DOXORUBICIN MAKES A COMPLEX WITH HORSERADISH PEROXIDASE: SPECTROSCOPIC STUDIES

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Abstract

Doxorubicin is an anticancer anthracycline inducing ROS-generation apoptosis in cancer cells. In this investigation, its consequence on the tertiary and secondary structure of HRPC, a critical enzyme involved in protection against oxidative stress, was studied. In vitro spectroscopic studies were done using, electronic absorption spectroscopy, fluorescence spectroscopy and circular dichroism spectroscopy. The electronic absorption spectra recorded from 300-700nm. $K_d$ and $\Delta G$ were calculated from changes in the absorbance of 403nm. The enzymes intrinsic fluorescence obtained upon excitation at 297nm for the only tryptophan residue of HRPC decreased as a function of Doxorubicin increasing concentrations. Circular dichroism showed a little change in random coil of secondary structure of the enzyme. All measurements performed in citrate buffer 0.1M pH 4.0. Results indicated that Drug-protein complex formation occurred through binding of one molecule of Doxorubicin independently. The heme and tryptophan environment became more polar and the Drug-protein complex quenched the only tryptophan residue in the enzymes structure. These alterations suggest that Doxorubicin which reduces the activity of catalase, peroxidase and superoxide dismutase in cells, could alter significant cell protein conformations like horseradish peroxidase C.

Key words: Doxorubicin, Horseradish peroxidase C (HRPC), Drug-protein complex, Apoptosis, Conformational changes, Spectroscopy.

Abbreviations: Reactive oxygen species (ROS), Horseradish peroxidase C (HRPC), Circular dichroism (CD), Ultra violet-visible (UV-VIS)
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