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STUDIES ON THE INTERACTION OF DNA AND WATER-SOLUBLE POLYMER-SUPPORTED SCHIFF BASE COMPLEX

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ABSTRACT

The modes and activities of the interaction of DNA and water-soluble polymer supported Schiff base nickel complex, which has been prepared by copolymerization, have been discussed according to the fluorescent probe method. It indicates that the polymer matrix effect and increasing solubility in water can increase the interaction of this polymer metal complex with DNA.

Key Words: DNA; Interaction; Water-soluble polymer metal complex; Fluorescent probe

INTRODUCTION

The interaction of transition metal complexes with DNA has been extensively studied in the past few years [1-3]. Due to the unusual binding properties, these metal complexes are suitable candidates as DNA secondary structure probe, photocleavers and anticancer or antiviral therapies, in which DNA is regarded as

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(PVP-AONiSGI) was prepared by copolymerization of AONiSGI and N-vinylpyrrolidone (NVP) in dimethylformamide using AIBN (1 wt% monomer) as initiator. The reaction mixture was degassed by passing nitrogen gas and kept in a thermostat at 75°C. After 48 hours, the polymeric nickel complex was precipitated in ether, further purified by reprecipitation by methanol from dimethylformamide solution and dried in vacuum at 50°C. The yield of 3 is 40-50%.

RESULTS AND DISCUSSION

The polymeric Schiff base nickel complex composition was estimated by analysis of metal and nitrogen content. In the UV/Vis spectra, compared with the Schiff base nickel complex (NiSGI), the four absorption peaks of polymeric Schiff base nickel complex 3 (PVP-AONiSGI) showed a red shift about 40-50 nm. In the IR spectra, the characteristic absorption bands of ν_{OH} (3067 cm^{-1}) and δ_{OH} (770 cm^{-1}) of the NiSGI disappeared in 1 (AONiSGI), and the characteristic absorption peak of 3 (PVP-AONiSGI) was presented at 1229 cm^{-1} by ($\nu_{\text{aS(C-O-C)}}$) and wide overlapped peaks appeared at 1657 cm^{-1} by δ_{COO} , $\nu_{\text{C=O}}$, and $\nu_{\text{C=N}}$. The polymeric Schiff base nickel complex has also been characterized by thermal analysis, $^1\text{H NMR}$ and Low Angle Laser Light Scattering (LALLS).

A fluorimetric method based on ethidium bromide (EB)/DNA system was used for investigating the interaction modes of PVP-AONiSGI with calf thymus DNA, and for evaluating the anticancer activities of PVP-AONiSGI. EB, a fluorescent dye, can intercalate into the double helix chains of DNA and greatly enhance the intensity of fluorescence [13], so do some metal complexes. Furthermore, when these complexes are added to the EB/DNA fluorescent system, the fluorescence intensity will be decreased. The measurement was performed in buffer [Tris-HCl (5 mmol/l) with 20 mmol/l NaCl, pH=7.4].

Samples Excited at 534 nm

When NiSGI and PVP-AONiSGI were added into EB/DNA system respectively, the fluorescence intensity of EB/DNA system decreased more quickly with increasing amounts of PVP-AONiSGI than that of NiSGI (Figure 1). Where, F and F0 are respectively the fluorescence intensity of EB/DNA system in the presence and the absence of metal complexes. $\text{C}_{\text{Ni}}/\text{C}_{\text{DNA(P)}}$ represents the ratio of the concentration of nickel to that of DNA(P) in the system. It is suggested that there is a strong interaction of PVP-AONiSGI with calf thymus DNA, and, it can be explained that a portion of the polymeric Schiff base nickel complex (PVP-AONiSGI) intercalate to adjacent base pairs of the DNA, which inhibits EB binding to DNA competitively. After decreasing the binding ability between EB and DNA, the fluorescence intensity of system quickly decreases. From Figure 1, we also concluded that low molecular weight metal complex NiSGI played an important role in the interaction system of PVP-AONiSGI and DNA. With increasing

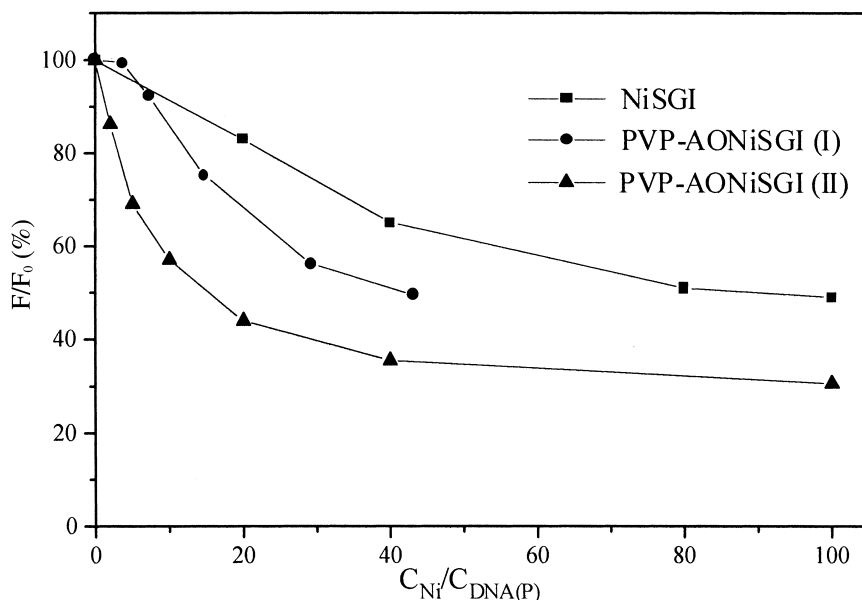


Figure 1. Relative fluorescent intensity of EB/DNA system in the presence of increasing metal concentration.

contents of AONiSGI in copolymer PVP-AONiSGI, the interactive activity of PVP-AONiSGI weakened, which attributed to the steric hindrance among of low molecular weight metal complexes.

