



Structure and stability of the Cu^{II} complexes with tandem repeats of the chicken prion.

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Prion protein (PrP) misfolding is one of the pivotal issues in understanding the rudiments of neurodegenerative disorders. The conformational change of mammalian cellular PrP to scrapie PrP is caused by an unknown agent, but there is reasonable evidence supporting the key role of copper ions in this process. The structure of the avian PrP was found to be very similar to the mammalian protein, although there is only 30% homology in the secondary structure. This work shows that copper ions are very effectively bound by hexarepeat fragments of chicken prion protein, although not as effectively as it was found in the case of mammalian protein. By means of potentiometric and spectroscopic techniques (nuclear magnetic resonance, circular dichroism, UV-vis, and electronic paramagnetic resonance), it was shown that Cu^{II} ions coordinate to the chicken PrP hexapeptide domain in physiological pH via imidazole nitrogen donors of His residue(s). The binding pattern changes the structure of peptide involved, indicating a possible impact of Cu^{II} ions in the biology and pathology of nonmammalian PrP, which could be similar to that found for mammalian PrP. The present study shows that, similar to the human prion octapeptide repeats, chicken prion hexapeptide repeats might bind copper ions in two different ways, depending on the number of repeats and metal/ligand molar ratio: (i) an intra-repeat coordination mode in which copper ion is chelated by His imidazole and deprotonated amide nitrogen in monomeric peptide and (ii) an inter-repeat coordination mode in which a polymeric peptide ligand (dimer and trimer) forms polyimidazole complexes that are very stable at physiological pH. Two proline residues inserted into the hexapeptide unit have a critical impact on the metal-binding ability.

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