CIRCULAR DICHROISM AND FLUORESCENCE STUDIES ON THE INTERACTIONS OF VINCRISTINE TO HOMOPOLYRIBONUCLEOTIDES

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Fluorescence study on the interactions of vincristine (VCR) with the polyadenylic (poly A), polyguanylic (poly G), polycytidylic (poly C), and polyuridylic (poly U) acids, in aqueous neutral buffer at 25° C, demonstrated complex formation. The exhibited effect involves quenching of their total overlapped fluorescence, indicating the formation of nonfluorescent complexes. It was possible to make precise measurements and to calculate the binding parameters from equations we derived for this purpose. The constants calculated include the equilibrium constant (K), number of binding sites (n), and the standard free energy changes. The K values were quite high and ranged from 0.4191×10^4 (VCR-poly A) to 2.3183×10^4 (VCR-poly G); while the n values assume the range from <0.01 (VCR-poly A) to 0.35 (VCR-poly U).

The circular dichroic (CD) difference spectrum of poly G in VCR-poly G is characterized by an increase in the intensity of the band at 285 nm, slight reduction of the 260 nm main positive band, and a very slight reduction in the intensity of the negative band at 240 nm associated with broadening extending to 220 nm. The pattern of change in the difference spectrum of poly A induced by the binding of VCR involves reduction in both of the positive and negative bands of poly A with retention of the original CD spectrum. The reduction seems to continue with increasing the concentration of VCR. The poly C difference spectrum is also affected by VCR. The positive band at 276 nm is reduced as well as slightly shifted towards longer wavelengths. The negative band is increased in intensity and blue-shifted. On the other hand a noticeable reduction in intensity of the positive band located at 271 nm, VCR concentration-dependent, is observed in the difference spectrum of poly U.

In order to account for the mechanisms of interactions from the observed effects, one may reasonably hypothesize the partial intercalation of the aromatic moiety of VCR between the bases. It may be concluded that the results presented in this work might add a piece of information contributing to basic understanding of the mechanism of action of the drug at the molecular level.