Study of the interaction of oxaliplatin with chromatin protein: Histone H1

Abstract: Oxaliplatin, L-OHP is a third generation platinum antitumor analog in which 1,2 diaminocyclohexane (DACH) ligand substitutes for the amine groups of cisplatin. This drug exerts its cytotoxic effect mostly through DNA damage and forms intra and interstrand crosslinks in cellular DNA. Histone H1 is a very lysine-rich histone fraction of histone proteins which binds to linker DNA between adjacent nucleosomes to facilitate the folding of the chromatin fiber. In the present study we have investigated the interaction of oxaliplatin with histone H1 in solution using UV/Vis and fluorescence spectroscopy techniques. Histone H1 was isolated from calf thymus and purified. The protein was incubated in the presence and absence of various concentrations of the drug for an hour and then spectrophotometric measurements were carried out at room temperature. The results showed that upon addition of oxaliplatin, absorbance of histone H1 at 210nm was significantly decreased. The fluorescence emission intensity of histone H1 in the absence of oxaliplatin exhibit a characteristic fluorescence emission intensity maximum at 305nm corresponding to the maximum fluorescence emission intensity of tyrosin. Addition of increasing amount of oxaliplatin to histone H1 solution at a constant protein concentration resulted in a reduction of its emission intensity because of fluorescence quenching. Stern-volmer curve shown positive and linear relationship. From the result presented above it is concluded that histone H1 can be considered as potent target for this drug which open a new insight into mechanism of oxaliplatin action.

oxaliplatin, histone H1, spectroscopy

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