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Spectroscopic studies on the interaction of γ-cyclodextrin–daunorubicin inclusion complex with herring sperm DNA

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ABSTRACT

The interaction of daunorubicin (DNR) with herring sperm DNA in cyclomaltooctaose (γ-cyclodextrin, abbrev. γ-CD) supramolecular system was studied by UV–vis absorption spectroscopy, fluorescence spectroscopy and viscosity method. On the condition of physiological pH, the results indicate that DNR prefers to form the 1:1 inclusion complex with γ-CD. These results are further supported by infrared spectrometry (IR), and X-ray diffraction (XRD). An inclusion constant (K) for the formation of γ-CD–DNR inclusion complex has been evaluated to be 9412.39 L mol^{-1} from the absorbance changes. It is observed that the interaction mode between γ-CD–DNR and DNA are a mixed binding, which contains partial intercalation and groove binding. The binding ratio of γ-CD–DNR with DNA is $n_{\gamma\text{-CD–DNR}}:n_{DNA}$ = 10:1, binding constant is $K^{\Theta}_{298.15\,K} = 2.44 \times 10^5$ L mol^{-1}, enthalpy and entropy work as driven force in this action.

1. Introduction

Investigation on the interactions of small molecules with DNA have attracted much attention over the past years owing to increasing researches in new efficient drugs and in many intracellular processes (Langer, 2001; Osborne & Ellington, 1997). Currently there are three primary binding modes of small molecules with nucleic acids (Song, Guo, Zhao, Shuang, & Dong, 2010): intercalative binding, grooving binding and electrostatic interaction. The studies on the interactions of small molecules with DNA are of great importance in many areas. Many anticancer drugs are known to interact with DNA to exert their biological activities.

Daunorubicin (DNR) is an anthracycline antibiotic with antiblastic and anticancer activity, which is linked by the formation of intercalative complexes with DNA and the inhibition of both DNA and RNA synthesis (Mizuno, Zakis, & Decker, 1975; Ward, Reich, & Goldberg, 1965; Xia et al., 2007; Zunino, Marco, Zaccara, & Gambetta, 1980). As shown in Fig. 1. Cyclodextrins (CDs) and their derivatives are a series of polysaccharides comprising six (α), seven (β) or eight (γ) D-glucose units which can provide a hydrophobic cavity in aqueous solution for the hydrophobic molecules or groups to form inclusion complexes (Martin del Valle, 2004; Misiuk & Zalewska, 2009). This "micro heterogeneous environment" can be used to control the equilibria of small molecules by including them into the cavity of CDs (Tafazzoli & Ghiasi, 2009), resulting in the changes of their electronic absorption and fluorescence properties. These unique amphiphilic characteristics make CDs particularly important and they have been employed as a host medium to study the interaction between small molecules and DNA (Wang & Zhou, 2007; Zhao, Zhu, Zhang, & Chen, 1999; Zhang et al., 2005; Zhang, Shuang, Dong, Liu, & Choi, 2004).

Through the binding studies of small molecules with DNA in γ-CD supramolecular system, it is possible to clarify their exact interactive modes. In this paper, the interaction of DNR with DNA in γ-CD medium is reported. Unlike α-CD medium, γ-CD can affect the interactive mode of DNR with DNA.

2. Experimental

2.1. Materials

Herring sperm DNA was purchased from Sigma biological Co. and used as received. Purity of DNA was checked by monitoring the ratio of absorbance at 260–280 nm. The ratio was 1.89, indicating the DNA was free from protein. The DNA was dissolved in doubly distilled deionized water with 50 mM NaCl and dialyzed for 48 h against a buffer solution at 277 K. The concentration of DNA stock solution was determined according to the absorbance at 260 nm by using the extinction coefficients of 6600 (mol cm)$^{-1}$.

All of the samples were dissolved in Tris–HCl buffer (pH7.40, examined by acidometer). Tris was purchased from Tianjin Kemi'ou Chemical Reagents Center. Acridine orange (AO) was purchased

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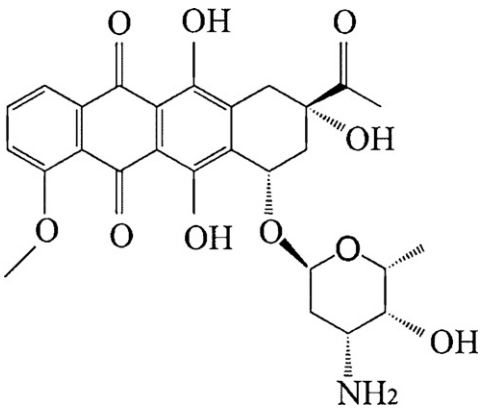

Fig. 1. Molecular structure of daunorubicin.

from Shanghai China Medicine Chemical Plant (A.R.). γ-CD was purchased from Sichuan Chengdu China Kelong Chemical Plant (A.R.). DNR was purchased from Jinan Wedo Industrial Co. Ltd. (A.R.). Other reagents were at least analytical grade, and were used without further purification.

