

Supplementary Materials for

Development and characterization of Lanthanide-HPDO3A-C16 based micelles as MRI contrast agents.

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Keywords

PARACEST agents; micelles; MRI; lanthanide; paramagnetic complex

High resolution ^1H - and ^{13}C -NMR spectra of the HPDO3A-C16 ligand.

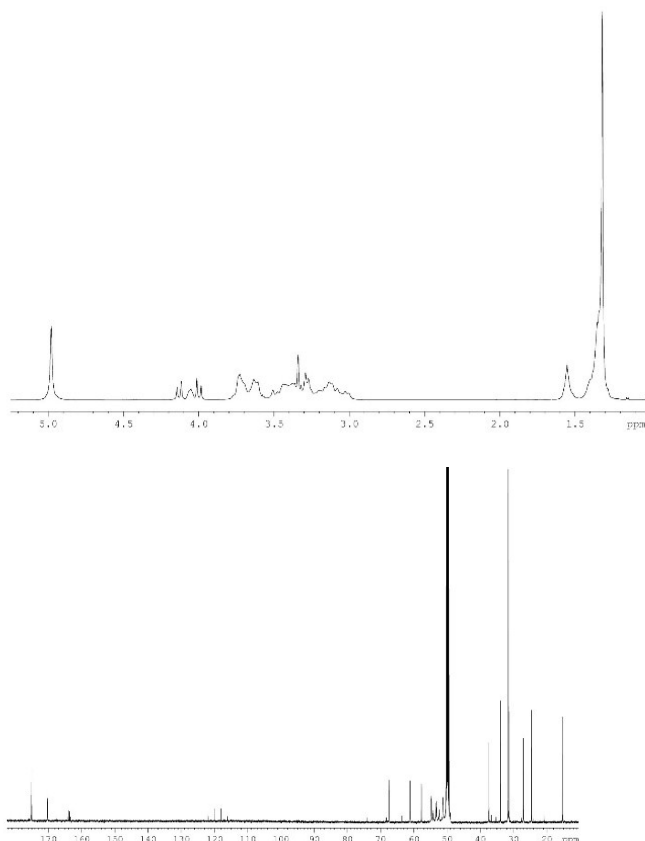


Fig.S1: ^1H - and ^{13}C - NMR spectra ($B_0= 14.1\text{ T}$) in MeOD of HPDO3A-C16 ligand.

High resolution ^1H spectra of the YbHPDO3A-C16 complex in CDCl_3 or D_2O .

The high resolution proton spectra of Eu- and Yb- HPDO3A complexes have been acquired at 14T both for YbHPDO3A-C16 in chloroform (CDCl_3) and in water (D_2O) in order to have the spectra of free complex and of the complex in micelle. The obtained spectra are quite similar to those obtained for Yb-HPDO3A without the hydrophobic chain. These results suggest that the presence of the additional C16 chain does not change the structure of the chelate.

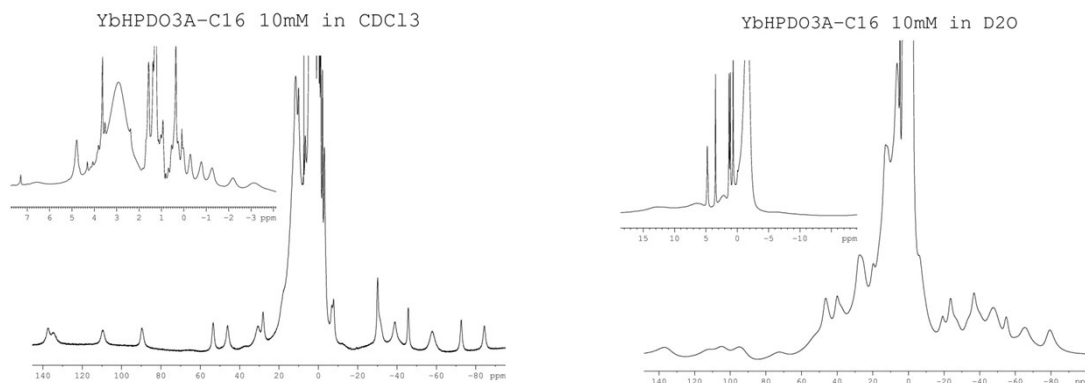


Fig.S2 ^1H -spectra ($B_0= 14.1\text{T}$) of Yb-HPDO3A-C16 10mM in CDCl_3 (left) or in D_2O (right), pH 7.0, 298K.

