Electronic Supplementary Material (ESI) for Nanoscale.

Supporting Information

for

Simple hybrid polymeric nanostructures encapsulating macrocyclic Gd/Eu based complexes: luminescence properties and application as MRI contrast agent

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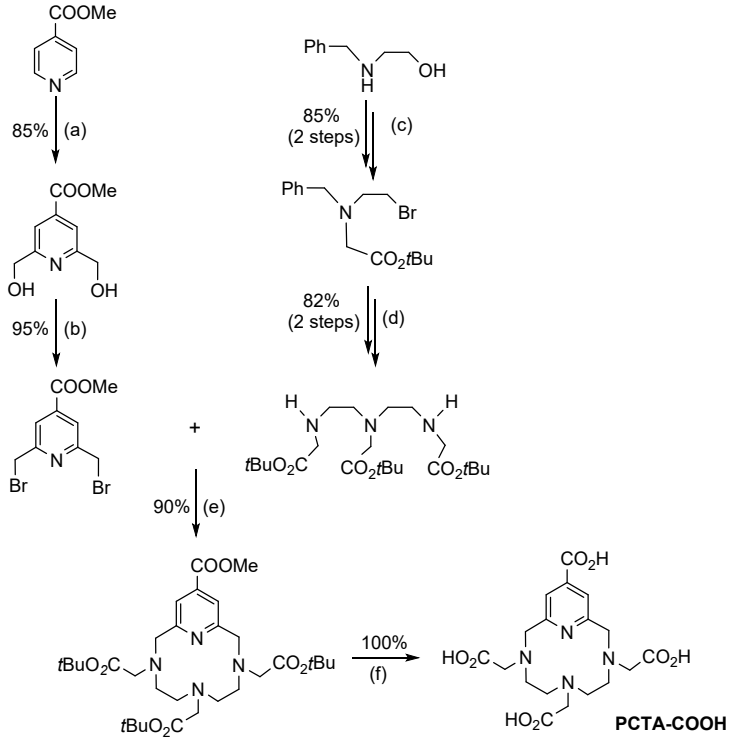
Scheme S1. Synthesis of the **PCTA-COOH** ligand described in **"**Efficient Synthesis of a Family of Bifunctional Chelators Based on the PCTA[12] Macrocycle Suitable for Bioconjugation". N. Leygue, M. Enel, A. Diallo, B. Mestre-Voegtlé, C. Galaup, and C. Picard. *Eur. J. Org. Chem.* 2019, 2899–2913.



Reagents and conditions: (a) $(NH_4)_2S_2O_8$, H_2SO_4 cat., MeOH, H_2O, reflux, 2 h; (b) PBr_3, CH_2Cl_2, reflux, 2 h; (c) i) $BrCH_2CO_2tBu$, K_2CO_3, CH_3CN, rt, 24 h, 100%; ii). *N*-bromosuccinimide, PPh_3, CH_2Cl_2, rt 16 h, 85%; (d) i) $NH_2CH_2CO_2tBu$ Hydrochloride salt, K_2CO_3, CH_3CN, reflux, 24 h, 82%; ii) Pd/C (10%), H_2 gas (6 bars), MeOH, rt, 12 h; 100%; (e) [reagents] = 2×10^{-3} M, Na_2CO_3, CH_3CN, reflux, 64 h. (f) 6*N* HCl_{aq}, reflux, 24 h.

