ABSTRACT

Structural, Relaxometric and Stability studies of selected Gadolinium (111) Complexes

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Complexes of Gadolinium (111) were synthesized in order to study their potential as contrast agents. The ligands used in the synthesis of these complexes were derivatives of 3,4-dihydroxycyclobutene-1,2-dione (squaric acid).

The first stage of this research project entailed the synthesis of a variety of ligands. Some of these ligands were synthesised using literature preparations and for others, procedures for their preparations had to be developed. After this synthesis was completed, the ligands were reacted with a salt of Gd(111). The resulting complexes were then characterized via X-ray Crystallography, Elemental Analysis, IR Spectroscopy and UV/VIS Spectroscopy. These techniques provided critical information on the structure of these complexes. Three complexes were successfully characterised.

Secondly, solubility studies in aqueous solution at various temperatures were then performed on the complexes. From these studies the enthalpies, entropies and Gibb's free energies of solvation were calculated. Potentiometric

titrations were then carried out in order to determine the number of species present on solvation and the various acid dissociation constants (K_a) of each of these complexes. These studies provided information pertaining to the extent of solvation, the number of species in solution and the thermodynamic feasibility of solvation in aqueous solution.

Thirdly, the relative kinetic stability of the Gd (111) complexes in aqueous media was determined via the use of challenger ions. The rates of breakdown of the complexes in the presence of the challengers were measured. These studies were performed in order to test the stability of the complexes in the presence of challenger ions similar to those in blood.

Fourthly, the longitudinal relaxation times of the coordinated water protons of each complex were measured on a 400 MHz instrument. From these values the relaxivities, in mM^{-1} s^{-1}, of the water protons were calculated. These values guided the researcher as to the efficiency of the complexes in enhancing the proton relaxation rates of water protons.

As a result of these studies, two Gd(111) complexes were recommended highly for further studies as potential contrast agents and one was rejected because of its inability to dissolve in aqueous solution. The recommended complexes dissolved and were stable in aqueous solution. They were also efficient in enhancing the proton relaxation times of coordinated water molecules.

It is hoped that this project will assist future researchers in the development of contrast agents that significantly increase the resolution of images

in Magnetic Resonance Imaging (MRI). MRI is rapidly becoming important as a clinical diagnostic tool. This has opened up a large market in the pharmaceutical industry for contrast agents.