DNA Binding of Iron(II)-Phenanthroline Complexes: Effect of Methyl Substitution on Thermodynamic Parameters

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The influence of methyl substitution on the thermodynamic parameters for the binding of $[Fe(DMP)_3]^{2+}$ and $[Fe(TMP)_3]^{2+}$ (DMP = 4,7-dimethyl-1,10-phenanthroline, TMP = 3,4,7,8-tetramethyl-1,10-phenanthroline) to calf thymus DNA (ct-DNA) has been studied by determining their equilibrium binding constants (K_b) at various salt concentrations and temperatures. K_b of the iron(II) complexes to ct-DNA decreases with the salt concentration in the solution, suggesting considerable electrostatic interaction in the ct-DNA binding of the iron(II) complexes. In contrast, K_b of the DNA binding increases with temperature, indicating that the DNA binding reaction of the complex is endothermic and entropically driven. The evaluation of the non-electrostatic binding constant ($K^0{}_t$) based on polyelectrolyte theory has revealed that the $K^0{}_t$ portions of the total binding constant (K_b) are relatively large and reach 46.4 % for $[Fe(DMP)_3]^{2+}$ at $[Na^+]$ = 0.075 M and 43.9 % for $[Fe(TMP)_3]^{2+}$ at $[Na^+]$ = 0.100 M. The contribution of non-electrostatic binding free energy (ΔG^0_t) to total binding free energy change (ΔG^0) is extremely large, *i. e.* > 90 % for both iron(II) complexes at $[Na^+]$ = 0.05 M, suggesting that the stabilization of the DNA binding is mainly contributed from the non-electrostatic process. The effect of methyl substitution on electrostatic (ΔG^0_{pe}) and non-electrostatic (ΔG^0_t) binding free energy changes has been systematically evaluated using the quantity of $\Delta\Delta G^0_{pe}$ and $\Delta\Delta G^0_t$ relative to that of the parent iron(II) complex, $[Fe(phen)_3]^{2+}$. The results indicate that the substitution of hydrogen atoms in the phen ligand by methyl groups decreases slightly the electrostatic binding free energy changes, but tremendously increases the non-electrostatic ones to yield net binding free energy changes which are more favorable for the ct-DNA binding.

Key words: DNA-binding Ligand, 1,10-Phenanthroline, Iron(II), Thermodynamic Parameters