

Original Research Article

Comparative DFT analysis of sulphadiazine and sulphathiazole: A quantum chemical study of sulphonamide derivatives

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Abstract

Purpose: To model the molecular structure and electronic properties of two sulphonamide derivatives, sulphadiazine (SDZ) and sulphathiazole (STZ), using quantum mechanics based on Density Function Theory (DFT) in order to provide theoretical evidence of differences in reactivity and biological activity of the two compounds.

Methods: Quantum mechanics calculations based on DFT were applied to SDZ and STZ. Charge distribution and electron density were calculated using the Kohn-Sham equations. Bond lengths and angles were calculated, and the energy gap was determined by calculating the energy of the two orbitals: the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO). The thermodynamic properties of both drugs, as well as their infrared vibrational frequencies, were also predicted.

Results: The DFT study showed the concentration of electron density around the sulphonyl oxygen of SDZ and STZ, as well as the nitrogen atoms of the pyrimidine ring of SDZ. However, STZ showed higher polarization due to the sulphur- and nitrogen-containing thiazole ring. STZ showed a lower energy gap, indicating higher reactivity and better biological activity than SDZ. STZ also showed lower thermodynamic values than SDZ. The key infrared vibrations showed a high level of similarity for both compounds, although SDZ displayed slightly higher values than STZ.

Conclusion: The findings from this study have provided theoretical evidence in support of the observed differences in the reactivity and effectiveness of SDZ and STZ. The data obtained have laid a strong theoretical foundation for the design of safer and more effective drugs.

Keywords: Density Function Theory, Quantum Mechanics, Sulphonamide derivatives, Sulphadiazine, Sulphathiazole

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INTRODUCTION

Sulphonamides are considered the first synthetic antimicrobial agents, developed before the widespread use of penicillin. Sulphonamides have demonstrated powerful efficacy against a wide range of bacteria, inhibiting their growth and reproduction [1-4]. These compounds consist of

a benzene ring linked to an amine group and a sulphonyl group ($-\text{SO}_2\text{NH}_2$) [5]. Sulphadiazine (SDZ) and sulphathiazole (STZ) are two antibacterial sulphonamides with interesting chemical properties and therapeutic efficacy [6].

Sulphadiazine (4-amino-N-pyrimidin-2-yl-benzenesulphonamide) consists of a pyrimidine

ring linked to a 4-aminobenzene sulphonamide group. It is poorly soluble in water and is chemically stable, making it an effective and safe antibacterial agent [7-9]. It is mostly used as silver sulphadiazine in the treatment of burns [10]. Due to its poor solubility in water, lipid-based formulations are used to improve its solubility. Sulphathiazole (4-amino-N-thiazol-2-yl-benzene sulphonamide), on the other hand, consists of a thiazole ring linked to a 4-aminobenzene sulphonamide. Studies have shown major differences between SDZ and STZ in terms of their therapeutic efficacy; the compound STZ is more toxic and tends to crystallize in the kidneys more readily due to its lower solubility compared to SDZ. For this reason, STZ is limited to topical and veterinary applications, whereas SDZ can be used systemically in the clinic [11,12]. Density function theory (DFT) is a prominent quantum mechanical modelling method used to study the electronic structure of many-body systems [13]. It has been used to study large molecules that are difficult to characterize experimentally. This theory is based on the principle that all properties of the ground state are determined by electron density, which depends on three (x, y, z) coordinates regardless of the number of electrons [14,15]. The theory also relies on the Hohenberg-Kohn principle, which states that the external potential is a function of the electron density; that is, electron density determines everything [16].

In the present study, DFT-based computational quantum mechanics was used to study the electronic structure of SDZ and STZ in order to better understand the chemical basis of their antibacterial action, identify the active sites of the molecules and understand the effect of ring substitution on biological activity. This information will lay the foundation for the design and development of safer, less toxic, and more effective therapeutic alternatives.

