

Interaction of Cu(II) ions with a fragment of Park9 protein

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Keywords: copper(II), Parkinson's disease

Parkinson Disease (PD) is a neurodegenerative pathology whose causes have not yet been fully clarified. For this reason it is also called an idiopathic (with no known or identifiable causes) syndrome, although some PD types can have a genetic or a post-traumatic origin, and different risk factors like exposure to some pesticides. Recently it emerged that also exposure to manganese (i.e. in welders or miners) can cause a PD-like syndrome (Parkinsonism), and a connection between genetic and environmental causes of Parkinson's disease has been discovered regarding a human protein, Park9, whose mutations can lead to a form of juvenile PD.¹

Shortly after, a study on a yeast gene, YPK9, which is very similar to human PARK9, revealed that deletion of this gene confers sensitivity for growth in the presence of several divalent cations, suggesting that the YPK9 protein may play a role in the sequestration of divalent heavy metal ions.² In the same way, a mutation on PARK9 may expose humans to these cationic species.

In this perspective, we have chosen short fragments of Ypk9 protein that include interesting sequences for metal binding and are highly conserved in a number of different organisms, located in domains of the protein readily accessible to the metals. We studied their behaviour towards divalent cations such as manganese and zinc, using NMR mono- and bidimensional techniques and EPR spectroscopy. As this study was going on,³ we also started the investigation on Cu(II) coordination, showing by a series of potentiometric and spectroscopic measurements that this metal too is able to effectively bind the chosen sequence. Here we would like to report our latest findings.

- 1) Gitler, A.D.; Chesni, A.; Geddie, M.L.; Strathearn, K.E.; Hamamichi, S.; Hill, K.J.; Caldwell, K.A.; Caldwell, G.A.; Cooper, A.A.; Rochet, J.-C.; Lindquist, S.; Nat. Genet. 2009, 41(3): 308-315
- 2) Schmidt, K.; Wolfe, D.M.; Stiller, B.; Pearce, D.A.; Biochem. Biophys. Res. Comm. 2009, 383: 198-202
- 3) Medici, S.; Peana, M.; Delogu, L. G.; Zoroddu, M. A.; Dalton Trans. 2012, 41 (15) 4378-4388

Copper(II) complexes of compartmental ligands: structural and stoichiometric aspects depending upon the anionic group of the copper salt

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Keywords: copper(II) complexes, compartmental ligands, structure

It has been found that anionic species of metal salts can lead to different geometries and stoichiometries in the synthesis of coordination compounds. Therefore, using the same cation but different polyatomic anion groups such as oxalate, sulfate, acetate, oxamate etc. [1], it is possible to obtain metal complexes with various structural and stoichiometric features upon coordination. In fact, these anionic groups can behave themselves, generally, as mono-, bidentate and bridged-bidentate ligands towards metal ions. In the last years, with the aim to design a multi-dentate ligand capable of supporting simultaneous coordination to three copper atoms and to mimic the multicopper active sites of blue copper oxidases (e.g., laccase, ascorbate oxidase and ceruloplasmin), we focused our studies on the synthesis and structural characterization of copper(II) complexes of compartmental acyclic bis(salicylhydrazone) ligands derived from imino- and methyl-iminodiacetic acid, finding a different behaviour using copper(II) sulfate, perchlorate and acetate salts. Thus, we have obtained, with a 1:3 (ligand-to-metal) molar ratio, a trinuclear coordination polymer from Cu(II) perchlorate [2], a sulfato-bridged hexanuclear dimer [3] and a mononuclear complex using Cu(II) acetate [4]. Microbiological investigations showed a good activity of the sulfato and perchlorato complexes. Studies concerning DNA binding of these compounds are now in progress.

- 1) S. Dey, S. Sarkar, T. Mukherjee, B. Mondal, E. Zangrando, J.P. Sutter P. Chattopadhyay. *Inorg. Chim. Acta* **376** (2011) 129.
- 2) H. Adams, D. E. Fenton, G. Minardi, E. Mura, A. M. Pistuddi, C. Solinas. *Inorganic Chemistry Communications*. **3** (2000) 24.
- 3) A. Bacchi, M. Carcelli, G. Pelizzi, C. Solinas, L. Sorace. *Inorganica Chimica Acta*. **359** (2006) 2275.
- 4) C. Juliano, A. Mattana, C. Solinas. *Transition Metal Chemistry*, **35**, issue 2 (2010) 253.

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