2.2. Instruments

The absorption spectra were recorded on an UV-3150 spectrophotometer, made by Japan Shimadzu. The fluorescence spectra were recorded on a PE LS55 spectrofluorophotometer, made by PerkinElmer Insrtument Co., USA. The X-ray diffraction patterns were collected on an X'Pert PRO diffractometer, made by PANalytical B.V. The infrared spectra were recorded on a Spectrum One spectrometry, made by PE Insrtument Co., USA. The pH was recorded on a pHS-2C acidometer (made in China). All of the spectroscopic work was carried out at pH 7.40 remained by a Tris–HCl buffer.

2.3. Procedures

Samples for absorption and fluorescence were prepared by mixing known amounts of stock solutions of DNR, DNA and γ-CD in Tris–HCl buffer (pH 7.40) and diluted to the required concentrations. The absorption and fluorescence titrations were performed by keeping the concentration of DNR constant while varying the concentration of γ-CD, or keeping the concentration of γ-CD–DNR inclusion complex constant while varying the concentration of DNA. All the absorption measurements were made against the blank solution. In fluorescence mode, both excitation and emission bandwidths were set at 5 nm, λ_{ex} = 411 nm. 1.0 cm path-length quartz cuvettes were used for absorption and fluorescence measurements.

The powder X-ray diffraction operated at a voltage of 35 kV and a current of 60 mA. The samples were analyzed in the 2θ angle range of (5–90)° and the process parameters were set as: scan step size of 0.02°, scan step time of 1.54 s.

The infrared spectra of the samples were mixed with KBr and compressed as disks. The selected wavenumber ranged between 400 and 4000 cm^{-1} being the spectra resolution of 4 cm^{-1} and 10 being the number of scans.

3. Results and discussion

3.1. Formation of γ-cyclodextrin–daunorubicin inclusion complex

Addition of γ-CD to DNR solution at pH 7.40 resulted in absorption spectral changes of DNR, indicating the formation of an inclusion complex between γ-CD and DNR. Fig. 2 shows the UV–vis spectra of DNR in Tris–HCl buffer solution (pH 7.40) containing various concentrations of γ-CD. The absorption peak decreases with the increase in the concentration of γ-CD. In general, the proper matching of sizes between the host and guest molecules plays a crucial role for the formation of host–guest inclusion complex. In here, the cavity of γ-CD can enclose DNR snugly with good protection from the aqueous environment.

In order to determine the stoichiometry of the formation of γ-CD–DNR inclusion complex, the mole ratio method (Xi et al., 2009) experiment was done at the peak 481 nm. The absorption spectra of DNR upon increasing the concentration of γ-CD were record at 481 nm, and then the graph was plotted by mole ratio method. The mole ratio plots of DNR with γ-CD are shown in Fig. 2. The inclusion complex has a 1:1 stoichiometry. The inclusion constant (K) is an important parameter to represent the inclusion capacity, which can be determined by the double-reciprocal method using the following equation (Ouameur, Marty, & Tajmir-Riahi, 2005; Priyadarsini, Mohan, Tyagi, & Mittal, 1994):

$$\frac{1}{\Delta A} = \frac{1}{(A_0 - A)} = \left[\frac{1}{(\alpha \cdot K_f)}\right] \cdot \left(\frac{1}{c_{\gamma\text{-CD}}}\right) + \left(\frac{1}{\alpha}\right) \cdot c_{DNR}$$

where A_0 and A are the absorbencies of DNR in the absence and presence of γ-CD, respectively. α is the constant. K_f is the binding constant between γ-CD and DNR. $c_{\gamma\text{-CD}}$ is the concentration of γ-CD. And the binding constants were calculated from the ratio of the intercept on the vertical: K_f = 9412.39 L mol^{-1}.

XRD was used to determine the structure period of inclusion complex. The host molecule (γ-CD) reacts with guest molecule (DNR) to form a 1:1 host–guest complex. X-ray powder diffraction patterns of the inclusion complex γ-CD–DNR (a), physical mixture γ-CD and DNR (b), DNR (c) and γ-CD (d) were collected in Fig. 3. The spectrum of a is clearly different from those of b, c and d. The X-ray diffraction peaks in the 2θ region of 7.92°, 11.62°, 20.88° and 23.32° for c are absent in those for a. And the X-ray diffraction peaks of 12.78°, 16.66°, 18.91° and 21.98° for d are still absent in those for a. However, they are all present in the physical mixture b. We have reason to believe that signals in the physical mixture are simply the signal superposition of the two components, c and d. Those differences and new peaks in a provide an indication of the formation of the inclusion complex.

