International Research Journal of Education and Technology
Peer Reviewed Journal
ISSN 2581-7795

MOLECULAR GEOMETRY, HOMO AND LUMO ANALYSIS AND DOCKING STUDIES OF PYRIMIDINE DERIVATIVE

S.MAHALAKSHMI [1], Dr.C.M.MAHALAKSHMI[2]

[1]Student, Krishnasamy College of Science, Arts And Management For Women, Cuddalore,India
[2]Assistant professor, Krishnasamy College of Science, Arts and Management for Women, Cuddalore, India

---

Abstract – *The theoretical calculations of the N-((1H-benzo[d]imidazol-2-yl)methyl) pyrimidin-4-amine has been carried out using the more popular density functional theory method, Becke-3-Parameter-Lee-Yang-Parr (B3LYP) in 6-311G++(d,p) basis set.. Moreover, the highest occupied molecular orbital, the lowest unoccupied molecular orbital, molecular electrostatic potential, chemical reactivity parameters and natural bond orbital of the optimized structure have been evaluated at the same level of theory. Besides, the molecular docking simulation of the mentioned molecule with target protein was also investigated. This research used the electrostatic molecular potential (MEP) and electrostatic contour to understand the regions of reactivity of the this molecule.*

***Key Words*: DFT, HOMO-LUMO, MEP, Molecular docking.**

1.INTRODUCTION

The majority of chemical entities, which are found in numerous natural goods, fine chemicals, and physiologically active medications essential for improving the quality of life[1], contain heterocyclic compounds that contain nitrogen. Due to the diversity of their structural makeup and connections to a wide range of biological activities, synthetic studies of fused pyrimidines have been widely published. Due to their anti-inflammatory, psychopharmacological, bactericidal, anticancer, antitubercular, antioxidant, anticonvulsant, antibacterial, antiplasmodial, antifungal, anticancer [2-4], antimicrobial, antibiotic, antiviral activity as HIV-1 reverse transcriptase inhibitors, antifolates [5] and antihismatic activity [6] properties, pyrimidines are also of pharmacological interest.

Pyrimidines are heterocyclic aromatic compounds with two nitrogen atoms at positions 1 and 3 of the six-membered rings, analogous to benzene and pyridine. Pyrimidine has a molecular weight of 80 and the chemical formula $C_4H_4N_2$. It is isomeric with two more diazene forms[7]. It is the source of a large group of heterocyclic compounds and is essential to many biological processes, as evidenced by the presence of nucleic acids, a number of vitamins, co-enzymes, and purines. Although the pyrimidine ring itself does not occur in nature, substituted pyrimidines and compounds that include it do. Additionally, pyrimidine[8] and its derivatives, such as fused pyrimidines, are among the most prominent structures in nucleic acids, including uracil, thymine, cytosine, adenine, and guanine, which are essential components of both DNA and RNA20.

It is now well established that theoretical calculations, such as the Density Functional Theory approach (DFT), are a useful method for assessing the structural and spectral properties of organic molecules. Several published DFT tests have documented a wide range of pyrimidine characteristics. The antioxidant, anticonvulsant, antibacterial, antiplasmodial, antifungal, anticancer, antimicrobial, antibiotic, antiviral activity as inhibitors of HIV-1 reverse transcriptase, antifolates, and antihismatic activity were also used to characterise newly synthesised pyrimidine by substitution groups in their derivative structure.

2. OPTIMIZED GEOMETRIES

Molecular geometry is a sensitive indicator of intra and intermolecular interactions. The accurate determination of geometrical deformation in substituted benzimidazole rings is an important tool for investigating the nature of the interactions between the ring and the substituent's .The geometry of N-((1H-benzo[d]imidazol-2-yl)methyl) pyrimidin-4-amine[9] was optimized at DFT (B3LYP) levels using 6-311++G (d,p) basis set. At the optimized geometry for the title molecule no imaginary frequency modes were obtained, so there is a true minimum on the potential energy surface. The optimized molecular structure with symbols and numbering of the title molecule is obtained from Gaussian 09W[10]and Gauss View programs[11] as shown in the Fig. (1). It is observed that most of the optimized bond lengths and bond angles are slightly shorter, as well as longer than the experimental value in B3LYP method. Selected geometrical parameters like bond length, bond angle and dihedral angle are listed in Table 4.1. As a result of partial protonation of both nitrogen atoms C1-N2 and C3-N2 bond lengths in benzimidazole moiety is 1.3747 and 1.3897.

