Southern Journal of Research Vol. 3(1), 2023

Computed Optical Analysis of an Antimicrobial Sulfanilamide Drug

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Abstract. We are reporting the theoretical studies on Sulfanilamide (SA) which is an important antibacterial drug. The molecular geometry was optimized at its lowest quantum mechanical energy using Density Functional Theory (DFT) at the B3LYP level with the 6-311+G (d, p) basis sets. The first principle examination of electronic characteristics, molecule electrostatic abilities, and quantum chemical identities has been studied. The UV-Vis analysis was carried out using the CAM-B3LYP/6-311+G (d,p) function and Time Dependent Density Functional Theory (TD-DFT). The natural bond orbital show that the maximum stabilization energy went up to 19.34kJ/mol, therefore was accountable for the molecule's added stability. The negative (red and yellow) zones on MEP have been linked to the possibility of electrophilic engagement, whereas the positive (blue) regions had been linked to the possibility of nucleophilic addition.

Keywords: Sulfanilamide, Density Functional Theory, UV-Vis, TD-DFT and MEP,

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1. Introduction

Sulfanilamide is an antibacterial organic Sulphur compound with a structure comparable to p-amino benzoic acid (PABA) (Sharaby, Amine and Hamed, 2017). Sulfanilamide competes with PABA for the bacterial enzyme dihydropteroate synthase, preventing PABA from being incorporated into dihydrofolic acid, the direct precursor of folic acid (Alaghaz *et al.*, 2014). This inhibits bacterial folic acid production as well as de novo purine and pyrimidine synthesis, ultimately leading in cell growth arrest and cell death (Thiede *et al.*, 2016). It is a sulfonamide with a 4-position sulfonyl functional group linked to aniline. It is an EC 4.2.1.1 (carbonic anhydrase) inhibitor, antibacterial agent, and drug allergen (Sumrra *et al.*, 2020). It is also a sulfonamide antibiotic, with a modified aniline, and a sulfonamide (Buldurun *et al.*, 2020). Following topical application or administration as a vaginal cream or suppository, a limited quantity of sulfanilamide is absorbed (through the vaginal mucosa). Like other sulfonamides, it is metabolized via acetylation and eliminated in the urine. It is also associated with antimicrobial resistance and is potentially hazardous to aquatic creatures (Hassan and Sumrra, 2021). It has also been found primarily in surface water (Johnson *et al.*, 1998). As a result, finding sensitive techniques for determining (**SA**) is crucial. Mass spectrometry, gas chromatography, fluorescence polarization immune assays, high performance liquid chromatography, and electrochemical procedures are examples of traditional detection methods. These procedures, however, are typically time-consuming, difficult, and costly (Fig 1).

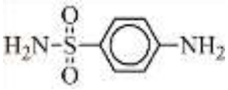

Fig 1: Chemical structure of Sulfanilamide

QSAR investigations are used to anticipate endpoints of interest in organic compounds that function as medicines (Sumrra *et al.*, 2020). The composition and structure of molecules can influence several physiological processes (Adam *et al.*, 2021). QSAR analysis employs molecular descriptors, which are numerical representations of molecular structures. In the literature, semi-empirical approaches such as AM1 and PM3 have mostly been employed to calculate the quantum mechanical molecule descriptors used in QSAR research. However, recent QSAR investigations have demonstrated that using DFT instead of AM1 or PM3 leads in a greater correlation across computed and experimental findings. By combining the semi-empirical approaches, the DFT technique is projected to produce a statistically more accurate model.

The DFT approach has seen considerable application in recent years for estimating molecular characteristics of somewhat big compounds (Komjáti *et al.*, 2016). DFT can determine molecular parameters like optimal shape and energy with the same precision as electron-correlated ab initio approaches like MP2, but it takes significantly less computing time. The selection of the basis set and technique for calculating molecular characteristics is a significant undertaking that varies depending on the kind of molecules of interest.

The current original study goal is to develop a technique for investigating the molecular characteristics of sulfonamide (SA) compounds.

2. Computational methodology

Lee, Yang, and Parr employed Becke's three-parameter hybrid (B3LYP) exchange as also as a semi linkage functional to perform the various theoretical estimates (Lee, Yang and Parr, 1988). We had employed some functions in addition to the B3LYP function to get the required findings across the density functional theory experiments (Sumrra *et al.*, 2022). Without the presence of single-crystal information, the (SA) was configured at their ground state (S°) energy levels to get insight onto their geometric forms (Hassan and Guleryuz, 2021). More exact values for Frontier Molecular Orbitals (FMO) and Natural Bond Orbitals (NBO) studies have been achieved by doing single-point studies with a rather robust basis set of 6–31+G* (d,p) (Sumrra, Zafar, *et al.*, 2021).

