

New Aryl-piperazine-Bis(3-Hydroxy-4-Pyridinonate)-IDA in Coadjuvation with a Deferiprone Derivative for Shuttle Metal Chelation

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The 3-hydroxy-4-pyridinones (3,4-HP) are well known chelating agents with potential applications in medicinal chemistry. The importance of these compounds has been mostly associated with their high affinity towards hard trivalent metal ions, such as Fe(III), Al(III) and Ga(III), and potential use as decorporating agents in situations of metal imbalance [1].

As part of an ongoing project, besides the polydentcity of 3,4-HP derivatives, we have decided to further explore their extra-functionalization aimed at improving the selectivity of the interaction with specific biological receptors. Therefore, a new arylpiperazine-containing bis-hydroxypyridone ligand was synthesized [IDAPIPr(3,4-HP)₂] (L¹) and its complexation behaviour was studied alone and coadjuvated by a peptide-mimetic mono-hydroxypyridinone derivative (L²) previously studied in our group [2].

This work reports equilibrium studies in aqueous solution for the characterization of this bis-hydroxypyridinone compound, in terms of acid-base properties and its binding affinity towards a set of M³⁺ ions (M = Fe, Al, Ga), as a simple binary and a ternary system (L¹:L²:M³⁺), using potentiometric and spectrophotometric methods. Biodistribution studies were also performed to assess the ability of this chelating system for the removal of a radiotracer (⁶⁷Ga) from overloaded mice.

References

1. M. A. Santos, *Coord Chem. Rev.* 228, **2002**, 187.
2. M. A. Santos, M. Gil, L. Gano, S. Chaves, *J. Biol. Inorg. Chem.*, **2005**, 000.