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# In vitro biomolecular interaction studies and cytotoxic activities of copper(II) and zinc(II) complexes bearing ONS donor thiosemicarbazones

**Nimya Ann Mathews**[1] | **M.R. Prathapachandra Kurup**[1,2]

[1]Department of Applied Chemistry, Cochin University of Science and Technology, Kochi, India

[2]Department of Chemistry, School of Physical Sciences, Central University of Kerala, Periye, Kasaragod, India

**Correspondence**
M.R. Prathapachandra Kurup, Department of Applied Chemistry, Cochin University of Science and Technology, Kochi 682 022, Kerala, India.
Email: mrp@cukerala.ac.in

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Among all the bio-metals, zinc and copper derivatives of ONS donor thiosemicarbazone have aroused great interest because of their potential biological applications. Multisubstituted thiosemicarbazone ligand $H_2$dspt (3,5-dichlorosalicylaldehyde-$N^4$-phenylthiosemicarbazone) derived new ternary complexes like [Zn(dspt)(phen)]·DMF (**1**) and [Cu(dspt)(phen)]·DMF (**2**), and another thiosemicarbazone, $H_2$dsct (3,5-dichlorosalicylaldehyde-$N^4$-cyclohexylthiosemicarbazone), derived [Cu(dsct)(bipy)]·DMF (**3**). These complexes have been characterized by elemental analysis (CHNS), Fourier transform infrared (FT-IR), ultraviolet–visible (UV–Vis) and proton nuclear magnetic resonance ($^1$H-NMR) spectra. The structures of the complexes were obtained by single-crystal X-ray diffraction analysis. Compounds **1** and **2** got crystallized in the monoclinic $P2_1/c$ space group. The complexes showed interesting supramolecular interaction, which in turn stabilizes the complexes. The ground state electronic configurations of the complexes were studied using the B3LYP/LANL2DZ basis set, and ESP plots of complexes were investigated. The interaction of the complexes with calf thymus DNA (CT-DNA) was studied using absorption and fluorescence spectroscopic methods. A UV study of the interaction of the complexes with calf thymus DNA (CT-DNA) has shown that the complexes can effectively bind to CT-DNA, and [Cu(dspt)(phen)]·DMF (**2**) exhibited the highest binding constant to CT-DNA ($K_b = 3.7 \times 10^4$). Fluorescence spectral studies also indicated that Complex **2** binds relatively stronger with CT DNA through intercalative mode, exhibiting higher binding constant ($K_q = 4.7 \times 10^5$). The DNA cleavage result showed that the complexes are capable of cleaving the DNA without the help of any external agent. Molecular docking studies were carried out to understand the binding of complexes with the molecular target DNA. Complex **2** exhibited the highest cytotoxicity against human breast cancer cell line MD-MBA-231 ($IC_{50}$ = 23.93 μg/mL) as compared to Complex **1** ($IC_{50}$ = 44.40 μg/mL).

**KEYWORDS**
cytotoxicity evaluation, DNA binding, molecular docking, thiosemicarbazone complexes, X-ray

  