Metal-Binding Peptides: From Occurrence in Nature to the Design for Chemical or Biological Applications

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Several d-block metal ions (such as Cu, Zn, Fe, Mn etc) play an essential role in biology, in particular as catalytic and structural centers in metalloproteins. Two properties makes certain of them very suited for catalysis: (i) they have several accessible redox states and (ii) they are able to bind and activate small substrates (like O_2, $O_2^{\circ -}$, NO,…) via coordination bonds. Coordination bonds are stronger than weak interaction but are generally more reversible compared to covalent bonds.
Essential d-block metal ions are mostly bound to structured proteins. Metallopeptides, i.e. peptides that natively bind essential d-block metals, are much less abundant than metalloproteins. However, under dishomeostasis of these metal ions or in case of metal-overload, binding to peptides might become more relevant.
Challenging reaction catalyzed by enzymes at mild conditions with mostly first row d-block metals inspired chemists to study structural or even functional mimics. To do so, mostly inorganic complexes were developed. Much less functional examples are reported based on small peptides mimicking the enzymes. One major reason for that is the high flexibility of short peptides, which hampers to have a well-controlled metal site with defined properties. Enzymes are generally a long chain folded in a well-defined 3D structure, allowing a control and stabilization of the environment of the metal. This structure is made on intra-molecular interactions, covalent (eg disulfide) or non-covalent. Hence, the shorter the protein (peptide), the lesser the intra-molecular interactions, the higher its dynamics. This might also be the reason why physiological relevant metallopeptides are scarce.
Based on our experience [1,2], the present lecture will discuss some examples of metallopeptides (mostly copper), of physiological or pathosphysiological relevance, and report on potential strategies to better structure metallopeptides in order to control better their chemistry.

References:

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