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Studies of interactions among cobalt(III) polypyridyl complexes, 6-mercaptopurine and DNA

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Abstract

The interactions between cobalt polypyridyl coordination compounds $Co(L)_3^{3+}$(L=1,10-phenanthroline(phen), and bipyridine(bpy)),6-mercaptopurine and calf thymus DNA have been investigated using electrochemical methods(cyclic voltammetry, differential pulse voltammetry), electronic absorption spectroscopy and viscosity measurements. Results indicate that there is an obvious interaction equilibrium between $Co(L)_3^{3+}$, 6-mercaptopurine and DNA. The phenomena are investigated for the first time, and believed to be helpful to use the anticancer drugs more efficiently.

Keywords: Cyclic voltammetry; Cobalt polypyridyl complexes; DNA; Antitumor

1. Introduction

Recently, the interaction of transition metal polypyridyl coordination compounds with DNA has been extensively studied. Due to the unusual binding properties and general photoactivity, these coordination compounds are suitable candidates as DNA secondary structure probe, photocleavers and antitumor drugs [1,2]. The effects of size, shape, hydrophobicity, and the charge on the binding of the complex to DNA have been studied by changing the type of heteroaromatic ligand or metal centre [3,4]. The vast majority of such studies have been focused on complexes of Ru(II) [5–7], but to a far lesser extent, on other metal complexes. Barton has reported that chiral phenanthroline–cobalt(III) complexes recognize different local structures of DNA [3]. In the previous work, we have synthesized many cobalt(III) complexes and investigate their DNA-binding properties [8–10].

6-Mercaptopurine (6-MP) has been used as an antineoplastic agent. For example, it constitutes an important part of the backbone for the treatment of childhood acute lymphoblastic leukemia (ALL). However, studies have showed that there are great individual differences in the pharmacokinetics of 6-MP in the patients with ALL [11]. It is difficult to keep optimal plasma levels of the drug in some patients with standardized treatment regimens, at least in children [12]. Normally, the 6-MP plasma concentrations are found to be unexpectedly low and highly variable, with marked individual differences found in the peak plasma concentration and the time to peak concentration [13]. Therefore, it is very important to control the 6-MP concentration and individualize dosage regimens, ensuring the adequate drug exposure required to prolong remission. Since both cobalt polypyridyl complex and the 6-MP have antitumor activity, it can be envisioned that the combined use of these two reagent complexes may exhibit strong antineoplastic action. In this regard, the interaction between cobalt polypyridyl complex, 6-MP and DNA has been investigated for the first time in our lab. The results should be valuable in understanding the mode of the complex binding to DNA, the sustained release of 6-MP, as well as laying the foundation for the rational design of DNA structure probes and antitumor drugs.

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2. Experiment

2.1. Materials

$[Co(phen)_3](ClO_4)_3$ and $[Co(bpy)_3](ClO_4)_3$ were prepared and purified according to the literature [14]. Calf thymus DNA was obtained from Shanghai Changyang Biochemical Reagent Company. Tris (where Tris is tris(hydroxy methyl)amino-methane) was purchased from Sigma Chemical Company. All other reagents and solvents were analytical grade reagents and were used as received.

All the spectroscopic titrations were carried out in buffer solution (10 mmol/L Tris-HCl, 50 mmol/L NaCl, pH=7.2) at room temperature. A solution of calf thymus DNA in the buffer gave a ratio of UV absorbance at 260 and 280 nm of ca. 1.8–1.9:1, indicating that the DNA was sufficiently free of protein. Other materials were commercially available and used without further purification unless otherwise noted, and doubly distilled water was used to prepare buffer solutions.

2.2. Measurements

Cyclic voltammetry (CV) and differential pulse voltammetry (DPV) were performed with an Autolab PGSTAT-30 electrochemical analytical instrument (Holand). The three-electrode cell comprised a reference saturated calomel electrode (SCE), auxiliary platinum foil and the working Pt disk (0.196 cm^2) electrodes. For all the electrochemical studies, Tris (10 mmol/L Tris-HCl, 50 mmol/L NaCl, pH=7.2) buffer was used as supporting electrolyte. All the experimental solutions were purged with nitrogen for 15 min prior to each set of experiments. Electronic absorption spectra were recorded on a UV-8500 spectrophotometer. Viscosity of 0.1 mmol/L DNA was measured using an Ubbelodhe viscometer, immersed in a thermostated water-bath maintained at 25±0.2 °C. Flow time was measured with a digital stopwatch and each sample was measured three times, and an average flow time was calculated. Data were presented as $(\eta/\eta_0)^{1/3}$ versus concentration of "cobalt polypyridyl complex–6-MP" complex in DNA solutions [15,16], where η is the viscosity of CT DNA in the presence of complex, and η_0 is the viscosity of CT DNA alone.

