

**Abstract No.28**

**Study on interaction of DNA from calf thymus with 1,10-phenanthroline diimine palladium(II) complex of short hydrocarbon chain ethyldithiocarbamate ligand as potential antitumor agent**

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The platinum complexes such as cisplatin (CDDP) and carboplatin are the subject of much attention because of their beneficial effects in the treatment of cancer. Although CDDP exhibits strong activities against ovarian, gastric, and prostate cancers, it has serious problems of nephrotoxicity and emesis. To reduce these side effects, a great deal of effort has been focused on the preparation of new complexes as well as on methods of administration. In the present study, we evaluated the effectiveness of the interaction of calf thymus DNA with a new palladium (II) antitumor complex of formula  $[Pd(Phen)(Et-dtc)]NO_3$  (where Phen = 1,10-phenanthroline and Et-dtc = ethyldithiocarbamate) in 10 mmol/L of Tris-HCl buffer of pH=7.0.

The complex show 50% cytotoxic concentration ( $CC_{50}$ ) value against chronic myelogenous leukemia cell line, K562, much lower than that of cisplatin. This water soluble complex has been characterized by spectroscopic and non spectroscopic methods and interacted with calf thymus DNA using UV-Vis isothermal titration method in Tris-HCl buffer solution (pH=7.0) at 300 and 310 K. In these interaction studies, binding parameters, thermodynamic parameters, and the types of bindings between this agent and DNA are described as follow:

The above compound can denature DNA and the concentration of this ligand in the midpoint of transition ( $[L]_{1/2}$ ) is decreased by improving temperature, from 0.0101 mM at 300K to 0.0099 mM at 310K. The conformational stability of DNA in the interaction with ligand ( $\Delta G_{(H_2O)}^\circ$ ) determined to be 8.85 kJ/mol and 12.39 kJ/mol at 300 K and 310K respectively. Thus DNA is more stable at 310K i.e. presence of ligand led to less stability of DNA. Values for  $m$ , (a measure of ligand strength for DNA denaturation) are 883.5 and 1216 (kJ/mol).(mol/L)<sup>-1</sup> at 300K and 310K respectively. The enthalpy of DNA denaturation by this complex ( $\Delta H_{conformation}^\circ$  or  $\Delta H_{denaturation}^\circ$ ) in the range of 300 and 310K find out to be 96.89 kJ/mol. In addition, the calculated entropy ( $\Delta S_{(H_2O)}^\circ$ ) of DNA denaturation by this complex is 0.29 kJ/mol.K at 300 K. The positive value of entropy change is related

to the more disorder of denatured DNA with respect to the native DNA. There is a set of 6 binding sites ( $g$ ) for the complex on the DNA with positive cooperativity in binding.  $n$ , the Hill coefficient (as a criterion of cooperativity) find out to be 1.43 at 300K and 1.24 at 310 K respectively.  $K_{app}$ , the apparent equilibrium constant are 1.90 mM<sup>-1</sup> and 1.77 mM<sup>-1</sup> at 300K and 310K respectively. Fluorescence studies showed that this complex does intercalate in DNA. Gel filtration suggests them to bind with DNA and the binding is strong and irreversible.

**Key words:** calf thymus DNA, 1,10-phenanthroline diimine palladium(II), Thermodynamic parameters.

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**Thermal unfolding molecular dynamics simulation of spinach plastocyanin**

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Thermal denaturation of spinach plastocyanin was investigated by molecular dynamics simulation in order to study of unfolding mechanism of this protein. Molecular dynamics simulation was carried out in high temperature within 18 ns by using Gromacs software. The radius of gyration ( $R_g$ ) and Root Mean Deviation (RMSD) have been used to follow the unfolding process. Moreover, distributions of  $R_g$  were used to identify states during the simulation. By using Gaussian curve fitted to distribution of  $R_g$  curves, three state and two transition ensemble was detected during the simulation.

**Key words:** spinach plastocyanin, sodium phosphate, MD simulation.