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Model of G-quadruplex Interactions with Heterocyclic Ligands

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We offer a contribution to methodology of targeting important regulatory nucleic acid structures, G-quadruplexes. A model of their interaction with potentially anticancer hetero-polycyclic molecules is developed using methods of its precision computation by quantum chemistry.[1] Further we use quantitative characterizations of biological activity of studied heterocycles.[2] We find meaningful relationships of computed molecular energetic values, namely affinity of heterocyclic ligands to a model G-quadruplex, and experimental values of pharmacological characteristics, e.g. **IC_{50}.**[3] Applied quantum chemistry theories are DFT, e.g. using wB97XD/6-31G*, and explicitly correlated MO theory,[1,3] e.g. in the RI-MP2 form. These types of QSAR may be significant in the quest for novel anticancer and other medications, provided G-quadruplex regulation of the key biological process is involved.

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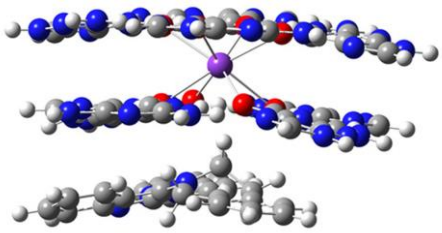

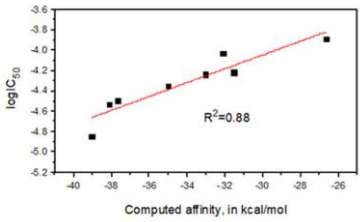

Keywords: G-quadruplexes, quantum chemical model, ligand affinity, cancer IC_{50}

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