EXPERIMENTAL

The study applied quantum chemical calculations using density function theory (DFT) at B3LYP/6-31G level and the Gaussian program was used to determine the electronic structure of two sulphonamides: Sulphadiazine (SDZ) and sulphathiazole (STZ), and the data obtained were linked to the biological activity of the two sulphonamides. The active sites in the two compounds were calculated by determining the charges and electron density of the atoms to identify the most active and nucleophilic sites, which represent the effective sites for protein and enzyme interaction to cause bacterial growth inhibition. The software used for the study

include ORCA, GAMESS, Psi4, ChemCraft, Molden, Avogadro 2, and Gabedit, were used for the study.

Determination of charges and electron density

The charges and electron density of the two sulphonamides, SDZ and STZ, were determined theoretically using quantum chemical calculations based on DFT. The exact ground-state electron density and energy were calculated using the Kohn-Sham equations [17].

$$\left[-\frac{\hbar^2}{2m} \nabla^2 + V_{eff}(\mathbf{r}) \right] \psi_i(\mathbf{r}) = \epsilon_i \psi_i(\mathbf{r})$$

$$V_{eff} = V_{ext} + V_H + V_{xc}$$

$$\rho(\mathbf{r}) = \sum_i^N |\varphi_i(\mathbf{r})|^2.$$

Where (∇^2): Laplacian operator, ($\hbar$): Reduced Planck constant, (m): mass of the electron, V_{eff} : Effective potential acting on the electrons, V_{ext} : External potential, V_H : Hartree potential

V_{xc} : Exchange-correlation potential, ψ_i : Kohn-Sham Orbitals, $\rho(r)$: electron density, r : position vector, ϵ_i : eigenvalue orbital energy.

For further simplification, approximations, local density approximation (LDA) and generalized gradient approximation (GGA), of the energies resulting from the exchange and correlation between electrons were used.

The positions and types of nuclei were input, and an initial estimate of the electrons in the system was made, and the Kohn-Sham equations were solved to calculate the electron density [18-21].

Determination of bond lengths and angles

DFT-based quantum mechanics was used to calculate the bond lengths and angles of the geometric shape of the two sulphonamides (SDZ and STZ) to identify the most stable geometry. The three-dimensional structures of the two compounds were modeled using Avogadro 2, Molden, and ChemCraft software.

Determination of energy gap, thermodynamic and vibrational properties

The energy gap between the two orbitals (ELUMO - EHOMO), the highest occupied

molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), was determined, which is an important indicator of biological activity and the ease with which the drug interacts with bacterial proteins. Under standard conditions ($T = 298\text{ K}$ and $P = 1\text{ atm}$), the thermodynamic values [Gibbs free energy (G°), enthalpy (H°), entropy (S°), internal energy (E°), Helmholtz free energy (A°), and heat capacity at constant volume (CV)], as well as important infrared vibrational frequencies of SDZ and STZ, were determined using DFT-based quantum chemical calculations.

RESULTS

Charge and electron density

The results obtained from the DFT study showed that the electron density of sulphadiazine was concentrated around the nitrogen atoms of the pyrimidine ring and the oxygen atoms of the sulphonyl group, while the carbon atoms of the pyrimidine ring showed a positive charge. Sulphathiazole, on the other hand, showed a higher polarization due to the presence of a thiazole ring, with the carbon atoms being less

electronegative and the oxygen atoms of the sulphonyl group more electron-dense (Tables 1 and 2).

Bond lengths and bond angle

As shown in Table 3, the sulphur-oxygen bond ($S=O$) in the two sulphonamides (SDZ and STZ) shows a high degree of similarity in bond length, ranging from $1.628\text{ \AA}$ to $1.643\text{ \AA}$, although it is somewhat shorter in the case of SDZ. The C-N bond length of the pyrimidine ring in SDZ was from 1.354 to $1.357\text{ \AA}$, while the C-N bond of the thiazole ring in STZ was shorter ($1.348\text{ \AA}$). The $O=S=O$ bond angle in both compounds ranged from 119° to 120° , but was slightly wider in SDZ. The bond angle for C-N-S in STZ was 121° , and was slightly higher (126°) in SDZ. The three-dimensional structures of the two compounds are shown in Figure 1.