For the 1A compound, pyrimidine ring attached to second position of benzimidazole were found to be planar with the ring. This result was shown by the fact that the dihedral angles for C10-N11-C14-N13 and C10-N11-C14-C15 in 1A are 0° and 180° respectively.

International Research Journal of Education and Technology
Peer Reviewed Journal
ISSN 2581-7795

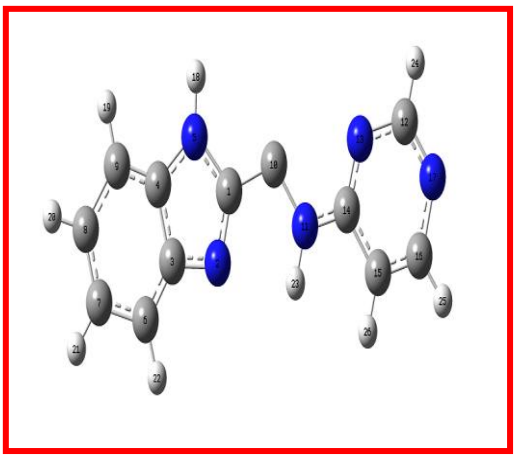
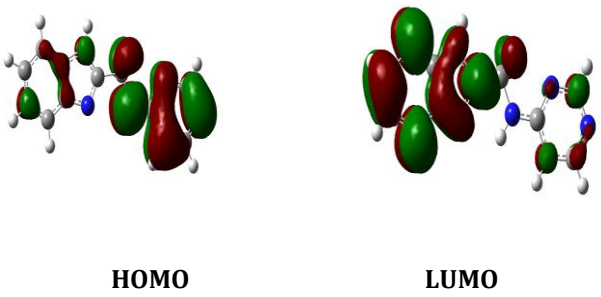


Fig -1: Optimized molecular geometries and atomic numbering of 1A

2.1. FRONTIER MOLECULAR ORBITALS:

The HOMO, LUMO and HOMO-LUMO energy gap of N-((1H-benzo[d]imidazol-2-yl)methyl) pyrimidin-4-amine in DFT level in 6-311++G(d,p) basis set has been calculated. Surfaces for the frontier orbitals were drawn for the title compound in the Fig..2. By careful observation of HOMO-LUMO plot we can provide insight into the nature of reactivity, and some of the structural and physical properties of molecules. The positive phase of the molecule is represented in red color and negative phase in green color



HOMO **LUMO**

Fig -2: HOMO-LUMO pictures of compound 1A

Compound 1A with higher energy E_{HOMO} = 6.2613 allows it to be the best electron donor and the lowest LUMO energy E_{LUMO} = 0.8844 which signifies that it can be the best electron acceptor. The two properties like I (potential ionization) and A (affinity) are so important, the determination of these two properties allow us to calculate the absolute electro negativity (χ) and the absolute hardness (η). These two parameters are related to the one-electron orbital energies of the HOMO and LUMO respectively.

2.2. MOLECULAR DOCKING:

A type of bioinformatic modelling called molecular docking includes the interaction of two or more molecules to produce a stable adduct. It makes predictions about the three-dimensional structure of any complex based on the binding characteristics of ligand and target. Several potential adduct structures are generated by molecular docking and are ranked and categorised using the software's scoring function. Based on the system's overall energy, docking simulations forecast an optimum docked conformer. Despite all viable strategies, the difficulties still lay in ligand chemistry (tautomerism and ionisation), receptor flexibility (single conformation of stiff receptor), and scoring function (differentiate actual binding mode). HIV-1 reverse transcriptase inhibitors, antifolates, and antihismetic activities

We have performed a molecular modeling study to investigate the possible binding conformation for the N-((1H-benzo[d]imidazol-2-yl) methyl) pyrimidin-4-amine compound by inhibiting *E.Coli* enzyme (biotin carboxylase) binding site which may be give an idea about the carboxylase activity and mechanism of action. The crystal structure (PDB code: 3JZI) was downloaded directly from the Protein Data Bank (www.rcsb.org). All the computations were performed using the Schrödinger suite[44]. The interaction between the protein and ligands were calculated using the Ligplot software .