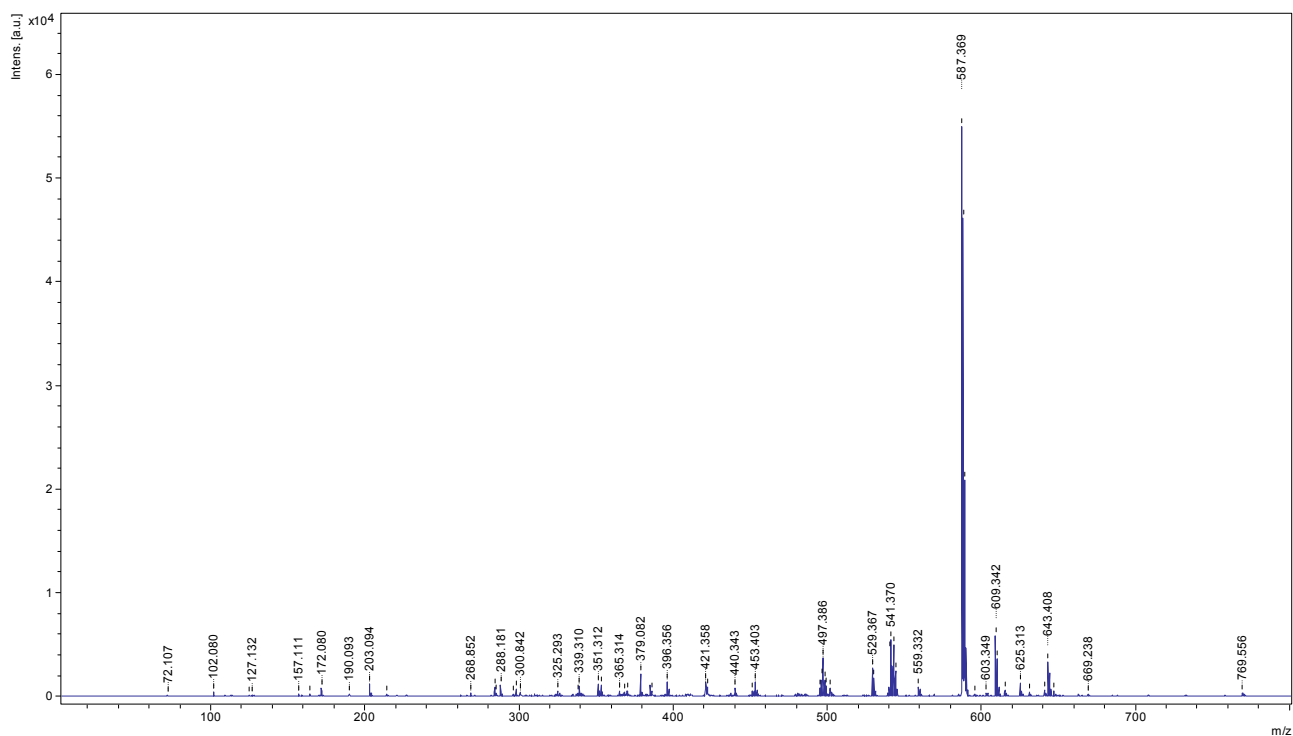


Fig.S3 MALDI-TOF spectrum of HPDO3A-C16 ligand

Evaluation of CMC and hydrodynamic size.

Hydrodynamic size and CMC have been evaluated by using Dynamic Light Scattering (pH 7.2, 25°C, in Saline Phosphate Buffer 1mM phosphate, 150mM NaCl).

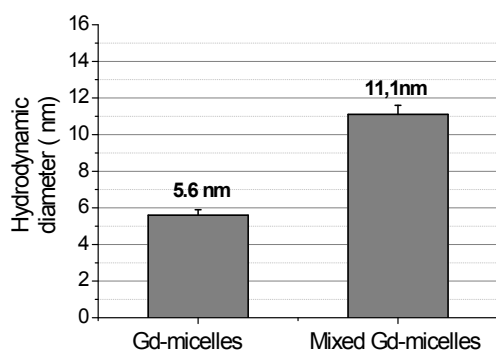


Fig.S4 Mean hydrodynamic diameter for Gd-Micelles and Mixed-Gd-micelles as evaluated by Dynamic Light Scattering (Mean ± SEM).

