Computational Affinity between Anthraquinone Derivatives and DNA

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Targeting DNA is a viable solution to treating cancer. Although many DNA intercalators are effective, they have deleterious effects on DNA structure and negative side effects for the patient. Anthraquinone drugs are used to manage symptoms of multiple sclerosis, fight antibacterial infections, and can facilitate tumorigenesis. Unlike DNA intercalators, anthraquinones interact with DNA using major and minor grooves which limit DNA disruption. In this study, the binding affinity of 4 anthraquinone derivatives: 9-aminoacridine (9-AA), 4-aminopyridine (4-AP), 3ß-cholesteryl N-(9-acridinyl) carbamate, 3ß-cholesteryl N-(4-pyridyl) carbamate was explored. AutoDock Vina determined the impact of anthraquinone size, polarity and lipophilicity on the binding affinity. In addition, the drug-like properties of the anthraquinones were calculated using the SwissADME webserver. The structure of DNA strand was obtained from the Protein Data Bank (1BDN). The study hypothesized that the binding will be stronger as polarity and number hydrogen bond donors and acceptors in the ligands increase. Our preliminary data indicates anthraquinones with cholesterol have a stronger affinity with DNA. The computed affinities for each ligand (9-acrininyl, 4-pyridyl, 9-AA, and 4-AP) are 17.34 kcal/mol, -16.00 kcal/mol, -12.60 kcal/mol, and -7.38 kcal/mol respectively. All the ligands studied mostly preferred the minor groove. The affinity between 9-AA and 4-AP with DNA is dominated by electrostatics and hydrogen bonds. In addition to electrostatics in 9-acrininyl and 4-pyridyl, binding seems to be enhanced by van Der Waals interactions through cholesterol hydrophobic patches. This data suggest that cholesterol has a major impact in enhancing the affinity between DNA and anthraquinones.

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