# Probing the role of (bis)phosphate in inhibitors toward $Cu^{II}$-amyloidβ-induced oxidative stress in Alzheimer's disease: Kinetics and NMR relaxation studies

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$Cu^{II}$ complexes of Alzheimer's disease related peptide β-amyloid (Aβ) exhibit metal-centered redox chemistry. The metallo-Aβ complexes are the hallmark of the disease and have been attributed to the generation of reactive oxygen species causing oxidative stress. Herein, the role of (bis)phosphate moieties in various compounds as potential inhibitors against the oxidative stress caused by $Cu^{II}$-Aβ complexes will be presented. Pyridoxal 5-phosphate and zoledronic acid afford a $K_i$ value of 200 and 2 μM, respectively, towards the oxidation of catecholamines by $Cu^{II}$-$Aβ_{1-20}$. Mutation of the $Aβ_{1-20}$ peptide at positions 5 and 16 gives insight into the interactions of the Arg/Lys side chains of the peptide with the (bis)phosphate moiety in the various inhibitors. $^{31}P$ NMR relaxation studies further supports the binding/interaction of (bis)phosphate moiety with the apo $Aβ_{1-20}$ and $Cu^{II}$-$Aβ_{1-20}$ complex. Correlation of (bis)phosphate moiety binding/activity will allow for the design of more potent inhibitors toward the $Cu^{II}$-Aβ induced oxidative stress.