Energy gap

The energy gap ($E_{\text{LUMO}} - E_{\text{HOMO}}$) of the two sulphonamide molecules is presented in Table 4. Sulphathiazole has a lower energy gap than sulphadiazine.

Table 1: Charge (e) and electron density (electrons) of sulphadiazine

Atom	Charge	Electronic Density	Atom	Charge	Electronic Density
O1	-0.6003	6.6003	C16	-0.0975	4.0975
S2	1.3317	4.6683	O17	-0.5556	6.5556
N3	-0.0794	5.0794	H18	0.3700	0.6300
C4	0.4977	3.5023	H19	0.1611	0.8389
N5	-0.3611	5.3611	H20	0.1480	0.8520
C6	0.0353	3.9647	H21	0.1567	0.8433
C7	-0.1316	4.1316	H22	0.1973	0.8027
C8	0.0414	3.9586	H23	0.1297	0.8703
N9	-0.3699	5.3699	H24	0.3240	0.6760
C10	-0.3089	4.3089	H25	0.3240	0.6760
C11	-0.0669	4.0669	H26	0.1320	0.8680
C12	-0.1500	4.1500	H27	0.1958	0.8042
C13	0.3410	3.6590			
N14	-0.8675	5.8675			
C15	-0.8075	4.8075			

Table 2: Charge (e) and electron density (electrons) of sulphathiazole

Atom	Charge	Electronic Density	Atom	Charge	Electronic density
N1	-0.825	5.825	O14	-0.5461	6.5461
C2	0.3397	3.6603	C15	-0.0974	4.0974
C3	-0.1398	4.1398	C16	-0.3270	4.3270
C4	-0.0921	4.0921	H17	0.3270	0.6730
C5	-0.3722	4.3722	H18	0.3271	0.6729
S6	1.3506	4.6440	H19	0.1374	0.8626
N7	-0.8144	5.8144	H20	0.1979	0.8021
C8	0.1785	3.8215	H21	0.3585	0.6415
N9	-0.3582	5.3582	H22	0.1663	0.8337
C10	0.0986	3.9014	H23	0.1725	0.8275
C11	-0.4514	4.4514	H24	0.1984	0.8016
S12	0.3679	5.6321	H25	0.1371	0.8629
O13	-0.5414	6.5414			