Fig. 4 shows the infrared spectra of wave number from 4000 to 400 cm^{-1} of γ-CD (a), DNR (b), the inclusion complex of γ-CD–DNR

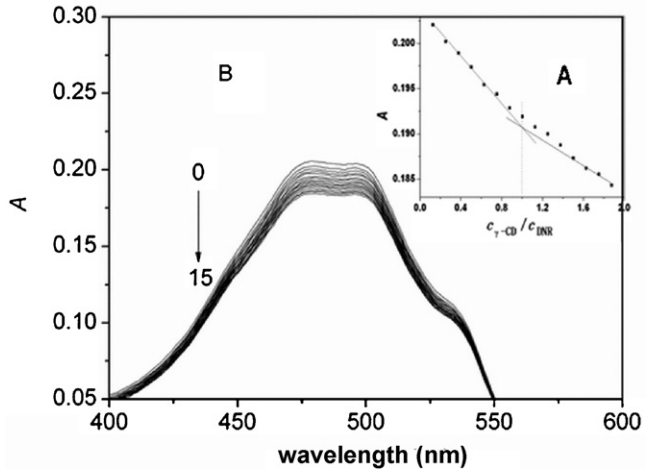

Fig. 2. (A) Mole ratio plots of γ-CD–DNR (pH 7.40; λ = 481 nm); $c_{DNR} = 2.00 \times 10^{-5}$ M; $c_{\gamma\text{-CD}} = 7.50 \times 10^{-4}$ M (10 μL per scan, 0–15:0–150 μL). (B) UV–vis absorption spectra of DNR in different concentrations of γ-CD (pH 7.40). $c_{DNR} = 2.00 \times 10^{-5}$ M, $c_{\gamma\text{-CD}} = 7.50 \times 10^{-4}$ M (10 μL per scan, 0–15:0–150 μL).

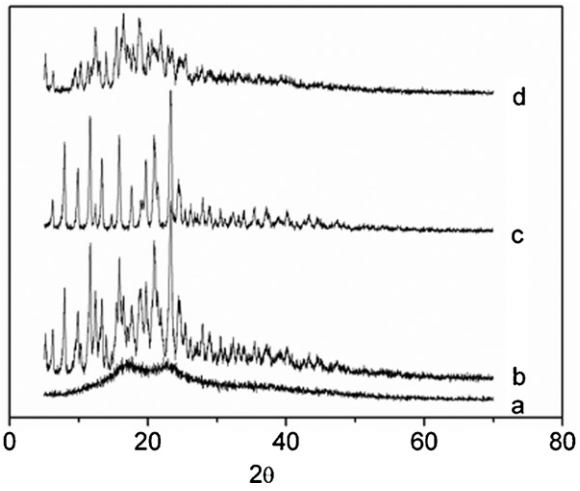

Fig. 3. X-ray diffraction patterns corresponding to the following products: (a) γ-CD–DNR; (b) physical mixture; (c) DNR; and (d) γ-CD.

(c) and physical mixture γ-CD and DNR (d). If γ-CD and DNR form an inclusion complex, the non-covalent interactions between them such as hydrophobic interactions, van der Waals interactions and hydrogen bonds will lower the energy of the included part of DNR, reduce the absorption intensities of the corresponding bonds (Wang, Han, Feng, & Pang, 2006). We can see that there are apparent differences between the spectra of b, c, and d and that some characteristic peaks of b change obviously by comparison of the spectrograms of c. c does not show any new peaks, indicating no chemical bonds were created in the formed complexes.

3.2. Absorption spectra studies

Generally, red shift and hypochromic effect are observed in the absorption spectra of small molecules if they intercalate with DNA. Fig. 5 depicts the UV–vis absorption spectra of γ-CD–DNR inclusion complex at various concentrations of DNA. The absorption of γ-CD–DNR at 496 nm decreases and 550 nm increases with the increase in DNA. The spectral changes of DNR in the presence of DNA are different with and without γ-CD, suggesting that γ-CD could affect the interaction of DNR with DNA. The new isosbestic

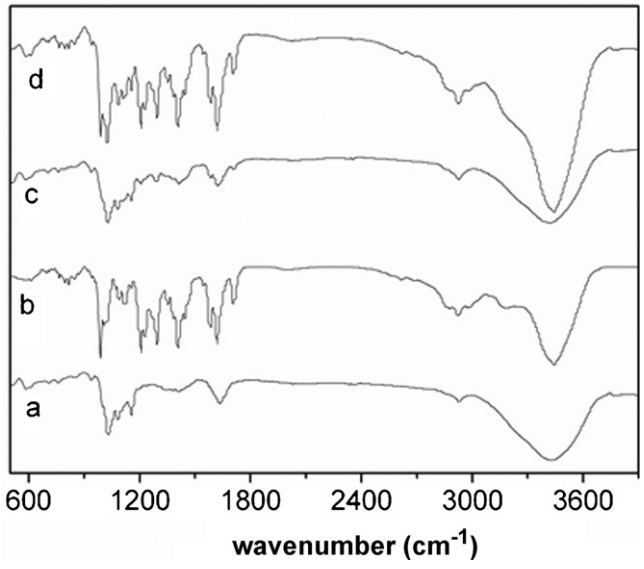

Fig. 4. IR spectra of γ-CD–DNR systems: (a) γ-CD; (b) DNR e; (c) γ-CD–DNR; and (d) physical mixture.