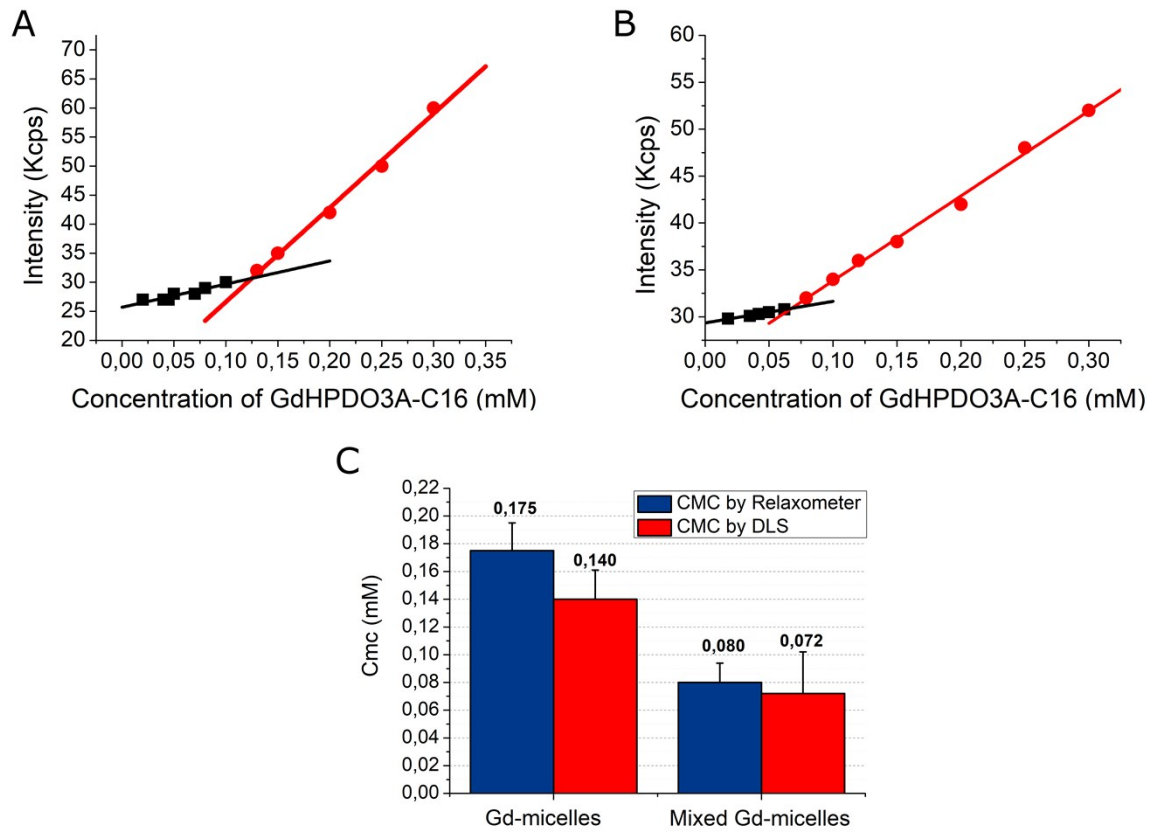


Fig.S5 Critical micellar concentration (CMC) evaluated by Dynamic Light Scattering (DLS) for Gd-micelles (A) and mixed Gd-micelles (B). (C) comparison between cmc evaluated by DLS and by relaxometric measurements.