The Gaussian 9 program was used to do these computations (Frisch *et al.*, 2013). To perceive the optimized structure, theoretical FT-IR and UV–Vis spectra, and descriptions of geometric forms such as bond angles and related length, *Chemcraft* (V 1.6) and *Gaussview* (V 5.0.9), along with *Gaussum* (V 3.0.2), were developed. The HOMO/LUMO energy band gap was used to investigate the global reactivity characteristics (Noreen and Sumrra, 2021).

3. Results and discussion

3.1. Optimized molecular structure

The SA geometry was optimized using the DFT/B3LYP scheme 6–31+G (d, p) sets. The vibrational frequency of molecule in the gaseous state was calculated using a B3LYP approach with a 6-31+G(d, p) basis set in the FT-IR spectrum with no negative values (Hassan *et al.*, 2021). DFT-optimized bond lengths were found to be 1.40–1.41, all through the phenyl (C–C) ring, with bond angles ranging from 119.9° to 120.6°. Based on the optimized geometric morphologies of the assessed sulfonamide molecule (**SA**), the S=O and S–N bond ranges were determined to be, 1.51–1.52, and 1.69–1.71, respectively, and their dihedral angles were determined to be 105–126°, respectively (Sumrra *et al.*, 2018)(Fig 2).

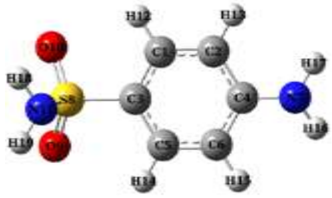

Fig 2: Optimized structure of SA at B3LYP/6-31 G+(d,p) level

Because the SA contained two nitrogen atoms in the molecular plane, their bonding was established at same length as its structure. Its stiffness influenced its consistency, leading the bond angles to deviate from 90°. The electron density contribution by active centers was also anticipated to lessen the conventional charge (Jacob *et al.*, 2020).

The vibration frequency of the title molecule in the gas phase was calculated using a B3LYP technique with a 6-31+G(d, p) basis set. In the FT-IR spectrum, the specified vibrational band values lacked any negative value. The phenyl system resembled the C-H vibrations of organic heterocyclic units and their derivatives. This comprises of several weak bands in the 3100-3000 cm-1 region, which correspond to the twisting C-H vibrations (Fig 3).

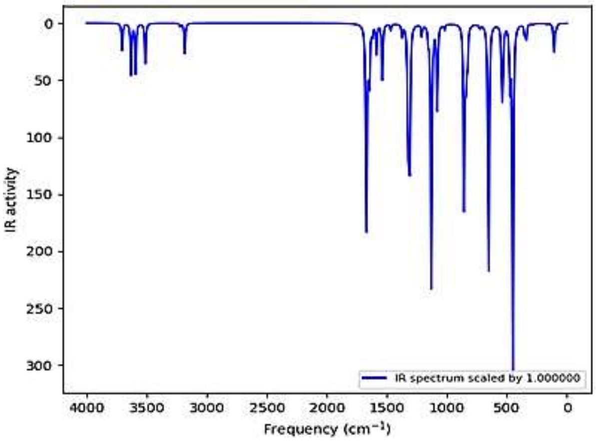

Fig 3: Computed FT-IR spectra of SA

3.2. Molecular orbitals

One of the primary goals of computational chemistry is to approximate the responsiveness of chemical entities, and much research has been done in this regard (Mahmoud *et al.*, 2019). The density functional theory (DFT) has been significant in establishing a theoretical foundation for the agreement of qualitative chemical terminology. FMOs and their quantum chemical features are being utilized to explain various sorts of processes and find the most responsive regions via conjugated arrangements. The calculations showed the charge dispersal to be mostly over HOMOs is frequently resolute by N and S containing lone pairs, as well as the phenyl moietiety. In contrast, the LUMOs vitality had the charge which was thoroughly dispersed over the phenyl moiety with an anti-bonding worth (Fig 4). The FMO mechanism, which can also be seen in the electronic transition, has confirmed intramolecular electrostatic interactions. Various quantum chemistry reactivity classifiers have been anticipated and used to study physicochemical characteristics and site specificity (Kutty *et al.*, 2020).