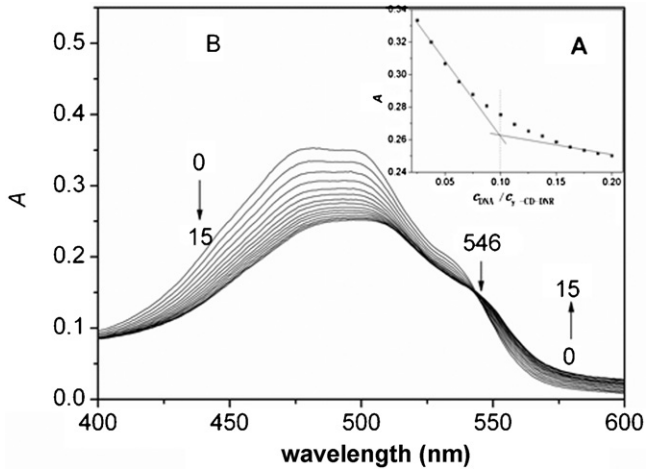

Fig. 5. (A) Mole ratio plots of DNA–γ-CD–DNR (pH 7.40; λ = 496 nm); $c_{\gamma\text{-CD–DNR}} = 4.00 \times 10^{-5}$ M; $c_{DNA} = 1.50 \times 10^{-4}$ M (10 μL per scan, 0–15:0–150 μL). (B) UV–vis absorption spectra of γ-CD–DNR in different concentrations of DNA (pH 7.40). $c_{\gamma\text{-CD–DNR}} = 1.00 \times 10^{-5}$ M, $c_{DNA} = 1.25 \times 10^{-4}$ M (10 μL per scan, 0–15:0–150 μL).

point at 546 nm also confirms that a new complex of DNA–γ-CD–DNR is formed (Hamai & Ohshida, 2004).

Fig. 5 exhibited the hypochromism on the addition of DNA with varying degrees of red shift, indicating interaction of γ-CD–DNR with DNA. The intercalative binding of γ-CD–DNR to a DNA helix has been characterized by large changes in the absorbance and an appreciable shift in wavelength due to the interaction of a DNA π stack and DNR π system.

In order to determine the stoichiometry of the formation of DNA–γ-CD–DNR complex, the mole ratio method experiment was also done at the peak 496 nm. The mole ratio plots of DNA with γ-CD–DNR were shown in superscript of Fig. 5. The binding ratio of the complex was: $n_{\gamma\text{-CD–DNR}}:n_{DNA} = 10:1$. According to Lambert–Beer law:

$$A = \varepsilon bc$$

where A is the absorbance of the DNA–γ-CD–DNR; ε is the molar absorptivity of DNA–γ-CD–DNR; c is the concentration of DNA–γ-CD–DNR. The apparent mol absorption coefficient of DNA–γ-CD–DNR was counted: $\varepsilon = 6.88 \times 10^4\ \mathrm{L\,mol^{-1}\,cm^{-1}}$.

3.3. Double reciprocal method

The absorption relationship between the complex and DNA was expressed by double reciprocal equation:

$$\frac{1}{(A_0 - A)} = \frac{1}{A_0} + \frac{1}{(K \times A_0 \times c_{DNA})}$$

where A_0 and A are the absorbance of γ-CD–DNR in the absence and presence of DNA, respectively. K is the binding constant between γ-CD–DNR and DNA, c_{DNA} is the concentration of DNA.

