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BIOPHYSICS

M. Khvedelidze, T. Mdzinarishvili, G. Khelashvili, G. Gogoladze, G. Mrevlishvili

Thermodynamic and Hydrodynamic Study of DNA-Anticancer Antibiotic (Adriablastin) Interaction

Presented by Member of the Academy M. Zaalishvili, February 8, 2005

ABSTRACT. **Investigation of DNA-adriablastin complex has shown that interaction between adriablastin and DNA occurs. It was shown that the result of this interaction becomes apparent both in calorimetric and viscometric experiments.** *© 2005 Bull. Georg. Acad. Sci.*

Key words: calorimetry, viscometry, adriablastin, DNA.

It is well known that various anticancer agents, which appear to suppress uncontrolled growth of tumor cells, are widely used against cancer diseases. One of the supposed targets for these drugs is DNA molecule. The data concerning interaction between DNA and different anticancer drugs are given in [1-4].

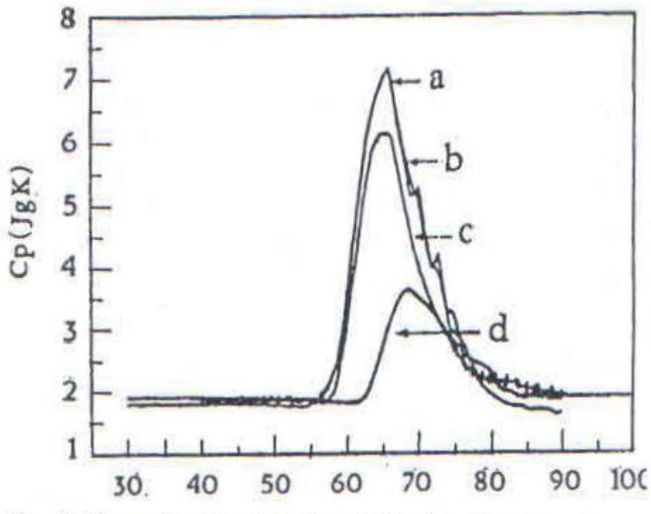

Fig. 1. Dependence of heat capacity function on temperature at different ratio of [DNA-bp]/[adriablastin] (20 mM HEPES, 0.1 mM EDTA, pH7.4). Curve a-DNA without adriablastin; b-[DNA-bp]/[adriablastin]=50/1; c-[DNA-bp]/[adriablastin]=10/1; d-[DNA-bp]/[adriablastin]=1/1.

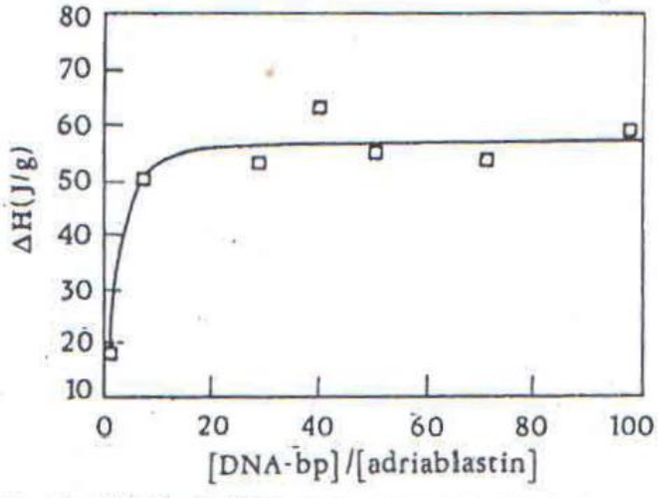

Fig. 2. Adriablastin-DNA complex transition enthalpy dependence on [DNA-bp]/[adriablastin].

Due to importance of the problem, we carried out a number of microcalorimetric and viscometric experiments. Adriablastin is characterized by anticancer activity and due to its wide action spectrum differs from other anticancer antibiotics.

The temperature dependence of DNA heat capacity at various [DNA-bp]/[adriablastin] ratio is given on Fig. 1. (Solvent: 20 mM HEPES, 0.1 mM EDTA, pH 7.4). Calculations have shown that the melting enthalpy ΔH of transition dramatically decreases from 55 J/g to 20 J/g while the [DNA-bp]/[adriablastin] ratio varies from 30 to 1. Fig. 2 shows the dependence of denaturation enthalpy on the concentration of Adriablastin. No significant changes of enthalpy are detected when the ratio of [DNA-bp]/[adriablastin] increases from 10/1 to 100/1, while the dramatic decrease of enthalpy takes place at the ratio of [DNA-bp]/[adriablastin] under 10/1.

The dependence of η_{sp} on differ-

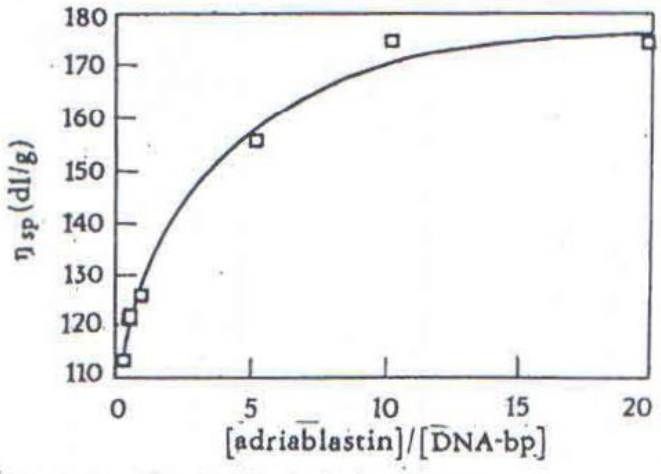

Fig. 3. Specific viscosity (η_{sp}) dependence on [adriablastin]/[DNA-bp] at T=30°C. (20 mM HEPES, pH7.4).

ent [adriablastin]/[DNA-bp] ratio is given on Fig. 3. As it is evident from the figure, at minor ratio of [adriablastin]/[DNA-bp], sharp increase of specific viscosity is observed; but at high ratio of [adriablastin]/[DNA-bp] the tendency of η_{sp} saturation occurs, what points to the DNA's saturation by Adriablastin molecules.

Obtained viscometric data point out that effect of Adriablastin on DNA molecule occurrs due to intercalation of antibiotic into the DNA structure. The intercalation has to be reflected also in calorimetric experiments. The intercalation should cause decrease of base stacking, what is represented by decrease of transition enthalpy.

I. Javakhishvili Tbilisi State University

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ბიოფიზიკა

მ. ხვედელიძე, თ. მძინარიშვილი, გ. ხელაშვილი,
გ. გოგოლაძე, გ. მრუელიშვილი

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რეზიუმე: ადრიაბლასტინ-დნმ-ის კომპლექსის შესწავლამ გვიჩვენა, რომ ადგილი აქვს ადრიაბლასტინის ურთიერთქმედებას დნმ-ის მოლეკულასთან. კერძოდ, ნაჩვენებია, რომ ამ ურთიერთქმედების შედეგი მჟღავნდება როგორც კალორიმეტრულკაკ, ასევე ვისკოზიმეტრულ ექსპერიმენტებში.