Table 3: Bond lengths and bond angles of sulphadiazine and sulphathiazole

Bond length (Å)		Bond angle (°)		Bond length (Å)		Sulphathiazole Bond angle (°)	
R (1-2)	1.637	A (5-4-9)	125.9	R (1-2)	1.375	A (4-3-19)	119.8
R (2-10)	1.849	A (4-5-6)	116.3	R (1-17)	1.006	A (3-4-5)	118.6
R (2-17)	1.628	A (4-9-8)	116.3	R (1-18)	1.006	A (3-4-20)	121.1
R (3-4)	1.375	A (5-6-7)	122.3	R (2-3)	1.417	A (5-4-20)	120.2
R (3-18)	1.015	A (5-6-19)	116	R (2-16)	1.417	A (4-5-6)	118.5
R (4-5)	1.357	A (7-6-19)	121.7	R (3-4)	1.391	A (4-5-15)	122.5
R (4-9)	1.354	A (6-7-8)	116.7	R (3-19)	1.085	A (6-5-15)	118.7
R (5-6)	1.348	A (6-7-20)	121.6	R (4-5)	1.395	A (5-6-13)	109.0
R (6-7)	1.399	A (8-7-20)	121.6	R (4-20)	1.084	A (5-6-14)	108.5
R (6-19)	1.085	A (7-8-9)	122.4	R (5-6)	1.856	A (5-15-16)	118.6
R (7-8)	1.398	A (7-8-21)	121.6	R (5-15)	1.394	A (5-15-24)	120.1
R (7-20)	1.082	A (9-8-21)	116.1	R (6-13)	1.629	A (13-6-14)	122.0
R (8-9)	1.348	A (11-10-16)	122.8	R (6-14)	1.631	A (8-7-21)	122.9
R (8-21)	1.085	A (10-11-12)	118.4	R (7-8)	1.368	A (7-8-9)	125.7
R (10-11)	1.393	A (10-11-22)	120.1	R (7-21)	1.011	A (7-8-12)	120.0
R (10-16)	1.394	A (10-16-15)	118.5	R (8-9)	1.298	A (9-8-12)	114.3
R (11-12)	1.391	A (10-16-27)	120.2	R (8-12)	1.859	A (8-9-10)	112.3
R (11-22)	1.082	A (12-11-22)	121.5	R (9-10)	1.397	A (8-12-11)	85.9
R (12-13)	1.416	A (11-12-13)	120.7	R (10-11)	1.358	A (9-10-11)	116.9
R (12-23)	1.086	A (11-12-23)	119.7	R (10-22)	1.080	A (9-10-22)	118.2
R (13-14)	1.376	A (13-12-23)	119.6	R (11-12)	1.818	A (11-10-22)	124.9
R (13-15)	1.416	A (12-13-14)	120.5	R (11-23)	1.078	A (10-11-12)	110.6
R (14-24)	1.005	A (12-13-15)	119.0	R (15-16)	1.391	A (10-11-23)	129.8
R (14-25)	1.005	A (14-13-15)	120.5	R (15-24)	1.084	A (12-11-23)	119.6
R (15-16)	1.391	A (13-14-24)	121.1	R (16-25)	1.085	A (16-15-24)	121.2
R (15-26)	1.085	A (13-14-25)	121.1	A (2-1-17)	121.2	A (15-16-25)	119.8
R (16-27)	1.084	A (13-15-16)	120.5	A (2-1-18)	121.1	A (8-7-6)	121.0
A (1-2-10)	109.0	A (13-15-26)	119.7	A (1-2-3)	120.5		
A (1-2-17)	120.5	A (24-14-25)	117.8	A (1-2-16)	120.5		
A (10-2-17)	109.8	A (16-15-26)	119.8	A (17-1-18)	117.7		
A (2-10-11)	119.4	A (15-16-27)	121.3	A (3-2-16)	119.0		
A (2-10-16)	117.8	A (4-3-2)	126.0	A (2-3-4)	120.6		
A (4-3-18)	119.3			A (2-3-19)	119.6		
A (3-4-5)	116.0			A (2-16-15)	120.6		
A (3-4-9)	118.0			A (2-16-25)	119.6		

