Available online at www.joac.info

ISSN: 2278-1862

Journal of Applicable Chemistry

2016, 5(1): 21-110

(International Peer Reviewed Journal)

Perspective Review

Computational Quantum Chemistry (CQC)
Part 2: Anticancer/anti-HIV drugs and DFT studies with Jaguar

K. Ramakrishna[1*], B. Venkata Sasidhar[1] andR. Sambasiva Rao[2]

1. Department of Chemistry, Gitam Institute of Science, Gitam University, Visakhapatnam, 530 017, **INDIA**
2 School of Chemistry, Andhra University, Visakhapatnam 530 003, **INDIA**

Email: karipeddirk@gmail.com, rsr.chem@gmail.com

Accepted on 10th January2016

ABSTRACT

Background: The FDA approved marketeddrugs for cancer and HIV increased the life span and comfort of patients. The motto of inventing better molecules to render AIDS-free and cancer-free human life and reducing the suffering is key in looking for new leads and toxic free/ high potency molecules for clinical trials. The results of CQC, structure activity relationships (SXR), HTS/virtual libraries, docking and conformer generators lead to complimentary and supplementary information in drug discovery to routine prescription through clinical trials. Earlier, we carried out the synthesis of substituted Uracil-5-Sulphonamides and confirmed their structures from spectral studies.

Scope of study: The quantum chemical investigations and biological (anti-cancer/anti-HIV) activity in vitro of four synthesized substituted Uracil-5-sulphonamides derivatives are reported.

Chemical models with CQC: The geometry optimization, chemical validity of CQC model, single point electronic point energies and physico-chemical properties of substituted aroyl sulphonamides are computed with Jaguar package of Schrodinger software suit. The level of theory employed is DFT with B3LYP hybrid functional for both optimization and vibrational frequency analysis. The anti-cancer and anti-HIVS activities of N-cyclobutyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-sulfonamide, Ethyl,1-((2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)sulfonyl)piperidine-4-carboxylate, ((2,4-dioxo-1,2,3,4-tetrahydro pyrimidin-5-yl)sulfonyl)-L-proline,(4aS,7aS)-6-benzyl-1-((6-methyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5yl) sulfonyl)tetrahydro-1H-pyrrolo[3,4-b]pyridine-5,7(6H,7aH)-dioneetc are reported here. A peda gogical research frame for pseudospectral method for solving PDFs (partial differential equations) and functional features of Jaguar in first order knowledge form are discussed. An intelligent database of drugs for cancer and HIV is under rigorous testing and passive form of a part of it is in supplementary material. The features of Schrodinger are described from an in-house hierarchical information/knowledge/method base for CQC with G09, HyperChem, ADF, Schrodinger and GAMESS for gaseous and solvent media.

Biological activity: The anticancer activity against survival of the colon carcinoma HCT-116 cell lines and anti-HIV data compared to Zidovudine (AZT) are experimentally determined. These second order tensors arecorrelated with quantum chemical derived parameters.

Conclusions: The present set of substituted sulphonamides show promising anti-cancer and anti-HIV activity. The results are valuable insights into the role in a multi-facet probing into the chemical properties of these new ligands and their physical-/bio-physical interaction energetics expanding assessment of the capabilities of molecules to explorative search in the drug-discovery pursuit. Further, detailed

investigations of toxicity, membrane permeability and protein-ligand interactions will throw light on the suitability for the next phase.

Keywords: Synthesis, Substituted Sulphonamides, CQC models, Gas phase, Jaguar package, 3D-Geo metric optimization, vibrational frequencies, Properties, biological activity, HIV, Cancer.