3. Results and discussion

3.1. Interaction between cobalt polypyridyl complex and 6-MP

3.1.1. Absorption spectroscopic studies

Absorption titration can monitor the interaction of metal complexes with biologically molecules. The absorption spectra of the complexes in the absence and presence of 6-MP were illustrated in Fig. 1. In the UV region, the intense absorption bands observed in the cobalt polypyridyl complexes were attributed to intraligand and π–$\pi*$ transition of the coordinated groups. With increasing 6-MP concentration, the hypochromism increased and was accompanied by a red shift for both of the two complexes. At the same time, a new absorption band appeared at 268 nm for the $Co(phen)_3^{3+}$ complex, as shown in panel A. In

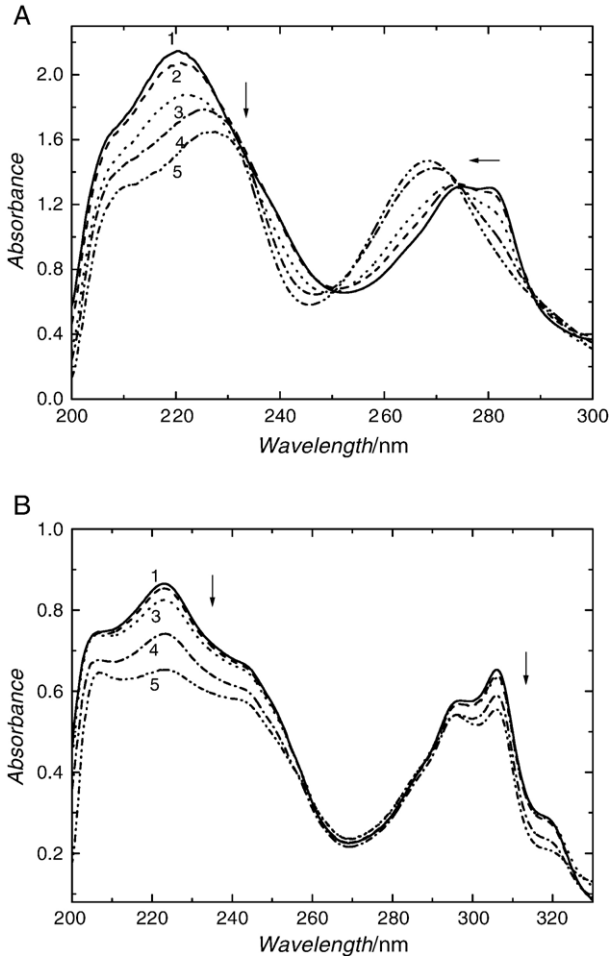

Fig. 1. Absorbance spectra of polypyridyl cobalt complexes (A) $Co(phen)_3^{3+}$ (B) $Co(bpy)_3^{3+}$. $C_{6\text{-MP}}$=1)0, 2)0.006, 3)0.02, 4)0.03, 5)0.06 mmol/L.

order to compare quantitatively the binding strength of the two polypyridyl complexes, the intrinsic binding constants K_b of them with 6-MP were obtained by monitoring the changes in absorbance at 220 nm for complexes 1 and 2, respectively, with increasing concentration of 6-MP. The following equation was applied:

$$C_{6\text{–MP}}/(\varepsilon_A-\varepsilon_f) = C_{6\text{–MP}}/(\varepsilon_B-\varepsilon_f) + 1/K_b(\varepsilon_B-\varepsilon_f)$$

Where $C_{6\text{-MP}}$ was the concentration of 6-MP, the apparent absorption coefficient ε_f, ε_A and ε_B corresponding, respectively, to the extinction coefficient of the free cobalt complex, the extinction coefficient for each addition of 6-MP to the cobalt complex and the extinction coefficient for the cobalt complex in the fully bound form. In the plot of $C_{6\text{-MP}}/(\varepsilon_A-\varepsilon_f)$ vs. $C_{6\text{-MP}}$, the binding constant K_b for phen complex was 7.7×10^4 L/mol, while the corresponding value for the bpy complex was 3.7×10^4 L/mol.