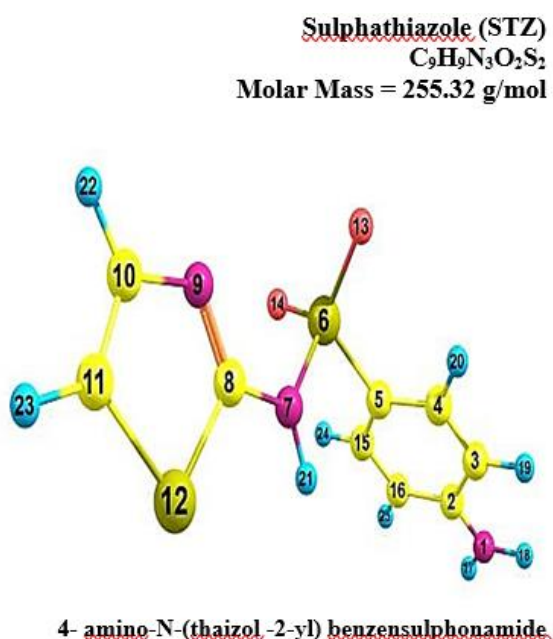
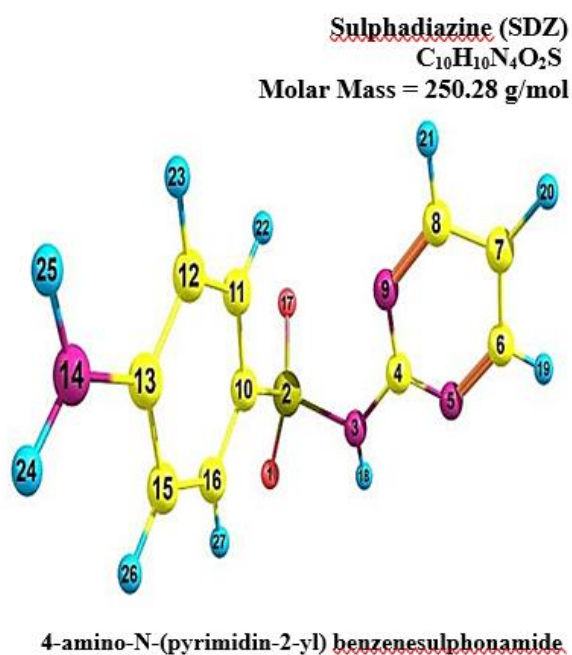
**Figure 1:** Three-dimensional structure of sulphadiazine and sulphathiazole

Table 4: Energy gap of sulphadiazine and sulphathiazole

Compound	E° HOMO (eV)	E° LUMO (eV)	Energy gap (LUMO – HOMO; eV)	IP (eV)
Sulphadiazine	-6.1353	-1.4359	4.6994	6.1353
Sulphathiazole	-5.9925	-1.7951	4.1974	5.9925

Table 5: Thermodynamic functions of sulphadiazine and sulphathiazole

Compound	S° kJ/mol.K	E°(thermal) kJ/mol	H° kJ/mol	G° kJ/mol	A° kJ/mol	Cv kJ/mol.K
Sulphadiazine	0.243	565.873	568.35	495.936	493.459	0.243
Sulphathiazole	0.553	507.602	510.079	345.285	342.808	0.243

G° = Gibbs free energy, H° = Enthalpy, S° = Entropy, E° = Internal energy, A° = Helmholtz free energy, Cv = Heat capacity at constant volume

Table 6: Comparison of the most important infrared vibrations for sulphadiazine and sulphathiazole

Sulphadiazine	Frequency cm ⁻¹ (DFT)	Frequency cm ⁻¹ Exp	Sulphathiazole	Frequency cm ⁻¹ (DFT)	Frequency cm ⁻¹ Exp
NH ₂ (Asy, Sy)	3638-3764	3352-3425	NH ₂ (Asy, Sy)	3319-3364	3280-3320
SO ₂ (Asy)	1358-1370	1320- 1330	SO ₂ (Asy)	1327-1364	1315-1320
SO ₂ (Sy)	1133-1180	1150-1160	SO ₂ (Sy)	1133-1180	1135-1145
-NH (Ring)	1610-1632	1580-1588	-NH (Ring)	1550-1555	1530-1535
-NS (Stretch)	966-997	925-940	-NS (Stretch)	964-996	910-925

Sy = Symmetric, Asy = Asymmetric

Thermodynamic functions

Sulphathiazole showed lower thermodynamic values than sulphadiazine, except for the entropy (S°), where sulphathiazole showed a higher value (Table 5).

Infrared Vibrational Frequencies

Table 6 compares the most important infrared vibrational frequencies for both sulphadiazine and sulphathiazole. The results showed that the theoretical values (calculated using DFT) were generally higher than the experimental values for both sulphonamides. It was observed that the key functional groups vibrate at slightly higher frequencies in sulphadiazine than in sulphathiazole, both theoretically and experimentally. All vibrational frequencies and their respective intensities for sulphadiazine and sulphathiazole are presented in Table 7 and Table 8, respectively, while Figures 2 and 3 show the infrared spectra for both compounds.