The double reciprocal plots of $1/(A_0 - A)$ versus $1/c_{DNA}$ are linear (at 298.15 K and 310.15 K, respectively), and the binding constants are calculated from the ratio of the intercept on the vertical: $K^{\Theta}_{298.15\,K} = 2.44 \times 10^5\ \mathrm{L\,mol^{-1}}$, $K^{\Theta}_{310.15\,K} = 2.10 \times 10^5\ \mathrm{L\,mol^{-1}}$. According to thermodynamic equation of K^{Θ}, $\Delta_r H_m{}^{\Theta}$, $\Delta_r G_m{}^{\Theta}$, $\Delta_r S_m{}^{\Theta}$ and T:

$$\ln \frac{K_2{}^{\Theta}}{K_1{}^{\Theta}} = -\Delta_r H_m{}^{\Theta} \left(\frac{1/T_2 - 1/T_1}{R} \right) \quad (1)$$

$$\Delta_r G_m{}^{\Theta} = -RT \ln K^{\Theta} \quad (2)$$

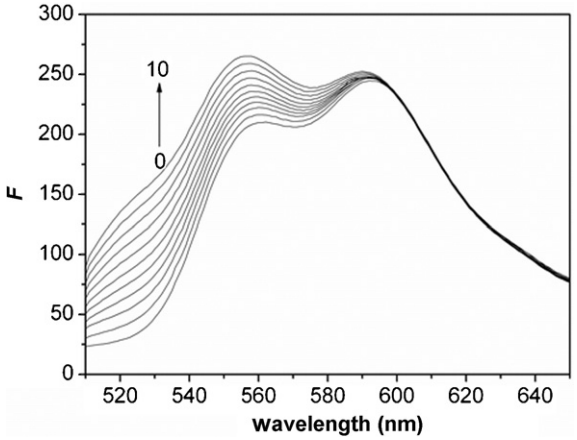

Fig. 6. Fluorescence spectra of DNA–γ-CD–DNR mixture in different concentrations of AO (pH 7.40). $c_{DNA-\gamma-CD-DNR} = 1.00 \times 10^{-6}$ M; $c_{AO} = 2.00 \times 10^{-5}$ M (10 μL per scan, 0–10:0–100 μL).

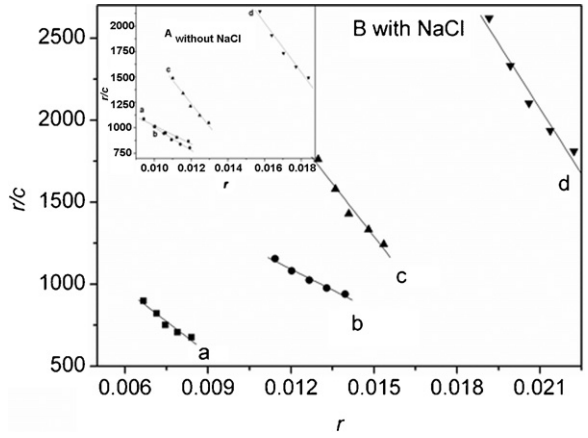

Fig. 7. Scatchard plots of DNA–γ-CD–DNR in different concentrations of AO ((A) without NaCl; (B) with NaCl) (pH 7.40). $c_{DNA} = 1.00 \times 10^{-4}$ M; $c_{AO} = 3.75 \times 10^{-4}$ M; RT = $c_{\gamma\text{-CD-DNR}}/c_{DNA}$; RT = a: 0.40, b: 0.80, c: 1.20, and d: 1.60.

$$\Delta_r G_{m,T}^{\Theta} = \Delta_r H_m^{\Theta} - T\Delta_r S_m^{\Theta} \quad (3)$$

where K_1^{Θ} and K_2^{Θ} refer to standard binding constants of γ-CD–DNR and DNA at 298.15 K and 310.15 K, respectively. T_1 is 298.15 K, T_2 is 310.15 K, $\Delta_r H_m^{\Theta}$ is standard molar reaction enthalpy. $\Delta_r G_m^{\Theta}$ refers to the standard molar reaction Gibbs free energy. $\Delta_r S_m^{\Theta}$ refers to the standard molar reaction entropy. Then $\Delta_r H_m^{\Theta} = -9.61 \times 10^3$ J mol^{-1} is deduced. The negative result showed it was an exothermic reaction. The $\Delta_r G_m^{\Theta}{}_{298.15\,K} = -3.07 \times 10^4$ J mol^{-1}. The negative result showed spontaneous interaction tide between γ-CD–DNR and DNA. The $\Delta_r S_m^{\Theta} = 70.74$ J mol^{-1} K^{-1}. The results suggested that the process of interaction of γ-CD–DNR and DNA were driven by entropy and enthalpy (Li, Tuo, Wang, Wang, & Ding, 2008; Ross & Subramanian, 1981).