From Figure 2, the plot of F_0/F vs. C_{Ni} was not a straight line and irrelevant to the reaction temperature. It indicated that the fluorescence of EB/DNA system was not being quenched by the classical mechanism, so it can be concluded that the pattern of fluorescence quenching of PVP-AONiSGI to the EB/DNA system was neither simply dynamic nor simply static quenching [14]. We think, perhaps, there are two interaction modes in the PVP-AONiSGI/DNA system. It was found, presumably that the fluorescence intensity of pure EB/DNA system was 100% ($C_{NaCl}=2(10^{-2}mol/l)$). The fluorescence relative intensity of EB/DNA system increased with increasing the ionic strength (C_{NaCl}) in the reactive system (Table 1). It is indicated that the intercalate degree of the polymeric Schiff base nickel complex in DNA weakened with increasing the ionic strength, because the Na^+ atmosphere inhibits positively charged polymeric Schiff base nickel complex electrostatic binding to negatively charged phosphate backbone of calf thymus DNA. The above results showed that the PVP-AONiSGI interacted with calf thymus DNA by two modes. At first, the cationic complex electrostatic bind to negatively charged phosphate backbone at the periphery of the double helix, then a portion of ligands intercalates between the base pairs on the DNA duplex strand. UV/Vis and CD spectra are also in accordance with this result.

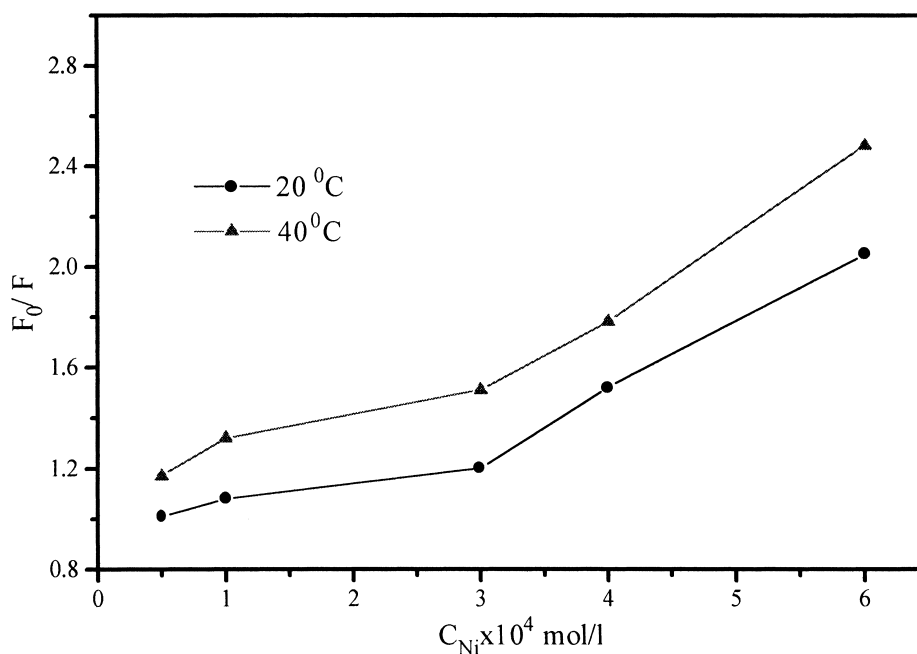


Figure 2. Fluorescence quenching of PVP-AONiSGI (I) to EB/DNA system at different temperatures.

Table 1. Effects of Ionic Strength on the Fluorescence Intensity of the PVP-AONiSGI/DNA-EB Systems

$C_{NaCl} \times 10^3 \text{ mol/l}$	20	30	40	50	60
Relative fluorescence intensity (%)	82.50	81.03	73.11	59.12	69.24

$C_{DNA(P)} = 1.378 \times 10^{-4} \text{ mol/l}$, $C_{EB} = 5 \times 10^{-6} \text{ mol/l}$, $C_{Ni} = 5 \times 10^{-5} \text{ mol/l}$.

CONCLUSION

In this work, the water solubility of PVP-AONiSGI was greatly improved by introducing hydrophilic groups. This water solubility and polymeric matrix effect jointly made DNA interact with PVP-AONiSGI stronger than NiSGI. The fluorescence intensity of EB/DNA system decreased about 55% in a low ratio of concentration of metal to DNA. So, it is possible [15] to design this kind of water-soluble polymer metal complexes as a polymer anticancer drug.

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