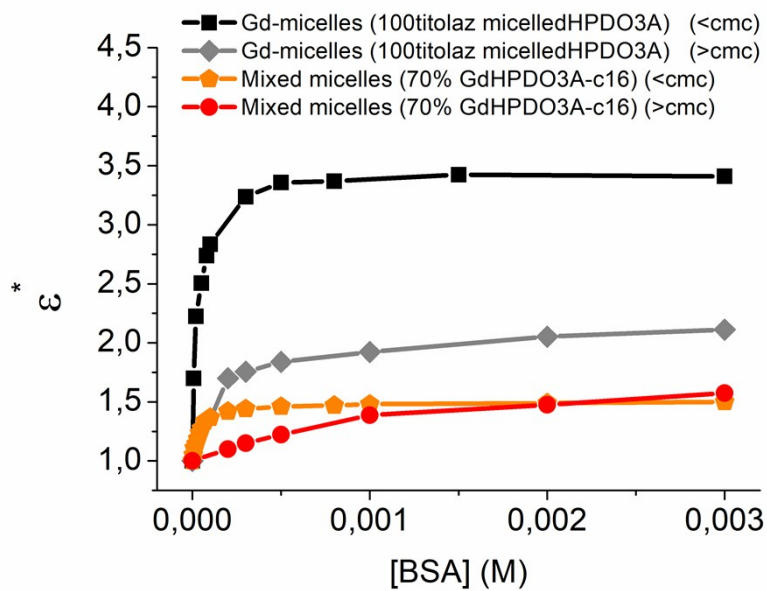


Fig.S6 Titration of micelles with BSA for GdHPDO3A-C16-micelles and mixed-Gd-micelles.