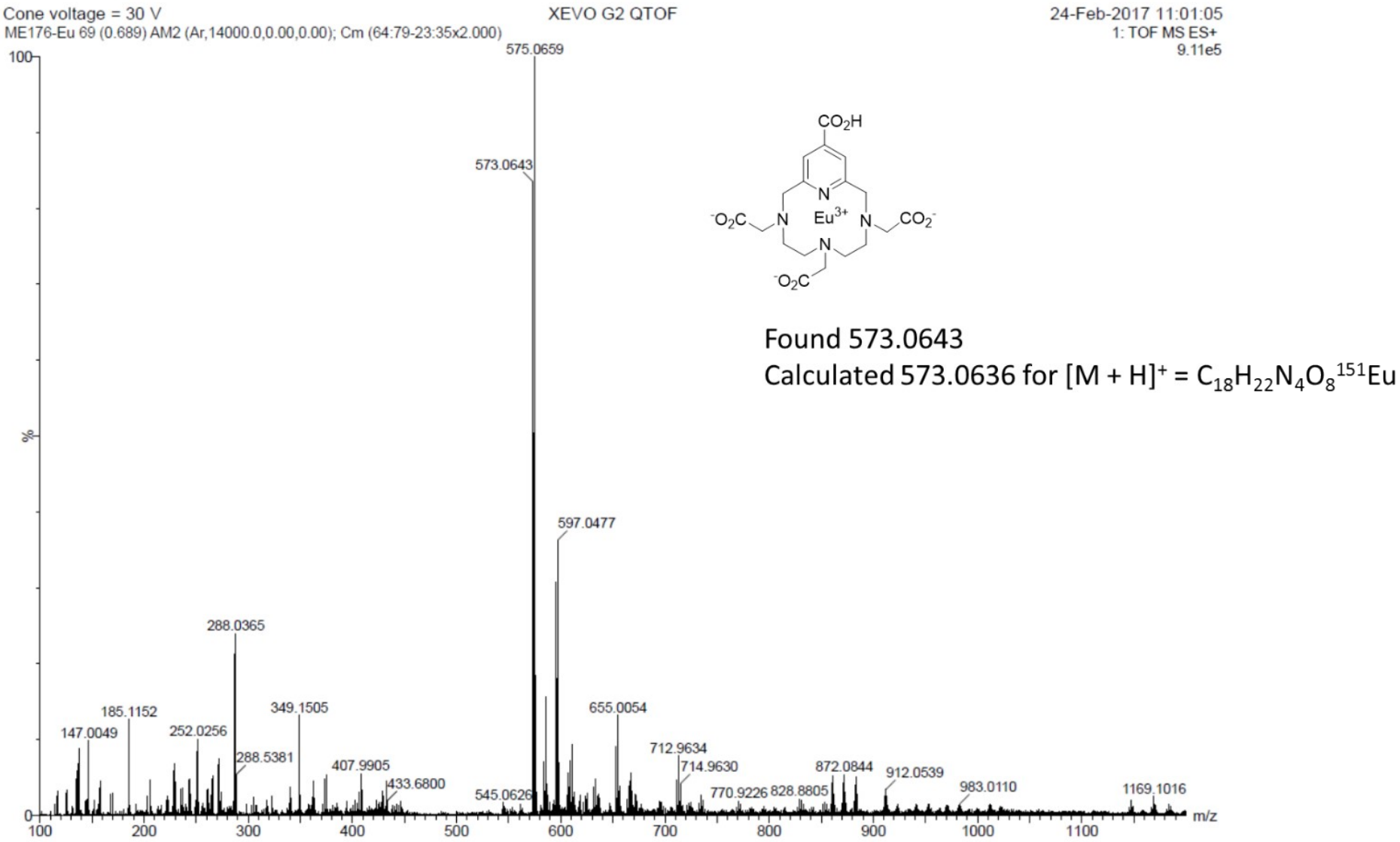


Figure S1. ESI$^+$ HRMS spectrum of **Eu^{3+}.PCTA-COOH complex**.