3.1.2. Electrochemical titration

CV has proved to be a very sensitive analytical technique to determine changes in redox behaviour of metallic species in the presence of biologically important molecules [17,18]. The redox

behaviour of metallic species is very sensitive to the coordination surrounding the metal centre (solvent, ligand, charge), therefore metal-based interaction can be detected using this technique. In the absence of 6-MP, the CV of the cobalt complexes in the buffer solution (pH=7.2) exhibited only one redox couples at the formal potential $E^{0\prime}$ of 155 mV, taken as the average of cathodic peak potential E_{pc} and anodic peak potential E_{pa} (PI). The redox peaks were attributed to Co(III/II) reaction as shown in curve 1 in Fig. 2A. The CV of $Co(phen)_3^{3+}$ (υ=100 mV/s) featured reduction of Co(III) to Co(II) at a cathodic peak potential (E_{PIc}=120 mV). The separation of anodic and cathodic peaks, ΔE_{PI} of 73 mV, indicated a quasi-reversible one-electron redox process [$I_{PIc}/I_{PIa}\approx 1$]. As shown in curve 5 of Fig. 2A, in the presence of 6-MP ($C_{6\text{-MP}}$:$C^{3+}_{Co(phen)3}$=4:1), the cathodic and anodic peak potentials were found to be at E_{PIc}=100 mV and E_{PIa}=158 mV. The peak-to-peak separation became narrow with ΔE_{PI}=58 mV, indicating that in the presence of 6-MP the electron-transfer process seemed to be improved, became reversible and the $E^{0\prime}$ value was shifted towards more negative region by about 26 mV. In the case of $Co(bpy)_3^{3+}$, in the absence of 6-MP (curve 1 in Fig. 2B) the peak potentials were found at E_{PIc}=72 mV, E_{PIa}=142 mV and ΔE_p=70 mV, which was considered to be also a quasi-reversible one. In the presence of 6-MP ($C_{6\text{-MP}}$:$C^{3+}_{Co(bpy)3}$=4:1), at the same concentration of complex, the peak potentials (E_{PIc}=40 mV and E_{PIa}=89 mV) were shifted to more negative potential and the redox couple with ΔE_p=49 mV was found to be reversible. Thus, the apparent $E^{0\prime}$ shifted to more negative potentials by 42 mV in the presence of 6-MP. For the two complexes examined, both of the redox couples were found to be reversible in the presence of 6-MP, which clearly indicated that these complexes on interaction with 6-MP facilitated electron transfer process in a better way.

Interestingly, a new redox couple (PII) appeared at negative potential direction in CV of both of the two cobalt complexes when 6-MP was added, accompanying by the decreasing of I_{PIc}, as shown in Fig. 2. As there was no redox reaction of 6-MP happened in the range of potential in the experiment condition, the new redox couple may be resulted from a new kind of complex "cobalt polypyridyl complex–6-MP", since

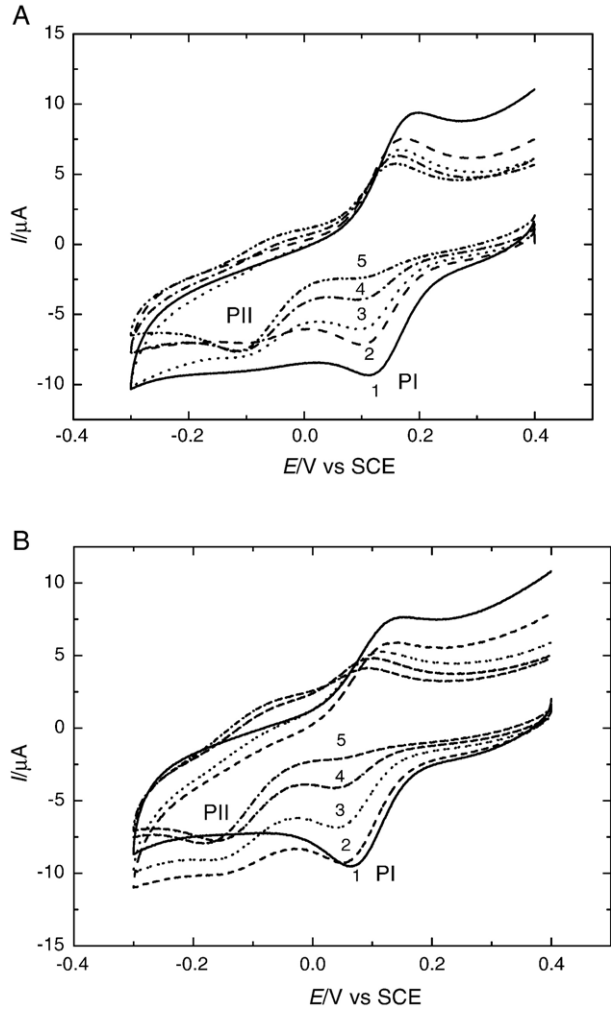

Fig. 2. Cyclic voltammograms of Pt electrode in solution containing 0.2 mmol/L (A) $Co(phen)_3^{3+}$ and (B) $Co(bpy)_3^{3+}$. $C_{6\text{-MP}}$=1)0, 2)0.2, 3)0.4, 4)0.6, 5)0.8 mmol/L, υ=100 mV/s.

