

Authentically Radiolabelled Mn(II) Complexes as Bimodal PET/MR Tracers

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The development of small molecule bimodal PET/MR tracers is mainly hampered by the lack of dedicated preparation methods. Authentic radiolabelling of MR contrast agents ensures easy access to such probes: a ligand, chelating a paramagnetic metal ion (e.g. Mn^{2+}) and the corresponding PET isotope (e.g. ^{52}gMn), leads to a "cocktail mixture" where both imaging reporters exhibit the same pharmacokinetics. Paramagnetic $[^{55}Mn(CDTA)]^{2-}$ shows an excellent compromise between thermodynamic stability, kinetic inertness and MR contrast enhancement. Therefore, the aim of this study was to develop new PET/MR tracers by labelling CDTA ligands with paramagnetic manganese and the β^+ -emitter ^{52}gMn .

N.c.a. ^{52}gMn ($t_{1/2}$: 5.6 d; E_{β^+} : 575.8 keV (29.6%)) was produced by proton irradiation of a ^{nat}Cr target followed by cation-exchange chromatography. CDTA was radiolabelled with n.c.a. $^{52}gMn^{2+}$ in NaOAc buffer (pH 6) at RT. The complex was purified by RP-HPLC and its stability tested in PBS and blood plasma at 37°C. The redox stability was assessed by monitoring the T1 relaxation (20 MHz) in HEPES buffer (pH 7.4). A functionalized CDTA ligand was synthesized in 5 steps.

$[^{52}gMn(CDTA)]^{2-}$ was quantitatively formed within 30 min at RT. The complex was stable for at least 6 days in PBS and blood plasma at 37°C and no oxidation occurred within 7 months storage at RT. Labelling CDTA with an isotopic $^{52}g/^{55}Mn^{2+}$ mixture led to the corresponding bimodal PET/MR tracer. Furthermore, a functionalized CDTA ligand was synthesized with an overall yield of 18-25%.

$[^{52}g/^{55}Mn(CDTA)]^{2-}$, the first manganese-based bimodal PET/MR tracer prepared, exhibits excellent stability towards decomplexation and oxidation. This makes the functionalized CDTA ligand highly suitable for designing PET/MR tracers with high relaxivity or targeting properties.

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