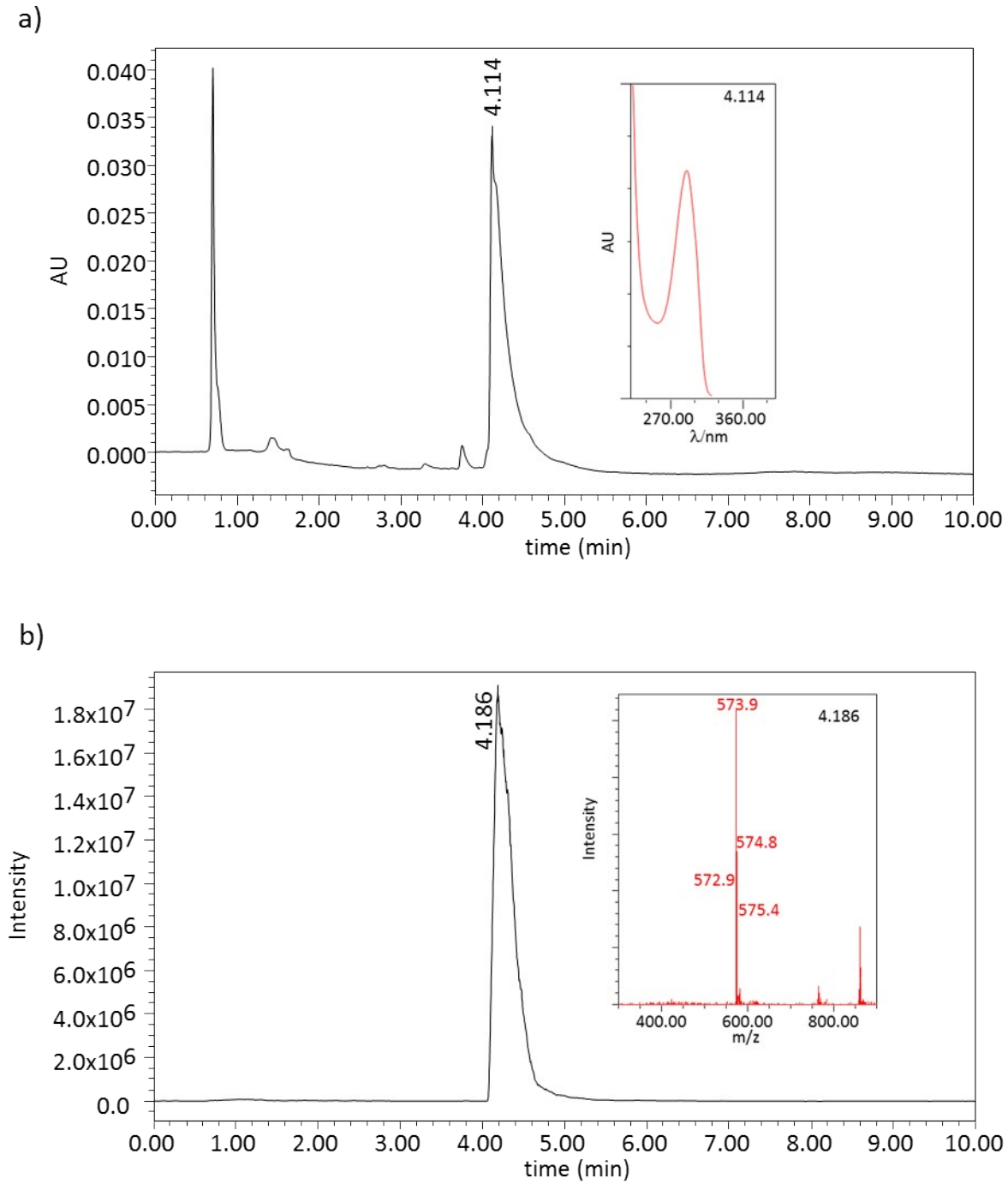


Figure S2. UPLC/UV-MS analysis of **Eu^{3+}.PCTA-COOH complex**. a) Chromatogram monitored at 290 nm (inset: UV absorption spectrum in arbitrary unit -AU- at 4.114 min) and b) trace chromatogram of *m/z* = 573 ($[M + H]^+$) (inset = ESI positive mode mass spectrum at 4.186 min). UPLC conditions are provided in the experimental part.