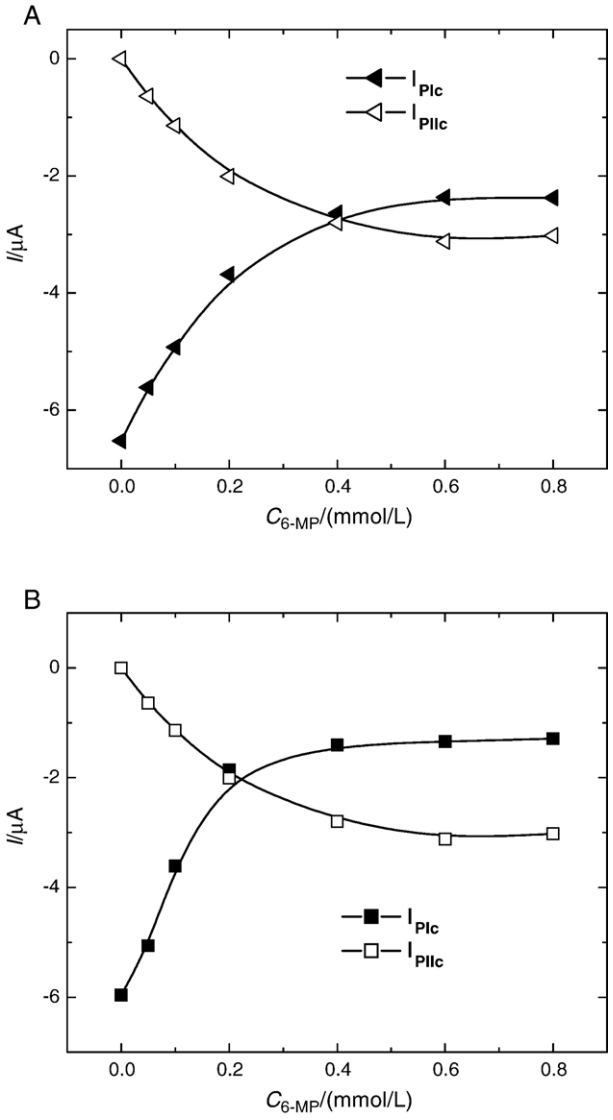

Fig. 3. Influences of 6-MP concentration on the peak current of (A)$Co(phen)_3^{3+}$ and (B) $Co(bpy)_3^{3+}$.

there is strong interaction between the cobalt polypyridyl complex and 6-MP, as revealed in the former absorption spectroscopic studies. The decreasing of I_{PIc} can be attributed to the slow diffusion of the metal complexes bound to the slowly diffusing 6-MP molecules.

Differential pulse voltammogram (DPV) of these complexes as a function of added 6-MP also indicated a large decrease in I_{PIc} and simultaneously an increase in I_{PIIc} with the increase concentration of 6-MP (Fig. 3). These can also be attributed to the strong interaction between 6-MP and the cobalt complex molecules. Moreover, when the ratio of $C_{6\text{-}MP}$:$C^{3+}_{Co(L)3}$ was great than 3, the PI peak became hardly resolved and I_{PIc} changed little with the more increase concentration of 6-MP, indicating that one molecule of cobalt polypyridyl complexes could take interaction with at less three molecules of 6-MP in the novel complex "cobalt polypyridyl complex–6-MP".

