Dinuclear Copper (II) Complexes as oxidative cleavage agents

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For its special stability under physiological conditions, DNA which contains the genetic instructions is one of the most important biomacromolecules in all living organisms. The half-life of DNA hydrolysis is estimated to be thousands to billions of years. However, it could be hydrolyzed with the help of artificial nucleases or be damaged by reactive oxygen species (ROS). Copper is among the most widely used metals for this purpose, since it was demonstrated that $[Cu(phen)_2]^+$ was able to break the DNA chain in the presence of H_2O_2. In this work we describe the capacity to cleave DNA of two novel dinuclear complexes $[Cu_2(HL_1)(\mu\text{-}OAc)](ClO_4)_2$ **(1)** and $[Cu_2(HL_2)(\mu\text{-}OAc)](ClO_4)$ **(2)**, where HL_1= *N,N',N'*-[tris-(2-pyridylmethyl)]-*N*-[(2-hydroxy-3,5-di-*tert*-butilbenzyl)]1,3-propano diamine-2-ol and HL_2= *N,N*-[bis-(2-pyridylmethyl)]-*N',N'*-[(2-hydroxybenzil)(2-hydroxy-3,5-di-*tert*butil benzyl)]1,3- propanodiamine-2-ol.
Initially, a series of experiments tested Complex **1** and **2** activities at different pH conditions. Results demonstrated that DNA cleavage activity is clearly pH-dependent since with increasing pH values, higher DNA cleavage is obtained. Kinetics experiments have been performed, and time-dependent and concentration-dependent cleavages were observed. The pseudo-Michaelis-Menten kinetic parameter k_{cat}, affinity constant (K_M) and specificity constant k_{cat}/K_M were determined. The obtained k_{cat} values of 0.12 and 0.45 h^{-1} for **1** and **2**, respectively (37°C, pH 9.0), indicate that these Cu(II) complexes exhibit very high cleavage activity, with 3.4 x 10^6 and 1.2 x 10^7 fold rate enhancement for **1** and **2** respectively. Mechanistic aspects also were investigated. The addition of hydroxyl radical scavengers, like DMSO, produces significant inhibition of the DNA cleavage activity of the complexes, suggesting an oxidative reaction mechanism. These results point out these complexes as potential chemical nucleases.

Key words: *Copper complexes, DNA Cleavage, Chemical nucleases.*

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