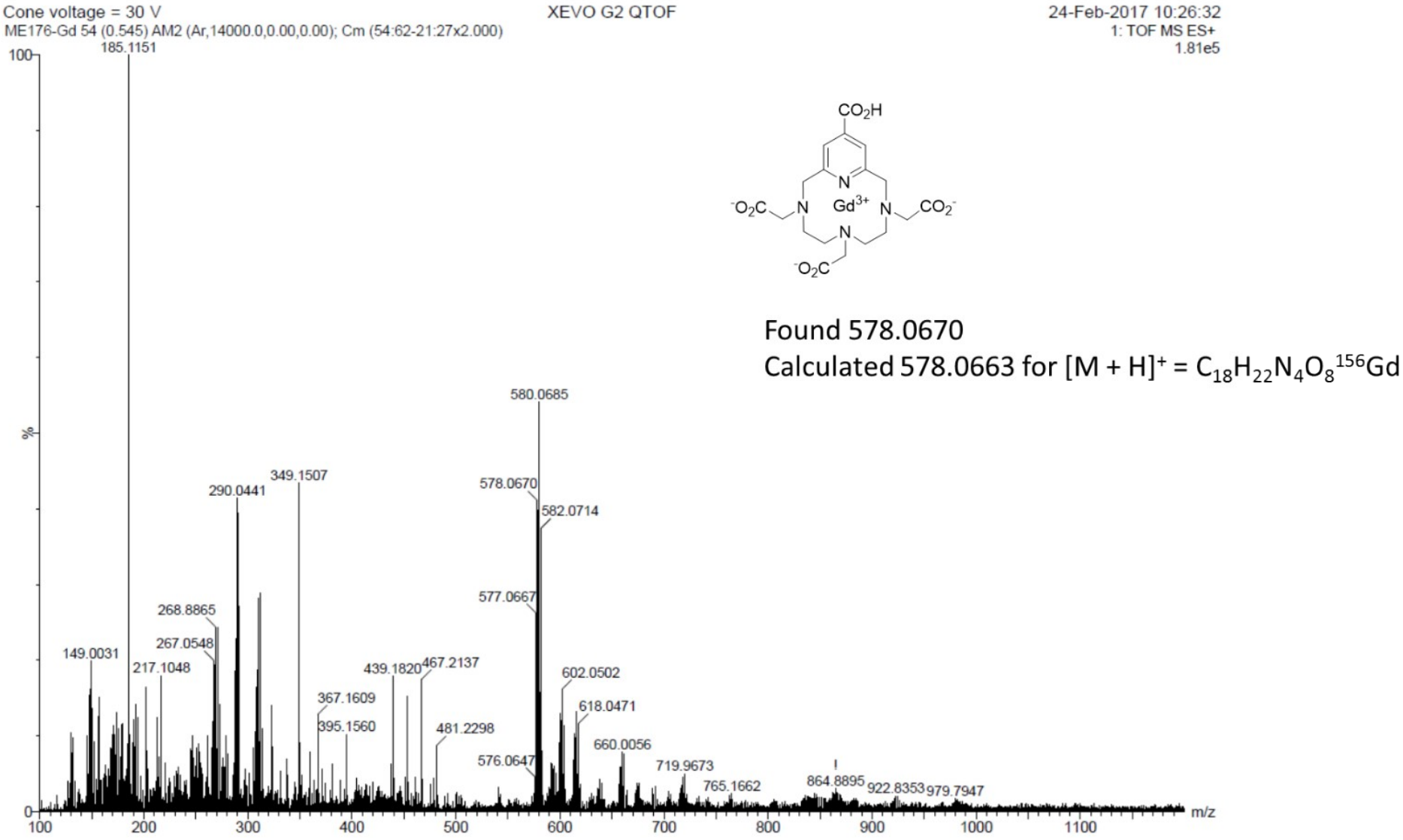


Figure S3. ESI^{+} HRMS spectrum of **Gd^{3+}.PCTA-COOH complex**.