DISCUSSION

The present study applied quantum mechanics calculations based on density functional theory (DFT) to determine the electronic structure of two sulphonamide derivatives: sulphadiazine (SDZ) and sulphathiazole (STZ). DFT is based on the principle that all properties of the ground state are determined by electron density [14,15]. Electron density not only represents probability density but also allows the determination of the

electronic structure, bonds, and physical and chemical properties of a compound [22], thus identifying the active sites for binding to biological receptors [23,24].

The results obtained from this study showed that the electron density in SDZ was concentrated around the nitrogen atoms of the pyrimidine ring and the oxygen atoms of the sulphonyl group, with the carbon atoms of the pyrimidine ring showing a positive charge due to the electron-pull effect of the nitrogen atom attached to the ring. Sulphathiazole contains a thiazole ring with sulphur and nitrogen, leading to a higher polarization. Sulphur has an electron pair that participates in the ring resonance, making the carbon atoms less electronegative. The study also used DFT to calculate bond lengths and bond angles of the geometric shape of the two sulphonamides (SDZ and STZ). The results showed that the S=O bond in the two compounds was similar in length, with SDZ's bond being slightly shorter. This difference can be attributed to differences in electron-withdrawing properties between the thiazole ring (five-membered heterocyclic) in STZ and the pyrimidine ring (six-membered heterocyclic) in SDZ. The equal length of the C-N bond in the pyrimidine ring of SDZ can be attributed to resonance and ring symmetry, while the difference observed in STZ is due to ring asymmetry.

Table 7: Infrared vibration frequencies and intensities of sulphadiazine

Number	Frequency (cm ⁻¹)	Intensity	Number	Frequency (cm ⁻¹)	Intensity
1	21.7175	1.2077	39	997.1123	0.4534
2	44.2604	0.5501	40	1000.8760	19.1315
3	61.6092	0.8042	41	1006.9570	0.1591
4	75.8630	0.3014	42	1015.7950	0.3393
5	103.6120	0.9617	43	1030.6540	8.3587
6	141.5620	0.7046	44	1068.2640	1.0566
7	168.6130	4.0024	45	1087.9760	53.7093
8	197.9170	2.3301	46	1100.4040	0.5574
9	224.7350	8.6905	47	1133.1570	3.2512
10	247.6479	7.5462	48	1180.4020	8.7259
11	274.1140	1.2696	49	1232.2620	11.5272
12	309.1435	24.8489	50	1235.6160	44.6192
13	334.0077	5.9284	51	1276.7890	21.8289
14	411.7483	1.3607	52	1358.0890	10.1812
15	420.0344	7.1369	53	1368.8160	33.8650
16	423.9057	4.8511	54	1370.7850	72.9170
17	428.1301	15.7452	55	1399.7960	0.74710
18	432.5124	0.2194	56	1411.6450	3.9702
19	447.2983	184.3926	57	1481.6470	17.7246
20	465.1914	402.9877	58	1488.2290	4.5492
21	529.2245	9.3921	59	1502.7710	722.2091
22	538.3233	28.8717	60	1554.6580	66.4916
23	574.7259	60.6088	61	1586.6180	68.1109
24	632.2095	6.7160	62	1610.7670	244.7050
25	652.6695	15.7478	63	1632.8280	11.7476
26	657.1886	25.1907	64	1655.6590	201.6403
27	659.2721	5.1553	65	1714.0680	188.4760
28	726.6983	2.0102	66	3203.5490	14.8107
29	761.5997	202.7813	67	3205.1180	16.0044
30	818.6106	40.4465	68	3212.1540	11.8260
31	821.2124	32.5596	69	3214.8970	23.0117
32	834.6815	2.96900	70	3239.7890	5.6140
33	837.7917	50.3509	71	3253.0220	12.4861
34	845.7679	53.3579	72	3260.4190	4.2661
35	856.2084	92.5869	73	3602.0230	96.3688
36	909.2424	51.4842	74	3638.8860	91.0669
37	966.0333	48.2413	75	3764.2710	25.1985
38	982.0314	1.3734			

