Interaction of the human prion PrP(106-126) sequence with copper(II), manganese(II), and zinc(II): NMR and EPR studies.

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Streszczenie

The synthetic peptide encompassing residues 106-126 (PrP106-126, KTNMKHMAGAAAAGAVVGGLG) of the human prion protein was considered for its binding properties toward copper(II), manganese(II) and zinc(II) at pH 5.7. 1H and 13C 1D spectra, 1H spin-lattice relaxation rates, and 1H-15N and 1H-13C HSQC 2D experiments were obtained in the absence and in the presence of metal ions. While Zn(II) was found to yield negligible effects upon any NMR parameter, metal-peptide association was demonstrated by the paramagnetic effects of Cu(II) and Mn(II) upon 1D and 2D spectra. Delineation of structures of metal complexes was sought by interpreting the paramagnetic effect on 1H spin-lattice relaxation rates. Exchange of peptide molecules from the metal coordination sphere was shown to provide sizable contribution to the observed relaxation rates. Such contribution was calculated in the case of Cu(II); whereas the faster paramagnetic rates of peptide molecules bound to Mn(II) were determining spin-lattice relaxation rates almost exclusively dominated by exchange. Proton-metal distances were therefore evaluated in the case of the Cu(II) complex only and used as restraints in molecular dynamics calculations where from the structure of the complex was obtained. The peptide was shown to bind copper through the imidazole nitrogen and the ionized amide nitrogen of His-111 and the amino-terminal group with the terminal carboxyl stabilizing the coordination sphere through ionic interactions. The data were interpreted as to demonstrate that the hydrophobic C-terminal region was not affecting the copper-binding properties of the peptide and that this hydrophobic tail is left free to interact with other target molecules. As for the complex with Mn(II), qualitative information was obtained on carbonyl oxygens of Gly-124 and Leu-125, beyond the terminal Gly-126 carboxyl, being at close distance from the metal ion, that also interacts, most likely, through a hydrogen bond of metal-bound water, with the imidazole ring of His-111.

Adres publiczny

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https://www.acs.org/content/acs/en.html