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# Potential therapeutic metallophore and electrochemical probe in the context of Alzheimer's disease: a ferrocene-containing aroylhydrazonic ligand.

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Zinc(II) ions are crucial in processing amyloid precursor protein (APP)[1] and are part of metalloproteins that degrade amyloid-β (Aβ) peptide, a key component of Alzheimer's disease (AD) senile plaques[2]. However, zinc also promotes neurotoxic Aβ aggregates, causing synaptic loss and memory deficits.[3] In this context, maintaining metal homeostasis in the brain is essential. Our group has been developing polydentate *N*-acylhydrazonic ligands over the past decade to prevent deleterious, abnormal metal-protein interactions, aiming to avoid aggregation and restore metal homeostasis.[4] On this basis, this work describes the synthesis and characterization of a dual *N*-acylhydrazone derived from ferrocene-carboxaldehyde, called **Ferfurone**, as a metallophore and electrochemical probe for AD. **Ferfurone** was characterized using mid-IR, Raman spectroscopy, $^{1}$H-NMR, and ICP-OES. The (*E*)-amido isomer, in *anti*-conformation, crystallized with a methanol molecule in the network, was confirmed by single-crystal X-ray diffraction. Due to its properties, ferrocene allows extensive studies using cyclic and square wave voltammetries. **Ferfurone** reacts with zinc(II) ions only in a strongly basic medium, suggesting it may be selective for copper(II) at physiological pH. A pKa value of 10.87 was estimated by voltammetry. Complexation assays showed current changes in the ferrocene process with addition of $Zn^{2+}$ or $Cu^{2+}$ ions. **Ferfurone** interacts with $A\beta_{1\text{-}40}$, confirming its role as a promising electrochemical probe for this peptide, and demonstrated an interesting antioxidant potential against superoxide radicals generated electrochemically. Further studies are ongoing to explore its electrochemical properties.

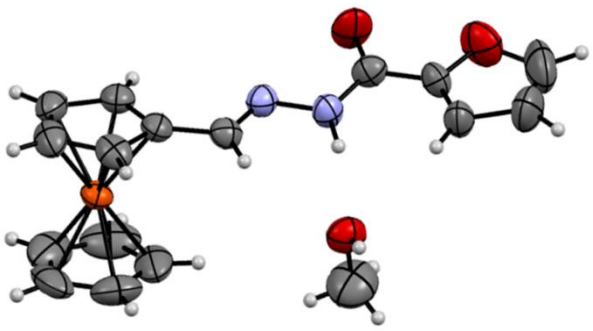

**Fig. 1.** ORTEP representation of the aroylhydrazonic ligand **Ferfurone**.

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