3.4. Fluorescence measurements using AO as probe

Fluorescence titration is a useful method in the studies of binding properties of small molecules to DNA (Huang et al., 2008; Valis, Mayer-Enthart, & Wagenknecht, 2006) and the studies of the host–guest interaction in cyclodextrin chemistry (McAlpine & Garcia-Garibay, 1996; Takakusa, Kikuchi, Urano, Higuchi, & Nagano, 2001; Tong et al., 2001). The fluorescence measurements were carried out with acridine orange as probe. Because of its conjugated planar, it can insert between two adjacent base pairs in a DNA helix to get the fluorescence intensity remarkably increased. If γ-CD–DNR has the same binding mode with DNA as well as AO, there is a competition mode between AO and γ-CD–DNR with DNA. So the fluorescence spectra will be changed (Bi et al., 2006; Shahabadi, Kashanian, & Purfoulad, 2009). The influence on emission spectra of AO to DNA–γ-CD–DNR is shown in Fig. 6. It can be seen that the peak at 557 nm increases upon the addition of AO. The fluorescence spectra of Fig. 6 show that the reaction competition between AO and γ-CD–DNR with DNA are remarkable. According to the intercalation binding mode between AO and DNA, intercalation binding mode between γ-CD–DNR and DNA is basically confirmed (Jing, Zhang, & Shen, 2004).

3.5. The influence of A, T, C, G to the inclusion complex system

In order to further confirm the action mode between γ-CD–DNR and DNA, we also conducted a study on the influence of A, T, C, G to the inclusion complex system, respectively. If the absorption spectra of the inclusion complex have an obvious change by adding of these base pairs, then there are two possibilities: first, γ-CD–DNR effects the base pairs of DNA through the major groove and minor groove of DNA molecule, which means that there are groove binding mode; second, the inclusion complex can through the domain π system occurred π–π interaction and hydrophobic interaction with the π system of base pairs, which means that there are intercalation binding mode.

The results show that the absorption spectra of inclusion complex decrease steadily with increasing the amounts of base pairs. The rates of change of base pairs are as follow: C: 13.3%; G: 13.2%; A: 9.6%; T: 10.4%. And as can be seen from results, in the vicinity of 560 nm and 593 nm, the binding force of the inclusion complex with C and G are greater than A and T, so that the inclusion complex main acts on the C–G enrichment regions of the DNA. And this is consistent with previous reports (Cheng et al., 2003). Combined with the probe method and Scatchard method, the results identify that the interaction mode between γ-CD–DNR inclusion complex and DNA is groove binding and intercalation binding.

3.6. Scatchard method

The binding mode between small molecules and DNA can be determined using the Scatchard's procedure (Mansuri-Torshizi, Mital, Srivastava1, Parekh, & Chitnis, 1991). Scatchard equation expresses the binding of AO-DNA in the presence of γ-CD–DNR:

$$\frac{r}{c} = K(n - r)$$

where r is the moles of AO bound per mole of DNA, c is the molar concentration of free AO, n is binding site multiplicity per class of binding sites and K is the association binding constant of AO with DNA. Generally, it is regarded as an intercalation-binding mode if the values of n are same in the presence and absence of the inclusion complex, and it is regarded as a dis-intercalation binding mode if the values of K are same. And it is regarded as mix binding mode including non-intercalation and intercalation binding if both the values of n and K are changed. Two groups of buffers in the presence of NaCl and absence of NaCl as a contrast were constructed in Fig. 7. From the Scatchard plot, we can get the value of K and n. The results are shown in Table 1.

As shown in Table 1, it can be seen that both values of n and K changed with the different concentrations of γ-CD–DNR. The variation of the parameter n and K suggest a mix interaction herein. Normally, the values of n in the present of NaCl are lower than those in the absence of NaCl, indicating there is an electrostatic interac-

Table 1
Data of Scatchard equation of the interaction between γ-CD–DNR and DNA.

Curve	$c_{\gamma\text{-CD–DNR}}/c_{DNA}$	NaCl %	Scatchard	$K/(\mathrm{L\,mol^{-1}})$	n
a	0.40	0.50	1.75×10^3 to 1.30×10^5	1.30×10^5	0.013
		0	1.91×10^3 to 0.89×10^5	0.89×10^5	0.021
b	0.80	0.50	2.11×10^3 to 0.85×10^5	0.85×10^5	0.025
		0	2.13×10^3 to 1.12×10^5	1.12×10^5	0.019
c	1.20	0.50	4.52×10^3 to 2.15×10^5	2.15×10^5	0.021
		0	3.97×10^3 to 10.61×10^5	2.27×10^5	0.017
d	1.60	0.50	7.63×10^3 to 2.65×10^5	2.65×10^5	0.029
		0	5.93×10^3 to 2.43×10^5	2.43×10^5	0.024

tion between small molecules and DNA. While in Table 1, the values of n in the present of NaCl are basically higher than those in the absence of NaCl, and combined with the results of base pairs, we can confirm that there are groove binding and intercalation binding between the inclusion complex γ-CD–DNR and DNA.

3.7. Viscosity method

Viscosity experiment is an effective tool to decide the binding mode of small molecules and DNA. Thus, to further clarify the interaction between γ-CD–DNR and DNA, we carried out viscosity measurements. A classical intercalation model demands the space of adjacent base pairs to be large enough to accommodate the bound ligand and elongate the double helix, resulting in an increase of DNA viscosity (Lerman, 1961). A partial non-classical intercalation of the complex would reduce the DNA viscosity. There is little effect on the viscosity of DNA if the non-intercalation binding occurs in the binding process (Satyanarayana, Dabrowiak, & Chaires, 1992).