Relaxometric characterization of Gd-HPDO3A-C16 micelles

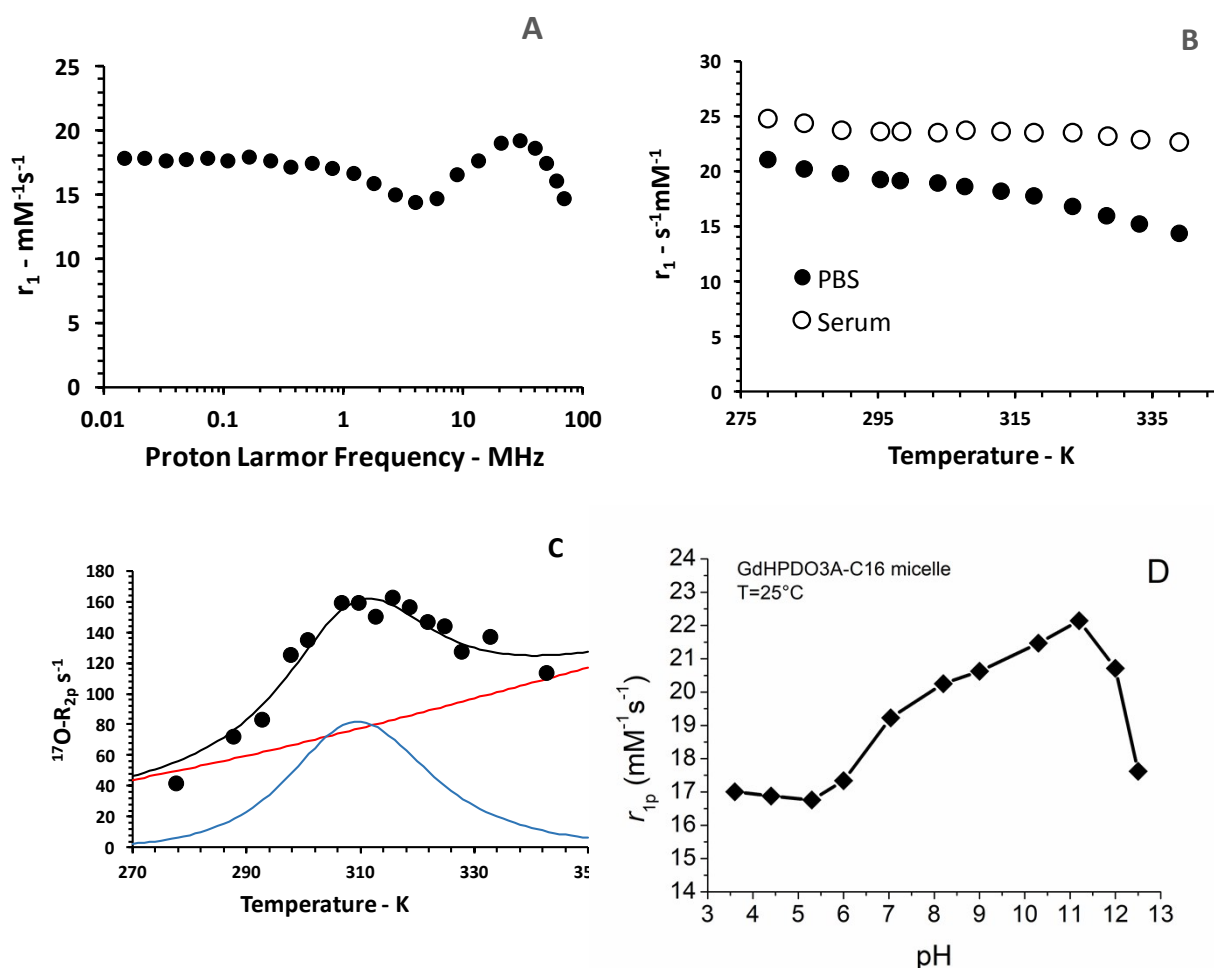


Fig.S7 (A) ^1H -NMRD profiles of Gd-HPDO3A-C16 micelles in PBS (1 mM of Gd-complex), pH 7.0, 25°C; (B) Relaxivity at variable temperature for 1 mM Gd-HPDO3A-C16 micelles in PBS or human serum; (C) Transverse ^{17}O NMR relaxation rates as a function of temperature for Gd-HPDO3A-C16 micelles recorded at 14.1 T. Data were analyzed with a model that considered the presence of two $q = 1$ isomers for the Gd-complex. The red and blue lines represent the calculated contributions of the predominant (> 90%, slow exchanging water) and the minority (< 5%, intermediate exchange water) isomers; (D) Relaxivity of Gd-HPDO3A-C16 micelles at variable pH values.

Hemolysis experiments

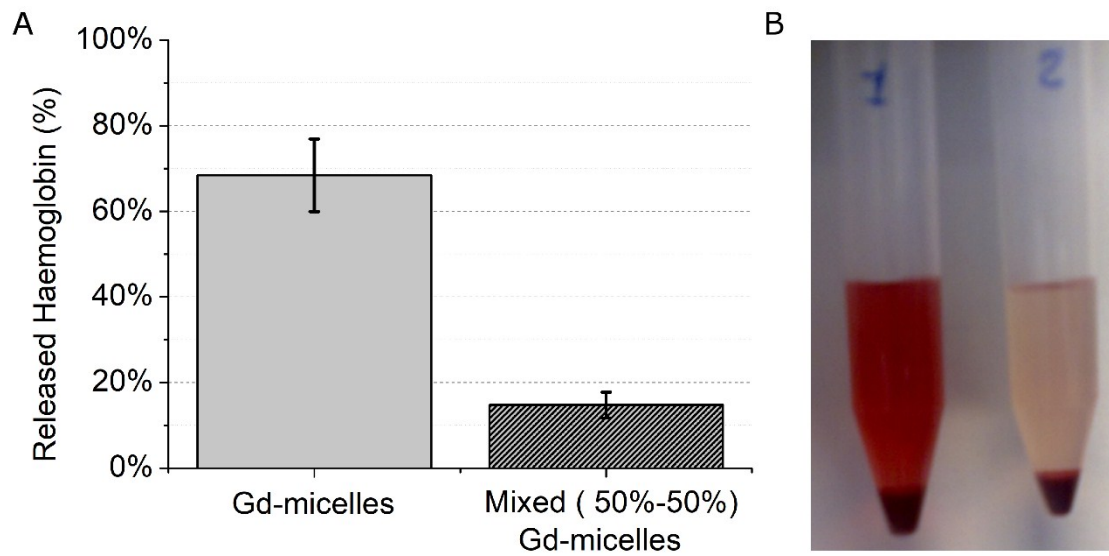


Fig.S8 Haemolysis experiment: (A) Percentage of Hemoglobin released in the RBCs' suspension after incubation with Gd-micelles or mixed Gd-micelles (50%-50%); (B) Representative tubes containing RBCs' pellet and supernatant with released Hemoglobin (left: incubated in presence of Gd-micelles, right: incubated in presence of mixed Gd-micelles)