MS28-1-3 Structural study of copper and zinc complexes of monoquinolines potentially active against Alzheimer's disease
#MS28-1-3

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Abstract
Loss of homeostasis of redox metals, particularly copper, in the brain of patients with Alzheimer's disease (AD) and the scavenging of copper by the amyloid peptide Aβ are responsible for oxidative damage leading to death of the cells neurons. To restore this copper homeostasis, without disturbing the abundant zinc in the brain, we have developed tetradentate chelators specific for copper, the TDMQs (for TetraDentate MonoQuinolines), formed of an 8-aminoquinoline unit substituted, on position 2, by a chelating side chain. In the metal complexes of TDMQ, the coordination of copper(II), provided by a square plane formed by the two nitrogen atoms of the 8-aminoquinoline unit and by the two nitrogens of the side chain, is very strong. The coordination of zinc, ensured only by the side chain, is much weaker. TDMQs are capable of completely extracting copper from Cu-Aβ complexes, and making it available to copper proteins. The complete structural characterization, by single-crystal X-ray diffraction, of eight TDMQ copper-zinc complexes is described here. The crystallographic structure is correlated with the affinity of the ligands for Cu(II) and Zn(II), and with their capacity to inhibit in vitro an oxidative stress induced by the Cu-Aβ complex. Such specific copper chelators should be able to regulate copper homeostasis in brain tissue and can therefore be considered as potential therapeutic agents for Alzheimer's disease.

References
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Restoration of copper homeostasis by TDMQs, specif