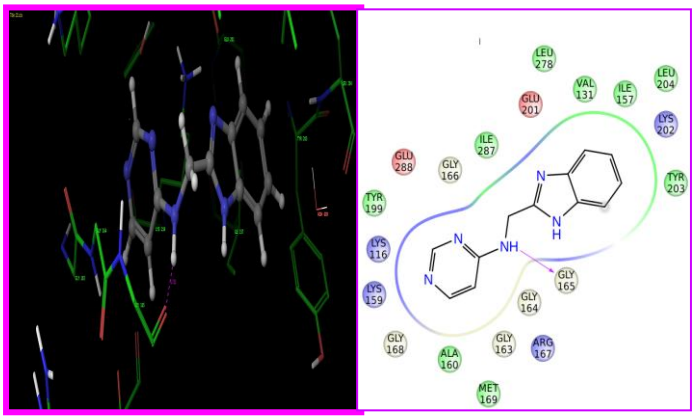


Fig -3: MOLECULAR DOCKING 3D AND 2D pictures of compound 1A

3. CONCLUSIONS

In this paper, we have performed the theoretical DFT analysis of a pharmaceutically important heterocyclic aromatic molecule, N-((1H-benzo[d]imidazol-2-yl) methyl) pyrimidin-4-amine for the first time. The optimized molecular geometry, energy gap between HOMO-LUMO and

in the ground state have been calculated by using DFT B3LYP/6-311G (d,p)basis set.. The calculated frontier molecular orbitals shows that eventual charge transfers takes place within the molecule and the molecule is chemically reactive. As a result of the docking study, it was determined that compounds substituted with amino groups had the best interactions with the microbial receptors, while compound substituted with pyrimidine and amino groups had the best interactions with the 3JZI receptor.

REFERENCES

[1] Bazgir, A., Amini, M. M. and Fazaeli, Y., 2009, "Dowex-50W-Promoted Synthesis of Oxazoline, Imidazoline and Thiazoline Derivatives". The Open Catalysis Journal, Vol. 2, pp. 163-165.

[2] Dansena, H., HJ, D., Chandrakar, K., 2015, "Pharmacological potentials of pyrimidine derivative" Asian Journal of Pharmaceutical Sciences, Vol. 8, pp.171-177.

[3] Fathalla, O. A., Zeid, I. F., Haiba, M. E., Soliman, A. M., Abd-Elmoez, S. I. and El-Serwy, W.S., 2009, "Synthesis, antibacterial and anticancer evaluation of some pyrimidine derivatives". World Journal of Chemistry, Vol. 4 pp. 127-132.

[4] Yerragunta, V., Patil, P., Anusha, V., Swamy, T., Suman, D. and Samhitha T., 2013, "Pyrimidine and Its Biological Activity". Pharma Tutor Magazine, Vol.1, pp. 41.

[5] Ansari, A., Ali, A., Asif, M., Rauf, M. A. and Owais, M. S.. Facile one-pot multicomponent synthesis and molecular docking studies of steroidal oxazole/thiazole derivatives with effective antimicrobial, antibiofilm and hemolytic properties. Steroids, 134: 22-36,2018

[6] Sharma, V., Chitranshi, Nitin. and Agarwal, A. K., 2014, "Significance and Biological Importance of Pyrimidine in the Microbial" World International Journal of Medicinal Chemistry, Vol. 14, pp. 31.

[7] Arikkatt, S. D., Baldwin, M. V., Joseph, J., Chandran, M., Bhat. A. R. and Krishnakumar, K., 2014 "pyrimidine derivatives and its biological potential". International Journal of Organic and Bioorganic Chemistry, Vol. 4, pp. 1-5.

[8] . Hill, M. D. and Movassaghi, M., 2008, "Synthesis of pyrimidine derivatives". Chemistry of European Journal, Vol. 14, pp. 6836 – 6844.

[9] C.M. Mahalakshmi and V. Chidambaranathan, "Synthesis, Spectral Characterization And Antimicrobial Studies Of Novel Benzimidazole Derivatives," *Int. J. Chem. Sci*.: 13(1), 2015, 205-212.

[10] Frisch, M.J., et al. (2009) Gaussian 09, Revision B. 01. Gaussian, Inc., Wallingford.

[11] Dennington, R.D., Keith, T.A. and Millam, J.M. (2008) GaussView 5.0.8, Gaussian

[12] Maestro, version 9.2, Schrödinger, LLC, New York, NY, 2011.