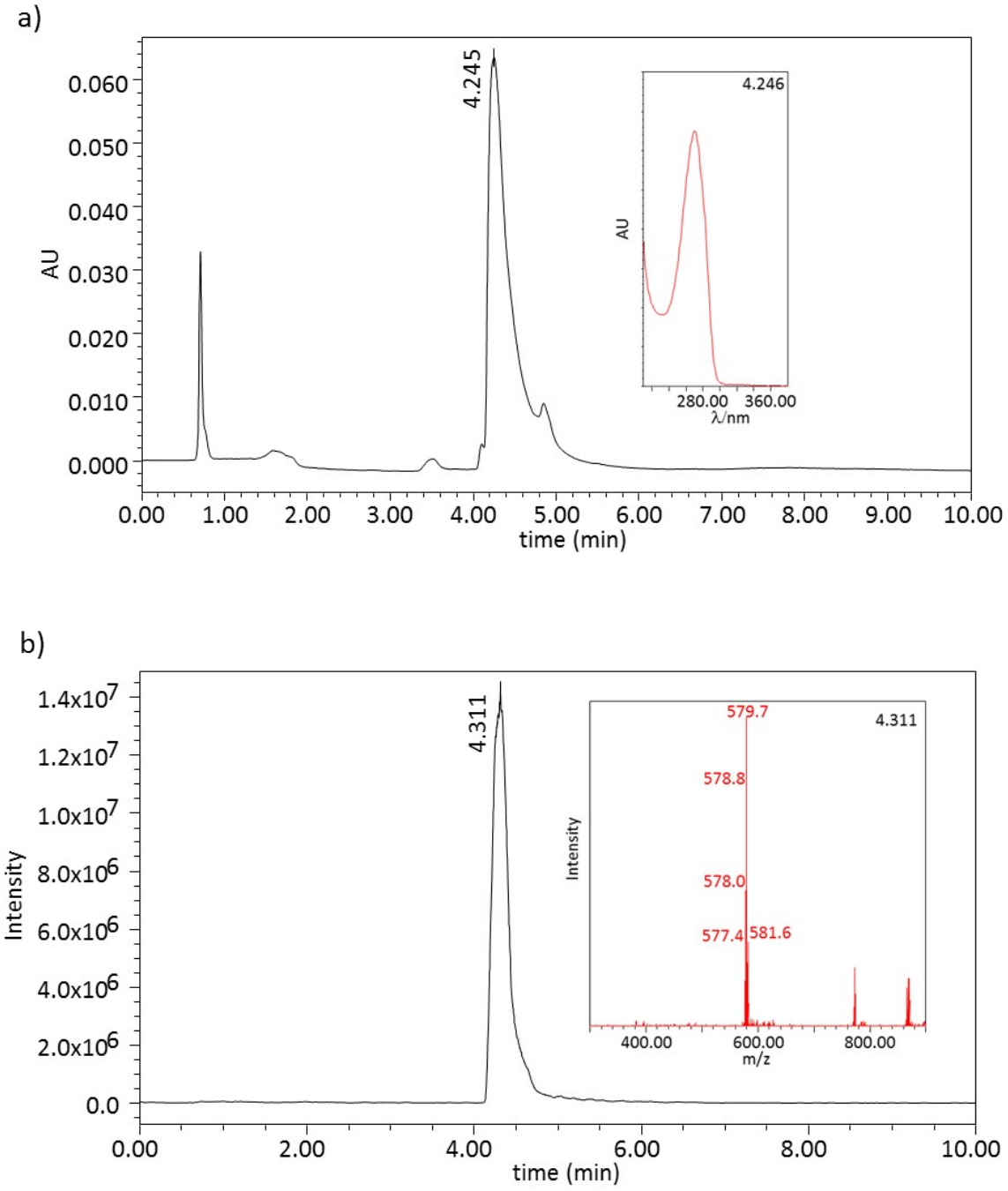


Figure S4. UPLC/UV-MS analysis of **Gd^{3+}.PCTA-COOH complex**. a) Chromatogram monitored at 290 nm (inset: UV absorption spectrum in arbitrary unit -AU- at 4.246 min) and b) trace chromatogram of *m/z* = 580 ($[M + H]^+$) (inset = ESI positive mode mass spectrum at 4.311 min). UPLC conditions are provided in the experimental part.

