# Investigation of a New Water Soluble Trinuclear Copper(II) Complex with Partial Cubane Cu3O4 Cores: Synthesis, Structure and DNA Binding Affinity

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## Abstract

A new water soluble trinuclear Copper(II) complex $K[Cu_3(cbal)_3(\mu_3\text{-}OH)(H_2O)]$ has been synthesized in good yield via the reaction of an unsymmetrical amino dicarboxylic ligand, N-(2-carboxybenzomethyl)-β-alanine ($H_2$cbal), $Cu(ClO_4)_2{\cdot}6H_2O$ and $K_2CO_3$ in methanol at room temperature. The complex has been characterized by several analytical techniques including single crystal X-ray crystallography. The X-ray crystal of complex shows that one Copper(II) ion is in a distorted square pyramidal geometry, the other Copper(II) ions are in a distorted trigonal bipyramidal and a distorted octahedral geometry forming a scalene triangle. The complex contains a partial cubane $[Cu_3O_4]$ core consisting of the trinuclear $[\{Cu(cbal)\}_3(\mu_3\text{-}OH)]^{-}$ unit. Complex is investigated for its binding affinity towards CT-DNA in aqueous medium at pH~7.5 using UV-vis and fluorescence spectroscopic techniques.

**Key words:** Trinuclear copper complex, Carboxylate bridging, X-ray structure, Spectroscopy, DNA binding

## 1. Introduction

Nature has constructed numerous polynuclear Copper complexes that perform an extraordinary array of catalytic transformations based on the cooperative interactions observed in biological systems[1-4]. In recent years, considerable attention has been devoted to the polynuclear metal complexes due to their implications in catalysis, magnetism and biology. In this context, investigation of trinuclear Copper(II) complexes should not only assist in the development of new low molecular weight catalysts and magnetic materials but could also shade light to biological processes that involve Copper biomolecules[5,6]. Within the scope of such applications, experimental and theoretical investigations of simple trinuclear

copper(II) complexes have turned out to be a promising route to the understanding of various biological functions[7,8]. Furthermore, the magnetic properties of such complexes reported in literature have indicated that the trinuclear complexes containing the [$Cu_3O$] core are a simple three-electron spin system. The three unpaired electrons in this core magnetically interact through super exchange involving Cu(II)-O-Cu(II) pathways resulting in the antiferro- or ferromagnetic complexes. Hence, it is vital to synthesize the low molecular weight trinuclear (II) complexes with triangular arrangement of metal ions in order to study these properties.

There are reports in the literature on multinuclear (II) complexes which can efficiently promote the binding and cleavage of biological macromolecules[9,10-12]. However, the systematic and detailed study of such binding and cleavage of biological macromolecules has been sporadic, probably due to the unavailability of structurally characterized highly water soluble trinuclear (II) complexes[13,14]. In this paper, we report the synthesis, structure, spectral properties and DNA binding affinity of two new water soluble $\mu_3$-hydroxo bridged trinuclear (II) complex containing partial cubane [$Cu_3O_4$] core.

## 2. Results and Discussion

**2.1. Synthesis and general characterization.** The unsymmetrical amino dicarboxylic ligand $H_2$cbal (Fig. 1) has been synthesized following our published procedure[15]. The ligand is fully characterized using the analytical techniques such as elemental analysis, FTIR, $^1$H and $^{13}$C NMR spectroscopy. The ligand $H_2$cbal is known to bind the (II) ions to yield a tetranuclear (II) complex showing the bridging potential of carboxylate functionalities[15].

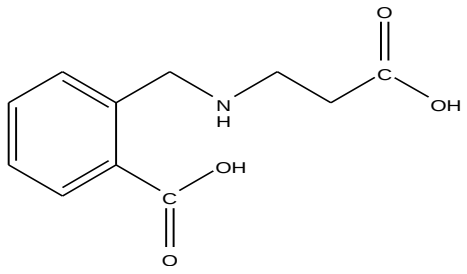


**Figure 1. The structure of ligand $H_2$cbal**

The reaction of $H_2$cbal with $Cu(ClO_4)_2 \cdot 6H_2O$ and $K_2CO_3$ in 1:1:2 molar ratio in methanol at ambient temperature in air yielded a blue trinuclear (II) complex, $K[Cu_3(cbal)_3(\mu_3\text{-}OH)(H_2O)]$ (Fig. 2). The molecular structure of complex has been established using different analytical techniques such as elemental analysis, FTIR, UV-vis, mass spectroscopy and single crystal X-ray crystallography.