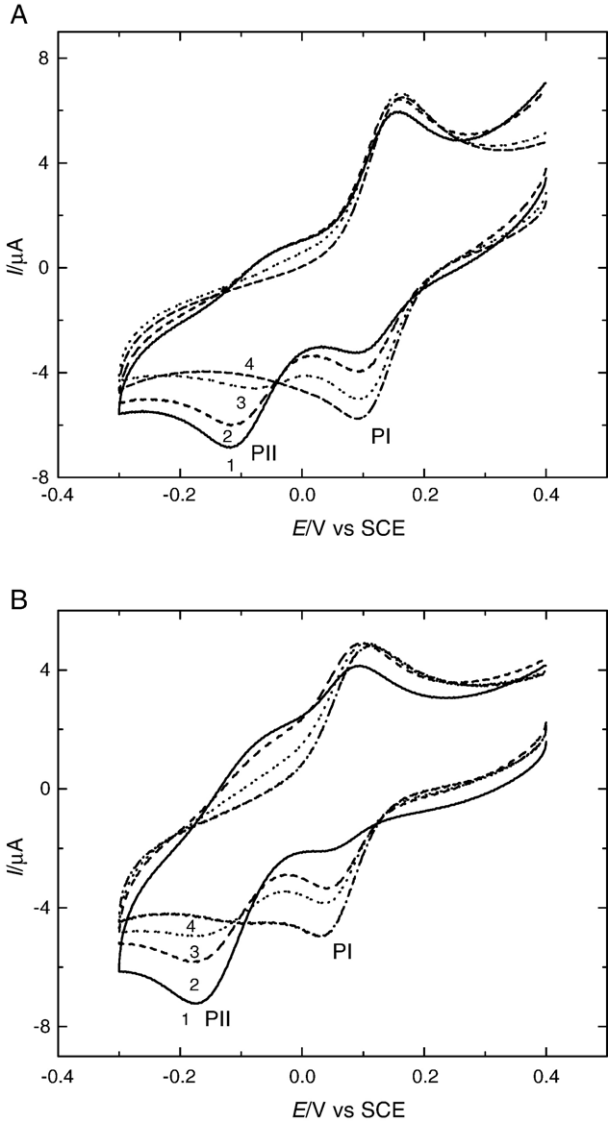

Fig. 4. Cyclic voltammograms of Pt electrode in solution containing (A)Co(bpy)$_3^{3+}$ –6-MP complex (B)Co(bpy)$_3^{3+}$–6-MP complex. υ=100 mV/s C_{DNA}=1) 0, 2)0.41, 3)0.96, 4)1.42 mmol/L.

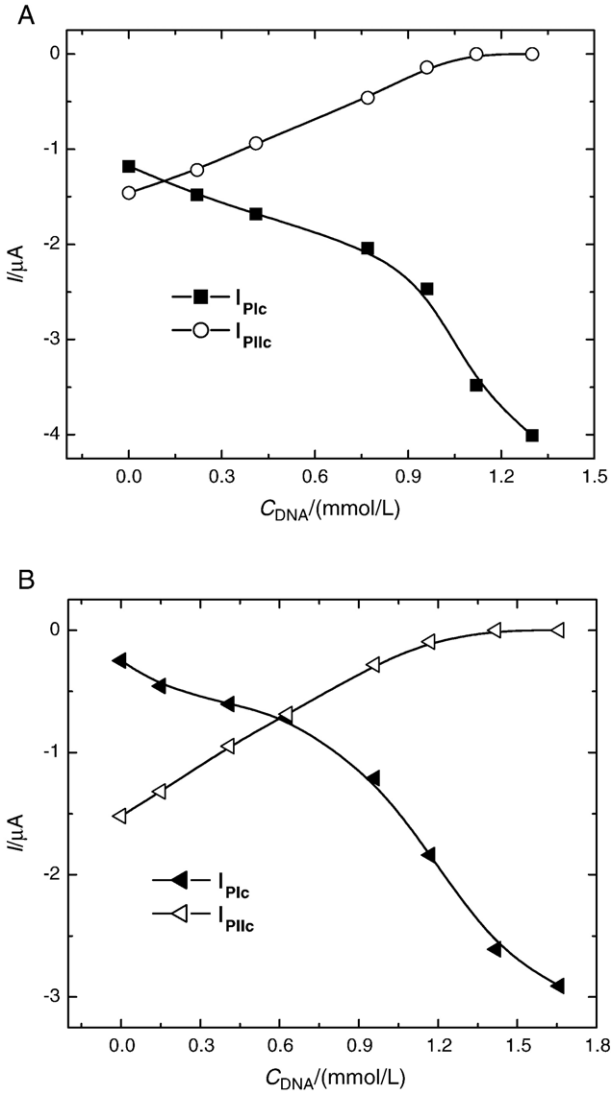

Fig. 5. Influences of DNA concentration on the peak current of Co(phen)$_3^{3+}$–6-MP complex (A) and Co(bpy)$_3^{3+}$–6-MP complex (B).

3.2. Interaction among cobalt polypyridyl complex, 6-MP and DNA

3.2.1. Electrochemical titration

Cyclic voltammetric techniques have also been employed to study the interaction among cobalt polypyridyl complex, 6-MP and DNA. The two cathodic peak currents were monitored as a function of added DNA (Fig. 4). In the absence of DNA, the separation between the anodic and cathodic peak potentials of cobalt polypyridyl complex–6-MP (ΔE_{PI}) was 58 mV for phen complex and 49 mV for bpy one, indicating a reversible redox process. The formal potential $E^{0\prime}$ was 129 mV and 65 mV, respectively. The presence of DNA (C_{DNA}=1.4 mmol/L) in the solution at the same concentration of two complexes caused a considerable decrease in I_{PIIc} and an obvious increase in I_{PIc}, as shown in curve 4 in Fig. 4. In addition, the peak potentials, E_{PIc} and E_{PIIc} had a shift to less positive potential. The separation of the anodic and cathodic peak potentials of cobalt polypyridyl

