of the slower motion of the bulk water and the faster motion of the water near to the paramagnetic centres, the difficulty in maintaining a suspension would mean that the slower motion would begin to dominate, thus causing the plateau effect.

This work demonstrates that concentrated suspensions of this resin, saturated with any of the paramagnetic metals used here, substantially enhance the relaxation properties of aqueous media. The metallated resins appear to be stable indefinitely in water and, at neutral pH, they show no sign of leaching of metal ions. In the presence of 2% carboxymethylcullulose they have the consistency of a thick gel. We suggest that such formulations, which are based solely on materials taken directly from the British Pharmacopoeia, may be suitable as a contrast agent for magnetic resonance imaging (MRI) of the gastrointestinal (GI) tract of man. Furthermore, given that MRI is non-invasive, this approach may well be suited to the study of GI tract transit times which are of importance, for example, to the estimation of nutritional uptake and pharmacological delivery.

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