The changes in relative viscosity of DNA with increasing concentrations of γ-CD–DNR reveal that the values of relative viscosity reduced with increasing the amounts of the γ-CD–DNR. Combined with previous conclusions, such behavior further suggests that partial intercalation should be the interaction mode of the γ-CD–DNR with DNA.

4. Conclusions

The interactions between the inclusion complex γ-CD–DNR and DNA have been investigated using UV–vis spectra and fluorescence spectra. Our results indicate that this complex can bind to DNA by groove binding and intercalation binding. These results are further supported by viscosity measurements where the binding mode of γ-CD–DNR with DNA is partial non-classical intercalation. The molecular structure of DNR contains anthracenenucleus, which is the internal structure reason of γ-CD–DNR can insert to DNA molecule. These results strongly support the idea that γ-CD–DNR inclusion complex has important theoretical and practical value for the mechanism of drugs and drug design.

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References

Bi, S. Y., Qiao, C. Y., Song, D. Q., Tian, Y., Gao, D. J., Suna, Y., et al. (2006). Study of interactions of flavonoids with DNA using acridine orange as a fluorescence probe. *Sensors and Actuators B: Chemical*, *119*, 199–208.

Cheng, G. F., Zhang, D. M., Ding, M., Qu, H. Y., He, P. G., & Fang, Y. Z. (2003). Studies on the interaction of daunomycin and the specific sequence of DNA. *Chemical Journal of Chinese Universities*, *24*, 1395–1399.

Hamai, S., & Ohshida, T. (2004). Inclusion complexes of cyclodextrins with tetrakis(4-carboxyphenyl)porphyrin and tetrakis(4-sulfonatophenyl)porphyrin in aqueous solutions. *Journal of Inclusion Phenomena and Macrocyclic Chemistry*, *50*, 209–217.

Huang, Y., Lu, Q. S., Zhang, J., Zhang, Z. W., Zhang, Y., Chen, S. Y., et al. (2008). DNA cleavage by novel copper (II) complex and the role of β-cyclodextrin in promoting cleavage. *Bioorganic and Medicinal Chemistry*, *16*, 1103–1110.

Jing, B. W., Zhang, M. H., & Shen, T. (2004). [Ruthenium(II)(bpy)2L]$^{2+}$, where L are imidazo[f]-1,10-phenanthrolines:synthesis photophysics and binding with DNA. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *60*, 2635–2641.

Lerman, L. S. (1961). Structural considerations in interaction of DNA and acridines. *Journal of Molecular Biology*, *3*, 18–30.

Langer, R. (2001). Drug delivery: Drugs on target. *Science*, *293*, 58–59.

Li, H. B., Tuo, H. G., Wang, X. M., Wang, S. Q., & Ding, L. S. (2008). Study on interaction between hematoporphyrin dihydrochloride and herring sperm DNA by spectroscopy. *Acta Optica Sinica*, *10*, 2015–2021.

Mizuno, N. S., Zakis, B., & Decker, R. W. (1975). Binding of daunomycin to DNA and the inhibition of RNA and DNA synthesis. *Cancer Research*, *35*, 1542–1546.

Mansuri-Torshizi, H., Mital, R., Srivastava1, T. S., Parekh, H., & Chitnis, M. P. (1991). Synthesis, characterization, and cytotoxic studies of α-diimine/1,2-diamine platinum(II) and palladium(II) complexes of selenite and tellurite and binding of some of these complexes to DNA. *Journal of Inorganic Biochemistry*, *44*, 239–247.

McAlpine, S. R., & Garcia-Garibay, M. A. (1996). Inside–outside isomerism of β-cyclodextrin covalently linked with a naphthyl group. *Journal of the American Chemical Society*, *118*, 2750–2751.

Martin del Valle, E. M. (2004). Cyclodextrins and their uses: A review. *Process Biochemistry*, *39*, 1033–1046.

Misiuk, W., & Zalewska, M. (2009). Investigation of inclusion complex of trazodone hydrochloride with hydroxypropyl-β-cyclodextrin. *Carbohydrate Polymers*, *77*, 482–488.

Osborne, S. E., & Ellington, A. D. (1997). Nucleic acid selection and the challenge of combinatorial chemistry. *Chemical Reviews*, *97*, 349–370.

Ouameur, A. A., Marty, R., & Tajmir-Riahi, H. A. (2005). Human serum albumin complexes with chlorophyll and chlorophyllin. *Biopolymers*, *77*, 129–136.