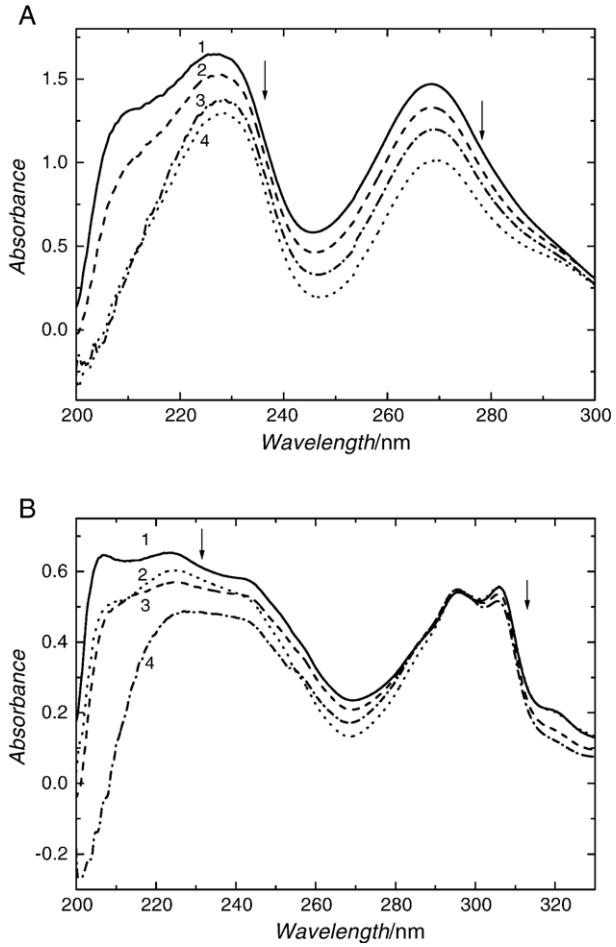

Fig. 6. UV-spectra of $Co(phen)_3^{3+}$–6-MP complex (A) and $Co(bpy)_3^{3+}$–6-MP complex (B) C_{DNA}=1)0, 2)0.008, 3)0.016, 4)0.024 mmol/L.

complexes, ΔE_{PI}=68 mV for phen complexes and 85 mV for bpy ones, which increased a few compared with the ones in the absence of DNA, indicating a similar reversibility in the electron transfer process in the presence of DNA.

DPV of these complexes as a function of added DNA also indicated a large decrease in I_{PIIc} and simultaneously an increase in I_{PIc}, as shown in Fig. 5. It can be seen clearly that the relationship is contrary to the one of Fig. 3, indicating the release of 6-MP from the formed "cobalt polypyridyl complex–6-MP".

These phenomena and the one reported in the part 3.1 can be explained with the equilibrium (1) and (2), as listed below. The peak II was resulted from the complex "cobalt polypyridyl complex–6-MP" and the peak I was due to cobalt(III) polypyridyl complex. As the concentration of DNA increased, the equilibrium moved to the right, then the concentration of "cobalt polypyridyl complex–6-MP" decreased and cobalt polypyridyl complex increased, resulting in the decrease of I_{PIIc} and increase of I_{PIc} in CV and DPV, as well as the release of 6-MP at the same time. On the contrary, when the concentration of 6-MP increased, the equilibrium moved to the left, which lead to the increase of I_{PIIc} and the decrease of I_{PIc} in CV (Fig. 2) and DPV (Fig. 3). It should be noted that the crystal of new formed "cobalt polypyridyl complex–6-MP" has not been obtained successfully although we have tried for many times.

$$Co(phen)_3^{3+}\text{–6–MP complex} \overset{DNA}{\rightleftharpoons} Co(phen)_3^{3+} + 6\text{–MP} \quad (1)$$

$$Co(bpy)_3^{3+}\text{–6–MP complex} \overset{DNA}{\rightleftharpoons} Co(bpy)_3^{3+} + 6\text{–MP} \quad (2)$$

3.2.2. Absorption spectroscopic studies

In general, the transition metal complex bound to DNA through intercalation usually results in hypochromism and red shift, due to the strong stacking interaction between aromatic chromophore of the complex and the base pairs of DNA. The absorption spectra of the cobalt polypyridyl complex–6-MP in the absence and presence of CT DNA were illustrated in Fig. 6. In the case of $Co(phen)_3^{3+}$–6-MP, with increasing DNA concentration, the hypochromism increased as evidenced from the decreasing intensity of the peaks at 227 nm and 268 nm, accompanied by the red shift and the peak at 206 nm disappeared. In the absorption spectra of $Co(bpy)_3^{3+}$–6-MP, a similar effect also appeared. These indicated there is strong interaction of "cobalt polypyridyl complex–6-MP" with DNA.

