

QUANTITATIVE DETERMINATION OF GADOLINIUM BASED MAGNETIC RESONANCE IMAGING CONTRAST AGENTS IN URINE AND HOSPITAL WASTEWATER BY HPLC-ICP-QMS

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Background

Rare earth elements (REE) are a class of 17 elements consisting of the lanthanide elements with atomic number 56 (La) till 71 (Lu) and yttrium and scandium. They generally have similar chemical and physical properties, hindering a complete element purification. [1] To some exceptions, most REE have a III+ oxidation state and 6 to 8 coordination number, so does also gadolinium (Gd). [2] The ion with electron configuration $^{64}\text{Gd}^{3+} : [^{54}\text{Xe}] 4f^7$ is known paramagnetic, having the highest spin magnetic momentum S of $+7/2$. Besides other applications such as in permanent magnets, glass additives and as shield in neutron radiography, it is therefore used in the medical field as a chemical contrast agent for magnetic resonance imaging (MRI) scan. The cation is chelated by organic linkers of diethylene triamine pentaacetic acid (DTPA), diethylene triamine pentaacetic acid bismethylamide (DTPA-BMA) or tetraazacyclododecane (DOTA). [3] Occurrence of free Gd^{3+} is highly toxic to humans as it interchanges with Ca^{2+} and Zn^{2+} in biomolecules [4] and accumulates in the liver, bones, lymph nodes and skin up to 4.6 mg kg^{-1} . [5]

Chromatographic speciation method

The chromatographic method [3] was adjusted for separation of three most currently applied MRI contrast agents to the optimal conditions. A Perkin Elmer 200 Series HPLC system was coupled through a six way switching valve to a Perkin Elmer Elan DRc Inductively Coupled Plasma Quadrupole Mass Spectrometer for detection of Gd. Limits of detection were calculated by formula with S_{bl} the blanc surface area and a the sensitivity obtained from calibration of 0 till $250 \mu\text{g L}^{-1}$ Gd standards in Milli-Q water and criteria of $R^2 > 0.995$. The resulting values for Gd-DTPA, Gd-DOTA and Gd-DTPA-BMA amount 44, 61 and 83 ng L^{-1} .

Degradation behavior of Gd based contrast agents and presence in hospital wastewater

The described method was used to analyze the wastewater of a medium sized hospital in Ghent, Belgium, where patients were treated with contrast agents for MRI. Gd was found in a total concentration of $18.4 \mu\text{g L}^{-1}$ at the pH of 7.7 and 660 mg L^{-1} of chloride, 102 mg L^{-1} of sulphate and 28 mg L^{-1} of nitrate ions present. From the obtained chromatogram (Fig 1), two peaks of Gd-DTPA and Gd-DOTA can be distinguished. The occurrence of native species in the effluent corresponds well to degradation studies in water that revealed 95%, 83% and 100% of Gd-DTPA, Gd-DOTA and Gd-DTPA-BMA respectively were unaffected after 14 days of incubation at $37 \text{ }^\circ\text{C}$. Degradation was expressed to a much further extend when performed in urine matrix, indicating the significant role of other ions or biomolecules.

Conclusions and perspectives

Quantification of Gd-DTPA, Gd-DOTA and Gd-DTPA-BMA contrast agents was successfully established by HPLC coupled to ICP-QMS. Ions and biomolecules present in the urine matrix showed a large influence on the degradation of Gd, but the impact of individual compounds requires further examination. In the specific hospital wastewater, mostly parent Gd-DTPA and Gd-DOTA was observed. A selective recovery strategy should therefore definitely take into account the organic nature of Gd based contrast agents. On this basis, the behavior of Gd in the environment and removal of single contrast agents is yet subject of study.

References

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