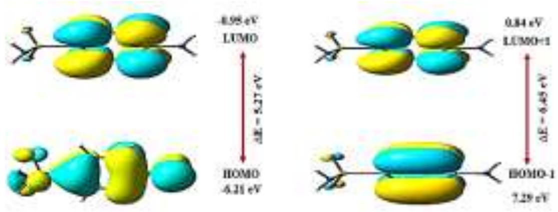

Fig 4: FMOs analysis of SA at B3LYP/6-31G+(d,p) level

The greater energy level of E_{HOMO} denotes how easy it can be to transfer an electron to an empty orbital, although the low quantity of E_{LUMO} indicates the low liability to accept electrons (Hassan *et al.*, 2020), showing that it might accept electrons easily (Table 1).

Table 1: Global reactivity parameters of SA

Parameter (eV)	Value
Ionization potential (*IP*)	6.25
Electron Affinity (*EA*)	0.94
Electronegativity (χ)	3.60
Potential (μ)	-3.60
Hardness (η)	2.66
Softness (σ)	0.19
Electrophilicity index (ω)	2.43

Chemical potential, μ, is really a propensity for electrons to leave out of a structural system; a minus chemical potential indicates that the solid is difficult to be and would not spontaneously breakdown into its constituents. SA had a value (-0.181eV) in the range that justifies their robust existence and capacity to withstand small external environment. *Hardness* measures a molecule's resistance to changes in electron distribution. The link between hardness and electronic structure is the same. The aromaticity of a range of non-substituted aromatics can be connected to general toughness (both absolute and relative), therefore "molecules should be as robust as feasible." Substances with such low E_{HOMO} values often have vulnerable exciton capacities, implying that (SA) had a superior electron-donating ability. As a result, they can contribute to their improved antioxidant as well as biological features. Antioxidant chemicals donate an electron to a free radical, causing it to form a radical charge.

3.4. Natural bond orbitals

This approach is a good tool for investigating hyper-conjugative involvement and electron transference by lone pairs present any chemical implications. The DFT/B3LYP/6-31G(d, p) method was used to assess the natural bond orbitals (Sajjad H Sumrra *et al.*, 2021), and a detailed description of the information acquired from the second order petulances analysis for this theory was estimated (Glendening, Landis and Weinhold, 2012). This is a powerful tool for analyzing charge transitions or conjugation in diverse parts of the molecule structure with higher accuracy. The quantity of stabilizing energy is related to the frequency of the hyper conjugative interaction between electron transfers.

Similarly, stronger interactions involving lone pairs (LP) were observed in another aromatic ring that exhibits substantial electron delocalization across the molecule. The same sort of binding energy, equivalent to molecular resonance, would be an electron transition with enormous stabilization energies (Sumrra, *et al.*, 2021). Significantly, the molecule's stabilization energy was around 81.03 kJ/mol, demonstrating the stability of the electron molecular system (Table 2).

Table 2: NBO analysis of title molecule SA

Donor (i)	**Type**	**Acceptor (j)**	**Type**	**E(2) [kcal /mol]**	**E(J) E(i) (a.u)**	**F (I,j) (a.u)**
C1-C2	π	1-C3	π^*	3.13	1.28	0.056
C1-C3	π	C1-C2	π^*	2.39	1.31	0.050
C1-C3	π	C1-C3	π^*	0.54	0.28	0.011
C1-H12	π	C1-C2	π^*	0.91	1.10	0.028
C2-C4	π	C1-C2	π^*	2.47	1.31	0.051
5-C6	π	C1-C3	π^*	15.04	0.28	0.059
S8-O9	π	C1-C3	π^*	1.28	1.56	0.040
S8-O10	π	C3-C5	π^*	1.39	1.56	0.042
S8-N11	π	2C1-C3	π^*	0.60	0.82	0.022
O9	LP	C3-S8	π^*	1.01	0.97	0.029
O10	LP	C3-S8	π^*	0.97	0.97	0.029
N11	LP	C3-S8	π^*	3.80	0.58	0.043
C1-C3	π	C5-C6	π^*	293.35	0.01	0.080
C3-S8	π	C1-C2	π^*	1.05	0.38	0.056
S8-O9	π	C1-C3	π^*	0.78	0.25	0.042
S8-O10	π	C1-C3	π^*	0.70	0.25	0.040
S8-N11	π	C3-S8	π^*	12.98	0.02	0.034

3.5. UV-Vis analysis

The UV-Visible (UV-Vis) interpretation was estimated using optimized designs, leveraging the CAM-B3LYP attribute as part of a TD-DFT simulation, at the same 6-31G(d,p)++ assumption.