3.2.3. Viscosity measurements

The binding modes of the cobalt polypyridyl complex–6-MP with DNA were further investigated by viscosity measurements. In the absence of crystallographic structure data, hydrodynamic methods, which are sensitive to DNA length increase, are regarded as the least ambiguous and the most critical tests of binding in solution [19,20]. A classical intercalation model results in lengthening the DNA helix, as base pairs are separated to accommodate the binding ligand, leading to the increase of DNA viscosity. However, a partial and/or non-classical intercalation of ligand may bend (or kink) DNA helix, resulting in the decrease of its effective length and, concomitantly, its viscosity [19,20]. The effects of the complexes $Co(phen)_3^{3+}$–6-MP, together with $Co(bpy)_3^{3+}$–6-MP on the viscosity of DNA were

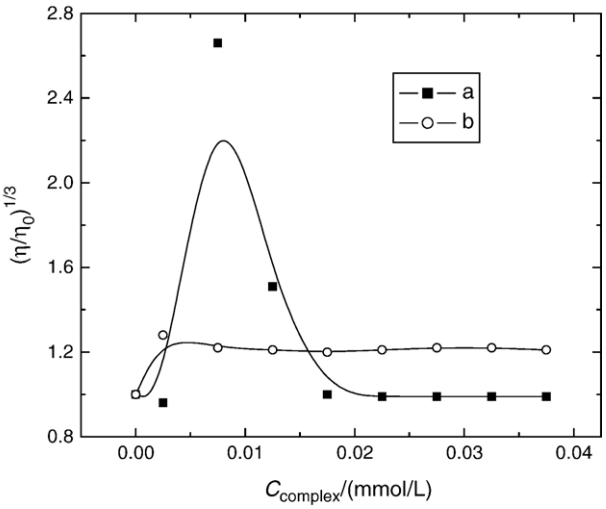

Fig. 7. Influences of $Co(phen)_3^{3+}$–6-MP (a) and $Co(bpy)_3^{3+}$–6-MP (b) complexes to the viscosity of CT DNA. C_{DNA}=0.1 mmol/L, T=(25±0.2)°C.

shown in Fig. 7. For the complexes $Co(phen)_3^{3+}$–6-MP, as increasing the amounts of complexes, the viscosity of DNA increased steadily, but upon further binding of the complex to DNA, the DNA viscosity decreased. While for the complexes $Co(bpy)_3^{3+}$–6-MP, it exerted essentially little effect on DNA viscosity as increasing the amounts of complexes. The experimental results suggested that the two complexes could bind DNA in two different modes: $Co(phen)_3^{3+}$–6-MP in partly intercalative mode, and $Co(bpy)_3^{3+}$–6-MP by electrostatic interaction. This may be related to the molecular structures of the complexes. As is well known, the two pyridyl rings in bpy may rotate away with large dihedral angles. On the other hand, for complexes containing phen, the rotated pyridyl rings are replaced with the phenanthroline ligands. It is coplanar and can construct a larger π framework compared to that of bpy. This helped the complexes intercalate into the DNA base pairs deeply [21]. At the same time, due to the greater planar area and higher hydrophobicity, complexes containing phen bind with DNA more strongly than the complexes containing bpy.

4. Conclusions

There is a strong interaction equilibrium between the cobalt polypyridyl (1,10-phenanthroline, and bipyridine) complexes, 6-MP and DNA, as indicated by the UV spectra and electrochemistry analysis. The cobalt polypyridyl complexes and 6-MP were believed to take interaction to form a new kind of complex, and the formed complex maybe decomposed in presence of DNA. The experimental results show that the interaction of $Co(phen)_3^{3+}$–6-MP complex with DNA is via the partly intercalative mode, however, the interaction between $Co(bpy)_3^{3+}$–6-MP complex and DNA is electrostatic. The research can be helpful to the control release of 6-MP in synthesis or design the antitumour drugs.

