Poster Session: Complexes of Phosphates, Nucleosides and Nucleotides

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Promotion of the Hydrolysis of Purine-Nucleoside 5'-Triphosphates by Metal Ions

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Enzyme-catalyzed transfer of nucleotidyl and phosphoryl groups depends on the presence of metal ions. In consequence, model systems involving metal ion-promoted dephosphorylation of nucleoside 5'-triphosphates (NTP) (with transfer of a phosphoryl group to water) continue to be the focus of considerable attention. While early studies provided useful comparisons on the influences of various metal ions [1], additional investigations have uncovered more subtle but essential features, including (a) the formation and participation of complexes containing more than one metal ion per NTP [2–4], (b) the importance of metal ion interactions with purine bases [2, 5], and (c), the involvement of dimeric purine-nucleotide complexes which arise through base-stacking [2, 5].

For pyrimidine-NTP systems containing Ni^{2+}, Cu^{2+} or Zn^{2+} the reactive species is a complex of type $M_2(NTP)(OH)^-$, where the nucleic base moiety of the pyrimidine-nucleotide is not involved [4]; this conclusion is confirmed by observations with methyltriphosphate.

In the case of purine-NTP systems the general situation is more complicated: for example, for ATP with Ni^{2+}, Cu^{2+} or Zn^{2+} the reaction proceeds by way of dimeric complexes such as $[M_2(ATP)]_2$ [2], which is possibly better formulated as $[M_2(ATP)]_2(OH)_{1\text{ or }2}^{-1/-2}$ [5]. The participation of dimers is in accord with the well-known self-association by base-stacking of purine-nucleotides [6]. The M^{2+}/N-7 interaction [6] is also crucial for rapid dephosphorylation [2]. Thus, if the Cu^{2+}/N-7 interaction in the Cu^{2+}/ATP system is prevented by addition of one equivalent of 2,2'-bipyridyl (Bpy), with formation of a ternary $Cu(Bpy)(ATP)^{2-}$ complex, the reactivity is reduced markedly and to the level shown by corresponding pyrimidine-NTP systems. The properties of binary Cu^{2+}/purine-NTP systems also vary, depending on the stacking properties of the base residues and the extent of the Cu^{2+}/N-7 interaction. Further, from ^{1}H-NMR shift experiments on the Cd^{2+}/ATP system, it is evident that the release of N-7 from the coordination sphere of the metal ion by the formation of hydroxo-complexes in the upper pH range parallels the decreasing dephosphorylation reactivity of the same system.

It appears that one of the nucleotides in the dimer is needed to facilitate transfer of the other into the reactive state. Accordingly, the reactivity of the Cu^{2+}/ATP 1:1 system is inhibited by adenosine and phosphate, while addition of AMP^{2-} further promotes the reactivity. We suggest that AMP^{2-} is able to take over the role of the 'structuring' ATP^{4-} in the reactive dimer, thus bringing more ATP into the reactive form. We postulate further that in the most reactive species one metal ion is coordinated to the α and β positions of the triphosphate moiety and a second metal ion is coordinated to the γ phosphate group, providing in this way a structure in which the terminal γ group is activated toward dephosphorylation. The metal ion/N-7 interaction seems to facilitate the formation of this reactive intermediate, a conclusion in accord with the lower reactivity of the pyrimidine-NTP and methyltriphosphate systems.

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