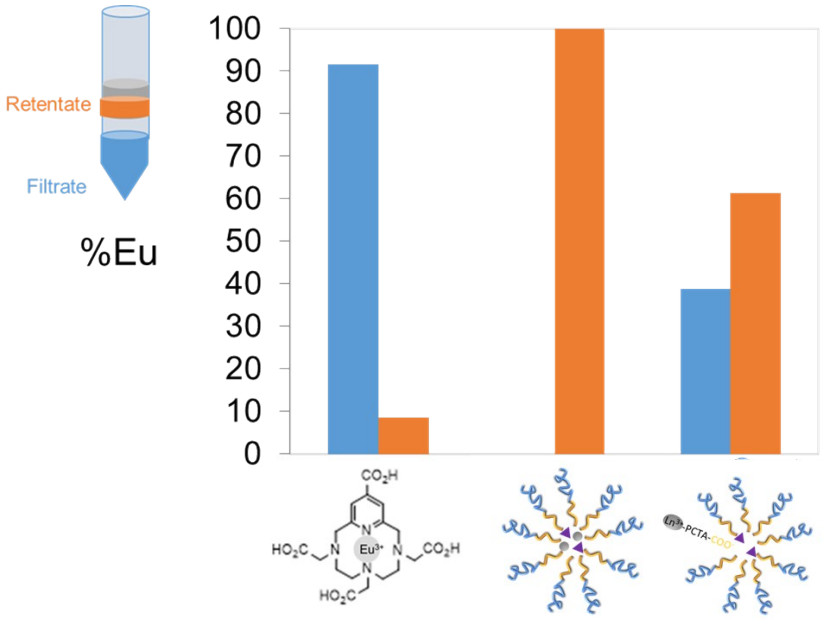


Figure S5. Evaluation of relative amount of Ln ions for the different systems of interest being submitted to a dialysis/centrifugation process. Solutions of Ln^{3+}/Zr@HPICs, Ln^{3+}.PCTA-COOH/Zr@HPICs and Ln^{3+}.PCTA-COOH were prepared according to the method depicted in supporting information. The composition of HPICs was adjusted in such way that electroneutrality between the positive charges of ZrO^{2+} and Ln^{3+} ions and the potentially available negative charges from the ionized or ionizable carboxylic acid, was reached. Once prepared, these samples were filtered with centrifugal filters (molecular weight cut-off 3 kDa) (Ultracel®-3K - Millipore Ireland Ltd) at 6500 rpm for 40 min. ICP-AES was further used to evaluate the relative amount of Ln ions in both retentate and filtrate. As expected, whereas Ln^{3+}/Zr@HPICs is exclusively present in the retentate part, most (90%) of Ln^{3+}.PCTA-COOH complex was found in the filtrate. In the case of Ln^{3+}.PCTA-COOH/Zr@HPICs, 40% of introduced complex was filtered through the dialysis membranes. This should correspond to complexes which are not trapped in HPIC structures.

