Evaluation of Selectivity of Binding of Diminazene and its Alkyne Analogs to DNA

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The binding of organic ligands to telomeric G-quadruplex DNA (gqDNA) may act as an anti-cancer therapy. The stabilization of gqDNA using polycyclic aromatic ligands, in particular, diminazene (DMZ) and its alkyne analogs, has been shown to prevent the rapid cell division that ultimately leads to cancer.[1] However, these ligands, when placed into an environment that contains double stranded DNA (dsDNA) and gqDNA, have displayed possible toxic effects due to their high affinity to dsDNA. A higher binding affinity to dsDNA may interfere with gene replication depending on the place of binding. The modeling presented here has been to test the relative affinities (binding energies) of DNA-ligand binding in order to establish the ligand structure that will provide the best selectivity for gqDNA. By simulating a natural molecular environment, an efficient assessment can be made using several computational trials conducted through various methodologies (e.g. molecular docking, molecular dynamics simulations). This work is focused on the testing of interactions of recently synthesized polycyclic aromatic ligands, namely DMZ and three of its analogs.

References

1. Wang C, Carter-Cooper B, Du Y, Zhou J, Saeed MA, Liu J, Guo M, Roembke B, Mikek C, Lewis EA, Lapidus RG, Sintim HO. *Eur. J. Med. Chem.* 118 (2016): 266-275.