Detection of Low Micromolar Gd^{3+} Concentrations via HyperCEST Using the Host-System Cryptophane-A Monoacid

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INTRODUCTION:

Gadolinium (Gd) is used in a wide range of scientific, industrial and medical applications. However, its use poses a problem, particularly in environmental and biomedical contexts. In recent years, concerns have been raised about the persistence of Gd in aquatic ecosystems due to its widespread use.[1] In addition, its accumulation in biological tissues, albeit at trace levels, has led to increased research of potential health risks.[2] In light of these concerns, the development of detection methods is of high importance. Accurate quantification and localization of Gd, particularly at low concentrations, not only facilitates environmental monitoring but also has significant implications for clinical diagnosis and treatment. This study demonstrates the suitability of Cryptophane-A monoacid (CrA-ma) for Gd detection through analysis of the depolarization rate of hyperpolarized (hp) ^{129}Xe during HyperCEST spectroscopy. It provides promising insights into studying the affinity of gadolinium ions for CrA-ma and its potential applications in sensitive Gd detection.

METHODS:

The affinity of CrA-ma to interact or bind with Gd^{3+} was investigated by acquiring z-spectra of a sample solution with a fixed concentration of 5.5 µM CrA-ma and different $GdCl_3$ concentrations from 2.5 µM to 100 µM. All HyperCEST experiments were performed on a Bruker Avance III HD console at 9.4 T. A gas mixture of 2% Xe, 10% N_2, and 88% He was dispersed into the 1 ml sample for 15 s at a flow rate of 80 ml/min and an operating pressure of 4.5 bar (abs.).

RESULTS:

Figure 1 shows the normalized signal intensities as a function of the offset frequency in ppm for two different saturation times. The typical HyperCEST response of ^{129}Xe bound to CrA-ma occurs at -133 ppm. A slight shift in peak position is mainly due to small temperature fluctuations, as the Larmor frequency of ^{129}Xe in CrA-ma is very temperature sensitive.[3] With increasing $GdCl_3$ concentration, a significant decrease in the HyperCEST response of hp ^{129}Xe bound to CrA-ma is observed. When fitting a Lorentzian function to the data, a more quantitative parameter, the depolarization rate λ, can be extracted. It is shown in Figure 2 as a function of $GdCl_3$ concentration.

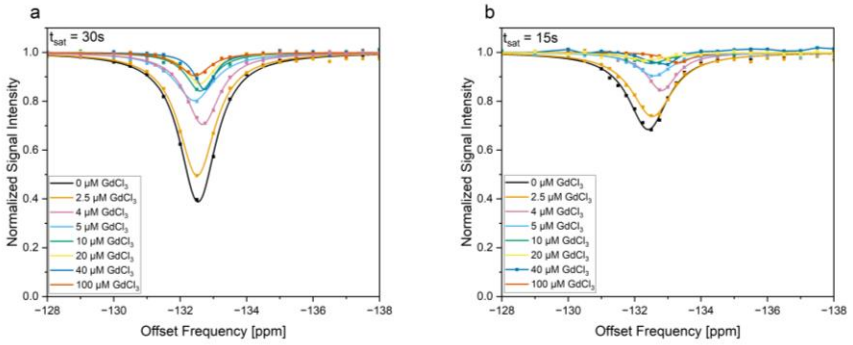

Figure 1: Normalized z-spectra of ^{129}Xe bound to 5.5 µM Cryptophane-A monoacid (CrA-ma) at different gadolinium chloride ($GdCl_3$) concentrations. Measurements were performed at saturation times of 30 s (a) and 15 s (b).

DISCUSSION:

The depolarization rate decreases strongly up to a concentration of 10 µM Gd^{3+}, probably because the depolarization of hp ^{129}Xe is less efficient when it is prevented from entering the molecular cage. A Gd^{3+} concentration of only 2.5 µM leads to a relative decrease in the HyperCEST response of 5 % and 10 % at saturation times of 15 s and 30 s, respectively. This may indicate a strong affinity of the gadolinium ions to the CrA-ma cage.

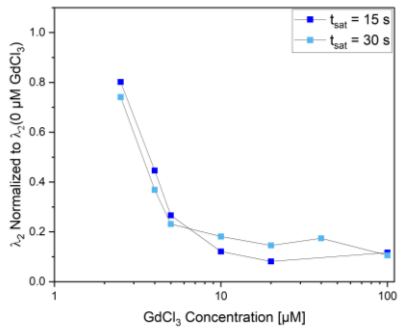

Figure 2: From a Lorentzian fit, the depolarization rate corresponding to ^{129}Xe bound to CrA-ma, λ_2, can be extracted. It is displayed as a function of the $GdCl_3$ concentration in µM for the two saturation times, and has been normalized to the case of o µM $GdCl_3$. λ_2 has the strongest decrease below 10 µM Gd^{3+}.

CONCLUSION:

This study has demonstrated the ability of CrA-ma to bind gadolinium ions and the detection of just small concentrations of Gd^{3+} in a low µM range via ^{129}Xe HyperCEST. This could be a novel tool in detecting and resorbing gadolinium impurities from aqueous solutions or even biological tissue.

REFERENCES:

1. Trapasso G, *et al.* SciTotalEnviron 2021;781: 146273 **2.** Werner P, *et al.* Sci Rep. 2021;11(1):21731, **3.** Schilling F, *et al*. ChemPhysChem 2010;11:3529-3533