The hypothetical UV-Vis spectra show the absorption spectrum, excitation energies, and oscillator strengths, with H→L (55%) as a major transformation (Table 3).

Table 3: Computed electronic analysis of SA				
No.	E (cm^{-1})	λ (nm)	O.S	Major contribs
1	37787	264	0.02	H→L+1 (50%)
2	40234	248	0.13	H→L (55%)
3	41072	243	0.19	H→L+2 (47%)

The calculated wavelength (max) was seen in the 264, 248, and 243 nm regions.

The first band was orientated to π* and n* transitions, with minor involvement from * and dd transitions (Fig 5). The second and third bands were attributed to π→π* shifts, separately.

3.6. Electron density

The electrostatic molecular potential (MEP) is related to charge density and provides a very useful indication for electron donating target sites and nucleophilic engagements with hydrogen bonds (Sumrra *et al.*, 2021). The surfaces have also been used to characterize reactive behavior, with negative domains referred to as potential electrophilic spots and positive sectors referred to as nucleophilic centers (Fig 6).

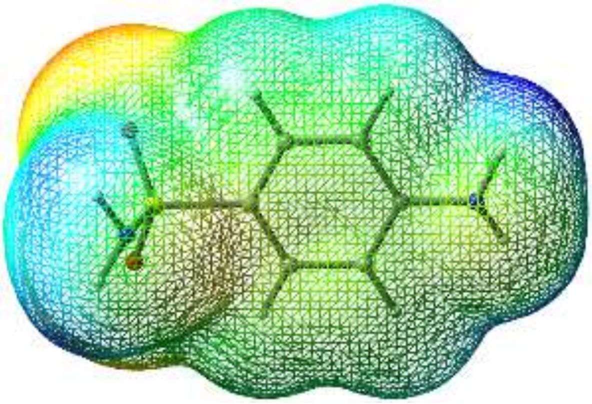

Fig 6: MEP plot of (SA)

During the current investigation, the electron donating sites had negative (red) regions and the electrophilic sites had positive (blue) portions over through the molecule (Kusmariya *et al.*, 2016). The negative charge density positions in (**SA**) were found on the title portion of sulfonamide Skelton.

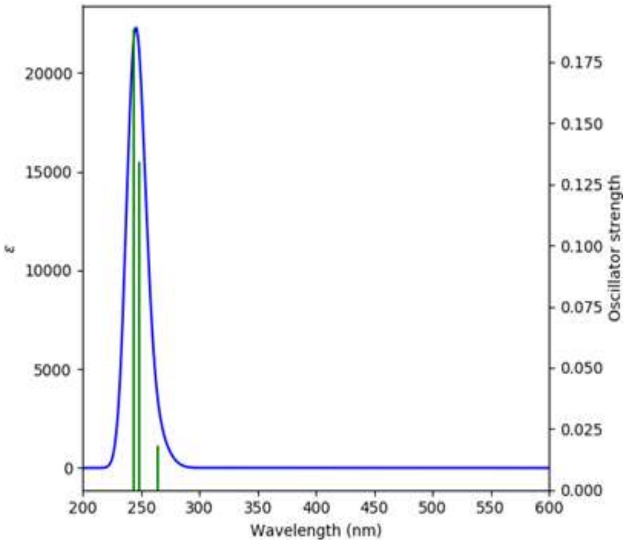

Fig 5: Computed UV-Visible spectra of (SA)

Positive charge was found in the confined vicinity of hydrogen atoms.

The current study discovered that nitrogen atoms had the most reactive impact. According to FMOs, this molecule has lower hardness and higher softness values. These results suggest that the chemical may be bioactive.

4. Conclusions

The current report reveals that the optimized bond lengths and bond angles agree well with the published X-ray and current DFT results.

The molecular chemical reactivity identifiers, electrostatic potentials, frontier molecular orbital analysis, one electrochemical response process, energy gap with electron transfer competence of this title molecule (**SA**) suggested that it is an efficient biological active drug.

The maximal stabilization potential is two times lower than the published work.

The FT-IR frequencies have increased as compared to stated values in all techniques, however there is considerable agreement across the evaluated methods.

Acknowledgments

Authors are thankful to higher education commission of Pakistan for assisting their research by financial means (NRPU 7800).

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