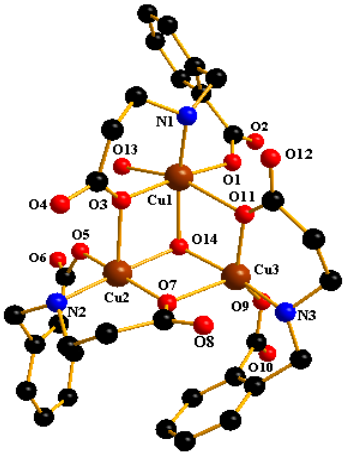


**Figure 2. Molecular structure of complex K[$Cu_3$(cbal)$_3$($\mu_3$-OH)($H_2O$)] with atom numbering scheme. Hydrogen atoms are omitted for clarity**

**2.2. DNA binding Study.** The trinuclear complex is highly water soluble and well stable in solution at physiological pH. Therefore, considering the important role and activity of ion and its complexes in the biological systems that they may act as biological probes, we were interested to study their DNA binding affinity in aqueous medium. The binding characteristics of complex with calf-thymus (CT) DNA have been examined by a combined approach of UV-vis and fluorescence spectroscopic techniques. The binding with DNA leads to a gradual increase in the absorption intensities in the UV-vis spectra (Fig.3) of complex accompanied by a significant blue shift. The intrinsic binding constant ($K_b$) value of complex has been calculated by monitoring the changes in absorbance at 276 nm with increasing concentration of CT-DNA and was found to be 3.500 x$10^4$ $M^{-1}$.

In an attempt to further investigate the DNA binding property of complex, the competitive ethidium bromide (EthBr) displacement assay has been carried out in aqueous solution. This assay is based on the quenching of ethidium bromide fluorescence upon displacement of the DNA-bound ethidium bromide by the complex (Fig.4). The extent of fluorescence quenching of ethidium bromide bound to DNA can be evaluated quantitatively using the classical Stern-Volmer equation: $I_0/I = 1 + K_{SV}[Q]$; where $I_0$ and I are the fluorescence intensities of the fluorophore in the absence and presence of quencher, respectively, $K_{SV}$ is the Stern-Volmer quenching constant and [Q] is the quencher concentration . Thus, the plots of log[$(I_0 - I)/I$] vs log [Q] can be used to find the binding constant value which is evaluated to be 3.161 x 104 $M^{-1}$.

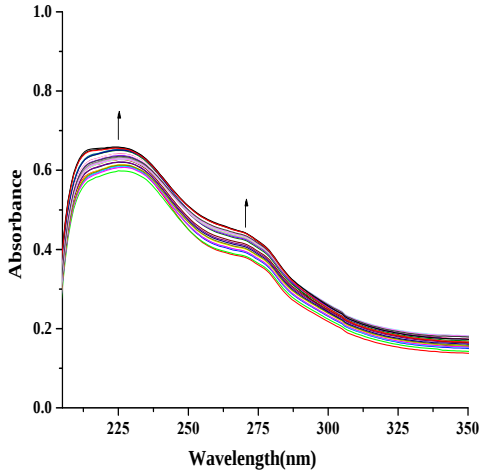


**Figure 3**. uv-vis spectra of DNA binding

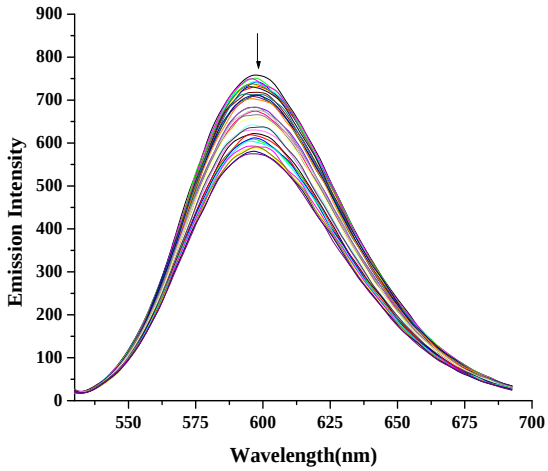


**Figure 4**. Fluorescence spectra of DNA binding

## 3. Conclusion

Water soluble clusters have become a promising class of coordination compounds in which variation of the metal salts, ligands, counter ions or experimental conditions lead to a variety of structural motifs showing the characteristic biological properties. The in-depth study on in vitro models of quantitative assay for developing target specific drug design based on structure-activity relationship is also a prevalent theme in the biological processes. This has spurred us to synthesize and characterize two new water soluble trinuclear (II) complexes containing a partial cubane [$Cu_3O_4$] core with an unsymmetrical amino dicarboxylic ligand. The new complex system shows evidence of binding with CT-DNA in aqueous solution at physiological pH indicating the significance in designing of water soluble new polynuclear transition metal complexes based on carboxylate rich ligands to be used as potential binding agents to different biological macromolecules and subsequent metal-based drugs.

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