Conformational changes of nesfatin-1 in the presence of Zn(II) ions

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Human nesfatin-1 is a small 82-amino acid (9.8 kDa) hormone peptide that is a product of proteolytical cleavage of N-terminus of Nucleobindin-2. Nesfatin-1 is comprised of three domains: N-terminal (N23), middle part (M30) and C-terminal (C29). Nesfatin-1 is thought to exert its biological functions, especially its anorexigenic properties through, the N23 domain. Nucleobindin-2/nesfatin-1 is engaged in the regulation of many important physiological processes, e.g. energy homeostasis, reproduction, epilepsy, anxiety, depression, regulation of circadian rhythm and carcinogenesis. Multifunctionality is a characteristic feature of intrinsically disordered proteins (IDPs) thus nesfatin-1 might be a member of this family as indicated by in silico analysis. Structural studies of nesfatin-1 are therefore essential to establish the relationship between its structure and function. Herein we utilized recombinant nesfatin-1 from *Homo sapiens* expressed in Bl21(DE3)pLysS *E. coli* cells. Intrinsic disorder of nesfatin-1 in the absence of ions was proven by circular dichroism spectroscopy (CD). Further CD experiments revealed a strong concentration-dependent increase in the α-helical content of nesfatin-1 under Zn(II) treatment. Sedimentation-velocity analytical ultracentrifugation confirmed structural changes of nesfatin-1 and compaction of its elongated structure in the presence of Zn(II) ions. We also observed a propensity of nesfatin-1 for oligomerization. Above findings suggest that nesfatin-1 may be engaged in Zn(II) homeostasis. Furthermore, our data demonstrating context-dependent structural flexibility of nesfatin-1 might help to elucidate multifunctionality of this peptide at the molecular level.

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