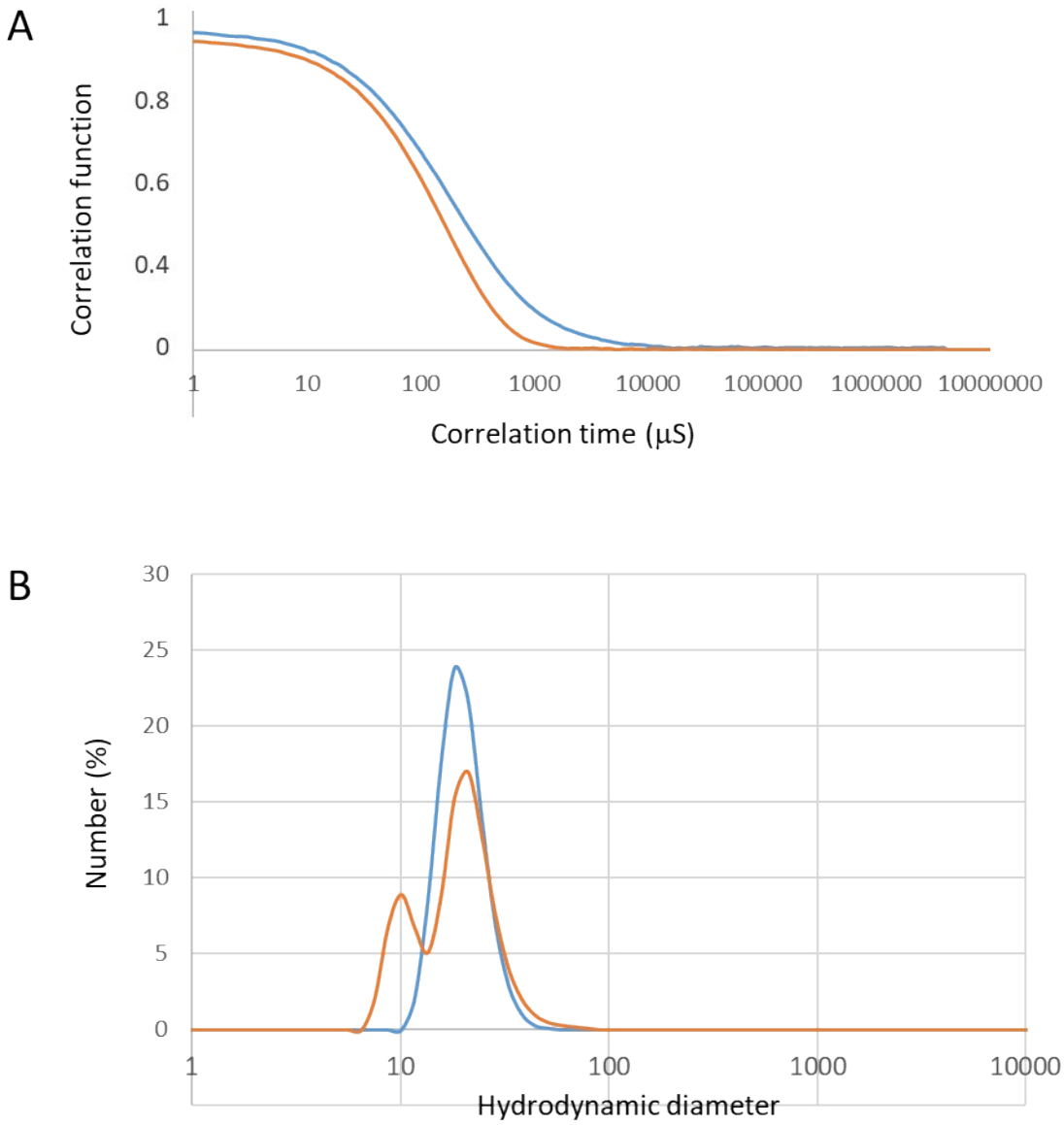


Figure S6. Correlation function (A) obtained for Gd^{3+}/Zr@HPICs (orange), Gd^{3+}.PCTA-COOH/Zr@HPICs (blue) and Gd^{3+}.PCTA-COOH (grey) solutions by DLS measurements (polymer concentration equal to 0.1%wt) at pH 7 and the corresponding the number-averaged hydrodynamic diameter distribution (B). In the case of Gd^{3+}.PCTA-COOH measured signal is too low to give an usable correlation function.

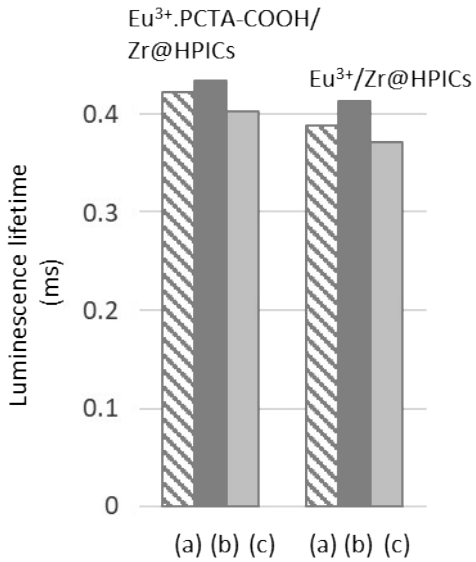


Figure S7. Effects of added ions on the emission lifetimes of HPIC particles. (a) **Eu^{3+}.PCTA-COOH/Zr@HPICs** or **Eu^{3+}/Zr@HPICs** ([Eu] = 0.12 mM) in Tris buffered saline 50 mM pH 7.4 ([NaCl] = 0.15 M), and after adding (b) phosphate (0.10 mM) and (c) calcium ions (0.25 mM).

