18th National and 3rd International Conference of Iranian Biophysical chemistry

هجدهمین همایش ملی و سومین همایش بین المللی بیوشیمی فیزیک ایران

25-26 Des, 2024, University of Hormozgan

۶-۵ دی ماه ۱۴۰۳، دانشگاه هرمزگان

The effect of guanine oxidation on the interaction of the doxorubicin whit four-stranded DNA

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Abstract

Four-stranded structure are guanine-rich sequences that are involved in the expression of proto-oncogene such as c-Myc.Doxorubicin is an anticancer drug belonging to the anthracycline family, which exerts its biological effect by inhibiting the topoisomerase II enzyme, chromatin instability and DNA breaks. In this research, the effect of guanine oxidation on the interaction of doxorubicin with the four-stranded structure of the NHE III region of the c-Myc gene promoter has been investigated. Absorption spectroscopy, Fluorescence emission and polyacrylamide gel electrophoresis were used to evaluate the interaction.The results of spectroscopy showed that the oxidation of guanine in the tetrad plane of the four-stranded structure causes a change in the binding of doxorubicin.The results of absorption spectroscopy indicated that percentage of the drug hypochromicity decreases upon addition of the oxidized G-quadruplex DNA structure in compared with the wild type structure. Fluorescence spectra implied that emission of doxorubicin decreases upon interaction of the both forms of G-quadruplex DNA, but the oxidation of guanine in the tetrad plane causes a remarkable decrease in the DNA concentration where binding saturation occurs. The binding constant of the G-quadrulex to doxorubicin and Stern-Volmer quenching constant decrease due to oxidation of the guanine nucleotide. In addition, the oxidation influences on stability of the interaction in the presence of urea and the electrophoretic mobility of the DNA structure in native polyacrylamide gel. Consequently, our results imply that

oxidative stress can mediate cancer initiation and development by molecular damage of the nucleotideshas remarkable effect on the interaction between doxorubicin anticancer drug and the G-quadruplex non-B DNA structure.

Key words: Four-stranded structure,Doxorubicin,Guanine oxidation,c-Myc gene

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