Acknowledgements

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References

[1] J.K. Barton, A.T. Danishefsky, J.M. Goldberg, Tris(phenanthroline) ruthenium (11): stereoselectivity in binding to DNA, J. Am. Chem. Soc. 106 (1984) 2172–2176.
[2] B. Nordn, P. Lincoln, B. Akerman, E. Tuite, in: A. Sigel, H. Sigel (Eds.), Metal Ions in Biological Systems, vol. 33, Marcel Decker, New York, 1996, p. 177.
[3] J.K. Barton, Metals and DNA-molecular left-handed complements, Science 233 (1986) 727–734.
[4] M. Carter, M. Rodriguez, A.J. Bard, Voltammetric studies of the interaction of metal chelates with DNA. 2. Tris-chelated complexes of cobalt(III) and Iron(II) with 1,l0-phenanthroline and 2,2′-bipyridine, J. Am. Chem. Soc. 111 (1989) 8901–8911.
[5] M. Ganesan, V.K. Sivasubramanian, T. Rajendran, K. Swarnalatha, S. Rajagopal, R. Ramaraj, Electron transfer reactions of tris(polypyridine) ruthenium(III) complexes with organic sulfides: importance of hydrophobic interaction, Tetrahedron 61 (2005) 4863–4871.
[6] V. Aranyos, A. Hagfeldt, H. Grennberg, E. Figgemeier, Electropolymerisable bipyridine ruthenium(II) complexes: synthesis, spectroscopic and electrochemical characterisation of 4-((2-thienyl) ethenyl)- and 4,4′-di((2-thienyl) ethenyl)-2,2′-bipyridine ruthenium complexes, Polyhedron 23 (2004) 589–598.
[7] L.F. Tan, H. Chao, Y.J. Liu, H. Li, B. Sun, L.N. Ji, DNA-binding and photocleavage studies of $[Ru(phen)2(NMIP)]^{2+}$, Inorg. Chim. Acta 358 (2005) 2191–2198.
[8] Q.L. Zhang, J.G. Liu, H. Xu, H. Li, J.Z Liu, H. Zhou, L.H. Qu, L.N. Ji, Synthesis, characterization and DNA-binding studies of cobalt(III) polypyridyl complexes, Polyhedron 20 (2001) 3049–3055.
[9] X.L. Wang, H. Chao, H. Li, X.L. Hong, Y.J. Liu, L.F. Tan, L.N. Ji, DNA interactions of cobalt(III) mixed-polypyridyl complexes containing asymmetric ligands, J. Inorg. Biochem. 98 (2004) 1143–1150.
[10] Q.L. Zhang, J.G. Liu, J.Z. Liu, H. Li, Y. Yang, H. Xu, H. Chao, L.N. Ji, Effect of intramolecular hydrogen-bond on the DNA-binding and photocleavage properties of polypyridyl cobalt(III) complexes, Inorg. Chim. Acta 339 (2002) 34–40.
[11] S. Zimm, J. Collins, R. Riccardi, D. Oneill, P.K. Narang, B. Chabner, D.G. Poplack, Variable bioavailability of oral mercaptopurine—is maintenance chemotherapy in acute lymphoblastic-leukemia being optimally delivered, N. Engl. J. Med. 308 (1983) 1005–1009.
[12] P. Lafolie, S. Hayder, O. Bjork, L. Ahstrom, J. Liliemark, C. Peterson, Large interindividual variations in the pharmacokinetics of oral 6-mercaptopurine in maintenance therapy of children with acute-leukemia and non-hodgkin lymphoma, Acta Paediatr. Scand. 75 (1986) 797–803.
[13] X.N. Cao, L. Lin, Y.Y. Zhou, G.Y. Shi, W. Zhang, K. Yamamoto, L.T. Jin, Amperometric determination of 6-mercaptopurine on functionalized multi-wall carbon nanotubes modified electrode by liquid chromatography coupled with microdialysis and its application to pharmacokinetics in rabbit, Talanta 60 (2003) 1063–1070.
[14] Chemical union of Japan, Translated by Cao Hui-Min, Hand Book of Inorganic Sythesis, vol. 3, Chemical Industry Press, Beijing, 1988, p. 506.
[15] J.B. Chaires, N. Dattagupta, D.M. Crothers, Studies on interaction of anthracycline of antibiotics and deoxyribonucleic-acid-equilibrium binding-studies on interaction of daunomycin with deoxyribonucleic-acid, Biochemistry 21 (1982) 3933–3940.
[16] G. Cohen, H. Eisenberg, Viscosity and sedimentation study of sonicated DNA-proflavine complexes, Biopolymers 8 (1969) 45–55.
[17] S. Srinivasan, J. Annaraj, PR. Athappan, Spectral and redox studies on mixed ligand complexes of cobalt(III) phenanthroline/bipyridyl and benzoylhydrazones, their DNA binding and antimicrobial activity, J. Inorg. Biochem. 99 (2005) 876–882.
[18] A.M. Leone, J.D. Tibodeau, S.H. Bull, S.W. Feldberg, H.H. Thorp, R.W. Murray, Ion atmosphere relaxation and percolative electron transfer in Co bipyridine DNA molten salts, J. Am. Chem. Soc. 125 (2003) 6784–6790.
[19] S. Satyanarayana, J.C. Dabrowiak, J.B. Chaires, Neither Δ- nor Λ-LAMBDA-tris(phenanthroline)ruthenium(II) binds to DNA by classical intercalation, Biochemistry 31 (1992) 9319–9324.
[20] S. Satyanaryana, J.C. Dabrowiak, J.B. Chaires, Tris(phenanthroline) ruthenium(II) enantiomer interactions with DNA: mode and specificity of binding, Biochemistry 32 (1993) 2573–2584.
[21] M. Brun, A. Harriman, Energy- and electron-transfer processes involving palladium porphyrins bound to DNA, J. Am. Chem. Soc. 116 (1994) 10383–10393.