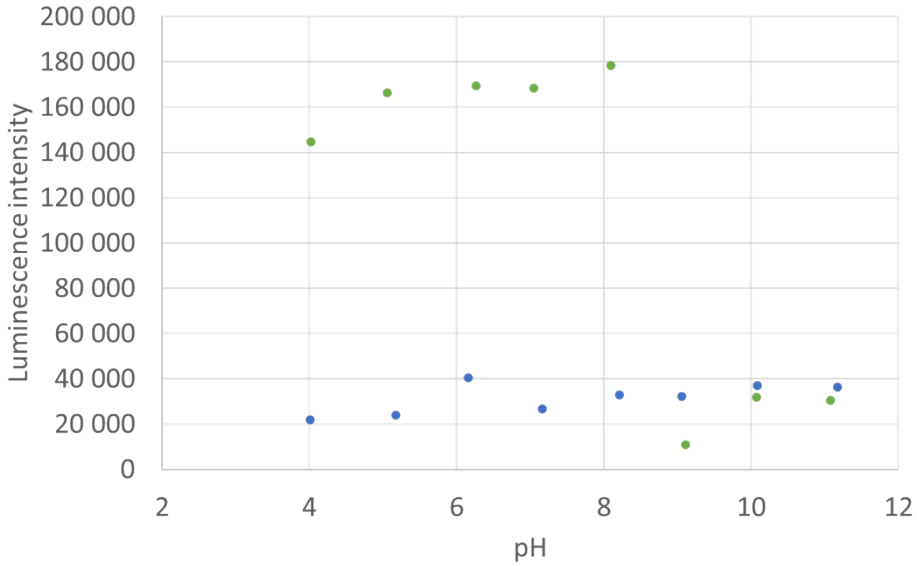


Figure S8. Effects of pH on the emission intensity (area-normalized emission spectra, l_{exc} = 249 nm) in HPIC particles. (blue circle) **Eu^{3+}/Zr@HPICs** ([Eu] = 0.14 mM) and (green circle) **Eu^{3+}@HPICs** ([Eu] = 1.96 mM)

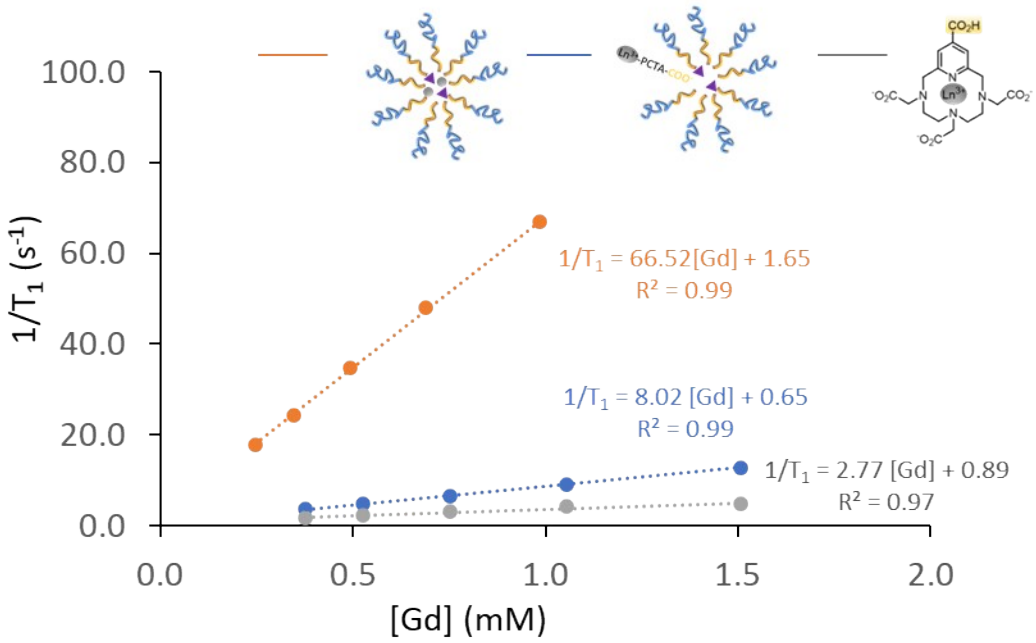


Figure S9. Change in the longitudinal relaxation time as a function of the concentration of Gd^{3+} ions in water at physiological pH (T = 298 K) for Gd^{3+}/Zr@HPICs (orange), Gd^{3+}.PCTA-COOH/Zr@HPICs (blue) and Gd^{3+}.PCTA-COOH (grey).