Priyadarsini, K. I., Mohan, H., Tyagi, A. K., & Mittal, J. P. (1994). Inclusion complex of γ-cyclodextrin-C60: Formation, characterization, and photophysical properties in aqueous solutions. *Journal of Physical Chemistry*, *98*, 4756–4759.

Ross, P. D., & Subramanian, S. (1981). Thermodynamics of protein association reactions: Forces contributing to stability. *Biochemistry*, *20*, 3096–3102.

Satyanarayana, S., Dabrowiak, J. C., & Chaires, J. B. (1992). Neither Δ- nor Λ-tris (phenanthroline) ruthenium binds to DNA by classical intercalation. *Biochemistry*, *31*, 9319–9324.

Shahabadi, N., Kashanian, S., & Purfoulad, M. (2009). DNA interaction studies of a platinum(II) complex, PtCl2(NN) (NN = 4,7-dimethyl-1,10-phenanthroline), using different instrumental methods. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *72*, 757–761.

Song, J. P., Guo, Y. J., Zhao, Q., Shuang, S. M., & Dong, C. (2010). Assemblies of brilliant cresyl violet to DNA in the presence of γ-cyclodextrin. *Talanta*, *82*, 681–686.

Takakusa, H., Kikuchi, K., Urano, Y., Higuchi, T., & Nagano, T. (2001). Intramolecular fluorescence resonance energy transfer system with coumarin donor included in β-cyclodextrin. *Analytical Chemistry*, *73*, 939–942.

Tong, A. J., Yamauchi, A., Hayashita, T., Zhang, Z. Y., Smith, B. D., & Teramae, N. (2001). Boronic acid fluorophore/beta-cyclodextrin complex sensors for selective sugar recognition in water. *Analytical Chemistry*, *73*, 1530–1536.

Tafazzoli, M., & Ghiasi, M. (2009). Structure and conformation of α-, β- and γ-cyclodextrin in solution: Theoretical approaches and experimental validation. *Carbohydrate Polymers*, *78*, 10–15.

Valis, L., Mayer-Enthart, E., & Wagenknecht, H. A. (2006). 8-(Pyren-1-yl)-2′-deoxyguanosine as an optical probe for DNA hybridization and for charge transfer with small peptides. *Bioorganic and Medicinal Chemistry Letters*, *16*, 3184–3187.

Ward, D. C., Reich, E., & Goldberg, I. H. (1965). Base specificity in the interaction of polynucleotides with antibiotic drugs. *Science*, *149*, 1259–1263.

Wang, H. Y., Han, J., Feng, X. G., & Pang, Y. L. (2006). Study of inclusion complex formation between tropaeolin OO and β-cyclodextrin by spectrophotometry and

Infrared spectroscopy. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, *65*, 100–105.

Wang, Y., & Zhou, A. H. (2007). Spectroscopic studies on the binding of methylene blue with DNA by means of cyclodextrin supramolecular systems. *Journal of Photochemistry and Photobiology A: Chemistry*, *190*, 121–127.

Xia, A. L., Wu, H. L., Li, S. F., Zhu, S. H., Zhang, Y., Han, Q. J., et al. (2007). Study of the interactions of berberine and daunorubicin with DNA using alternating penalty trilinear decomposition algorithm combined with excitation–emission matrix fluorescence data. *Talanta*, *73*, 606–612.

Xi, P. X., Xu, Z. H., Liu, X. H., Chen, F. J., Zeng, Z. Z., Zhang, X. W., et al. (2009). Synthesis, characterization, antioxidant activity and DNA-binding studies of three rare earth (III) complexes with 1-(4-Aminoantipyrine)-3-tosylurea ligand. *Journal of Fluorescence*, *19*, 63–72.

Zunino, F., Marco, A. D., Zaccara, A., & Gambetta, R. A. (1980). The interaction of daunorubicin and doxorubicin with DNA and chromatin. *Biochimica et Biophysica Acta*, *607*, 206–214.

Zhao, G. C., Zhu, J. J., Zhang, J. J., & Chen, H. Y. (1999). Voltammetric studies of the interaction of methylene blue with DNA by means of β-cyclodextrin. *Analytical Chemical Acta*, *394*, 337–344.

Zhang, G. M., Shuang, S. M., Dong, C., Liu, D. S., & Choi, M. M. F. (2004). Investigation on DNA assembly to neutral red-cyclodextrin complex by molecular spectroscopy. *Journal of Photochemistry and Photobiology B: Biology*, *74*, 127–134.

Zhang, G. M., Pang, Y. H., Shuang, S. M., Dong, C., Choi, M. M. F., & Liu, D. S. (2005). Spectroscopic studies on the interaction of Safranine T with DNA in β-cyclodextrin and carboxymethyl-β-cyclodextrin. *Journal of Photochemistry and Photobiology A: Chemistry*, *169*, 153–158.