



Interaction of the 5-fluorouracil analog 5-fluoro-2'-deoxyuridine with N and B isoforms of human serum albumin: a spectroscopic and calorimetric study.

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Abstract:

Drugs and metabolites are transported in the blood by plasma proteins, such as human serum albumin (HSA). The uridine analog 2'dFUrd, which is a cytotoxic prodrug metabolite of capecitabine, has remarkable activity against solid tumors when administered orally. We report the results of an in vitro experimental study on the interactions of 2'-dFUrd with the N-isoform (at pH 7.4) and B-isoform (at pH 9.0) of HSA, investigated using fluorescence spectroscopy, circular dichroism (CD), isothermal titration calorimetry (ITC), differential scanning calorimetry (DSC), and molecular docking. The binding constant (K_b) was higher for the N-isoform than for the B-isoform. Thermodynamic parameters, such as enthalpy change (ΔH°), entropy change (ΔS°), and Gibbs free energy change (ΔG°), were also calculated for both isoform interactions using calorimetric techniques. The thermostabilities of HSA and the HSA-2'dFUrd complex were found to be higher for the N-isoform. The interaction of 2'dFUrd with HSA was also explored in molecular docking studies, which revealed that 2'dFUrd was bound to the Sudlow site I in subdomain IIA through multiple modes of interaction, such as hydrophobic interactions and hydrogen bonding. These results suggest that 2'dFUrd has higher binding affinity for the N-isoform of HSA.

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