

DESIGN AND CHARACTERIZATION OF NOVEL STEALTH Gd(III)-DOTA CONJUGATES FOR MAGNETIC RESONANCE IMAGING (MRI)

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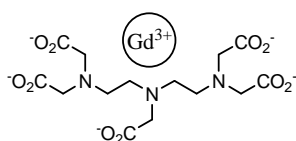
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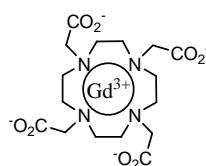
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Magnetic resonance imaging (MRI) is a non-invasive method that contributes to identify and characterize tumour tissues. The image contrast obtained in MRI depends essentially on the differences in the intensity of the water proton signals in different tissues. In order to increase the sensitivity of the technique, contrast agents (CA) containing paramagnetic metal ions such as Gd(III) are usually employed. For MRI applications, those paramagnetic species are strongly chelated by diethylenetriamine pentaacetic acid (DTPA) (**scheme 1**) or 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) (**scheme 2**) in order to avoid the deposition of the highly toxic Gd(III) species on bones. Although those contrast agents are commonly used in MRI studies, they present some limitations such as a short lifetime in blood and a poor contrast when high magnetic fields (1.5T actually) are used for imaging.



Scheme 1



Scheme 2

The aim of our work is to improve the blood lifetime and the contrasting efficiency of the contrast agent, and to target it to tumor tissues in order to reduce the dose of contrast agent needed for satisfactory image acquisition. For that purpose, we will therefore report on the immobilization of gadolinium complexes onto biocompatible functional micelles in mild aqueous conditions with the formation of novel macrocontrast agents. The synthetic procedure will be first detailed. Then, the superiority of our macrocontrast agents in term of contrasting efficiency compared to commercially available gadolinium based contrast agents will be demonstrated by comparing the full relaxometric data over a broad magnetic field range (from 0.01 to 100 MHz). The hemolytic CH50 test will also demonstrate that our macrocontrast agent is not recognize by the immune system, which should consequently avoid their fast elimination from the body. The improved relaxivity and the stealthiness of the macrocontrast agent make it an excellent candidate for MRI blood pool agent.

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