Full equilibria picture in aqueous binary and ternary systems involving copper(II), 1-methylimidazole-containing hydrazonic ligands and the 103-112 human prion protein fragment

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Full equilibria picture in aqueous binary and ternary systems involving copper(II), 1-methylimidazole-containing hydrazonic ligands and the 103-112 human prion protein fragment

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Abstract

In the present work, we describe two novel 1-methylimidazole *N*-acylhydyrazonic ligands and their interaction with copper(II) ions in solution. Binary systems constituted by each of these hydrazones and the metal were studied by potentiometric titrations. The magnitude of their affinities for zinc(II) was also determined for the sake of comparison. Additionally, a full evaluation of the copper(II) chelation profile of the new ligands in ternary systems containing a human prion protein fragment was performed. Mixed-ligand complexes comprising the $HuPrP_{103-112}$ fragment, copper(II) ions and an *N*-acylhydrazone were characterized by potentiometry, UV-Vis and CD. Some of these species were also identified by ESI-MS, and unequivocally assigned through their isotopic distribution pattern. As far as we know, this is the first report concerning the stability of ternary complexes involving a hydrazonic metal-protein interaction modulator, copper and a peptide. The *N*-acylhydrazones' ability in preventing this peptide's oxidation was examined as well. Both ligands are able to partially prevent the formation of the doubly-oxidized product, a process catalyzed by copper(II) ions. Oxidative stress is considered an important hallmark of neurodegenerative diseases, as prion-related spongiform encephalopathies. In this context, an active intervention on the deleterious copper-catalyzed methionine oxidation could represent an interesting therapeutic approach.

Keywords:

N-acylhydrazones; copper; PrP fragment; ternary complexes; potentiometry; oxidation.