The bond angle of the sulphonyl (O=S=O) group in both compounds indicates a distorted tetrahedral sulphonyl group (bond angle = 120°), although slightly wider in the case of SDZ to reduce the steric repulsion between the oxygen atoms and the adjacent rings. The C-N-S bond angle is affected by the type of ring attached. In STZ, it is smaller (121°) because the sulphur atom experiences less structural distortion, whereas in SDZ, the angle increases to 126° due to heightened angular ring strain and steric hindrance between the pyrimidine and benzene rings. Bond angles play a crucial role in determining the spatial orientation of drugs and their binding to target receptors [25].

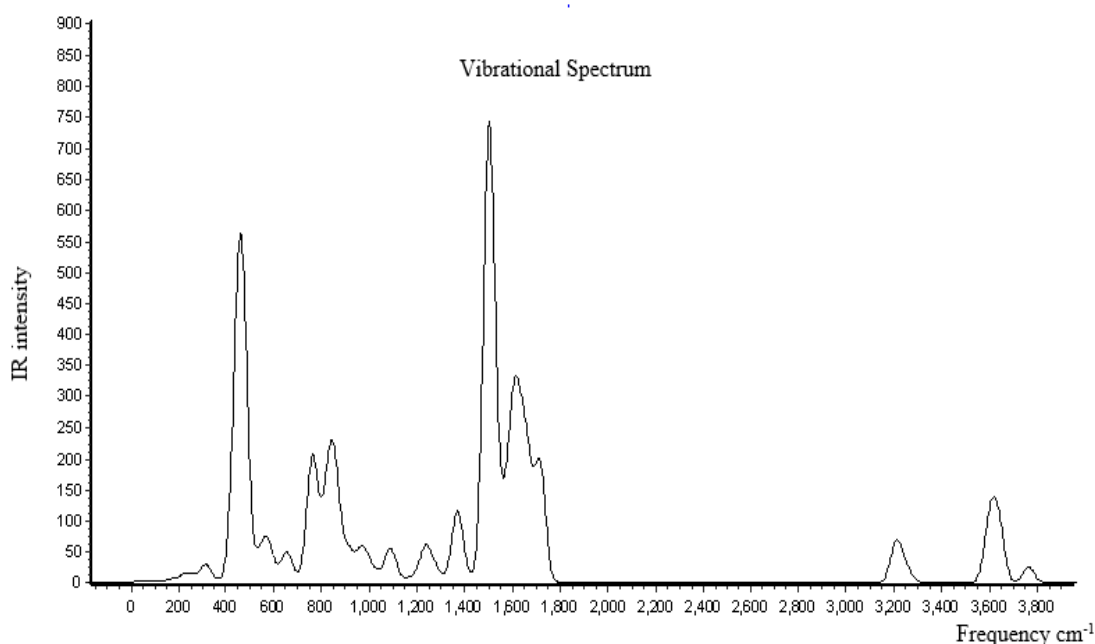
In computational chemistry, the energy gap ($E_{\text{LUMO}} - E_{\text{HOMO}}$) is a crucial indicator of drug stability, efficacy, and chemical reactivity. The smaller the energy gap, the easier it is to lose electrons, resulting in lower stability and higher activity [25]. Sulphathiazole has a lower energy

gap than sulphadiazine; hence, it readily reacts with bacterial target enzymes. This is due to its thiazole ring, which contains Sulphur and nitrogen, increasing sulphathiazole's polarization and making it highly reactive. This high reactivity may explain its instability in the human body, leading to the formation of toxic intermediates, kidney crystals, or skin damage. Therefore, it is not recommended for human use, while sulphadiazine is considered safer for clinical use [11,12].

The study showed lower thermodynamic values (G° , H° , E° , and A°) for STZ compared to SDZ. This indicates higher chemical and thermodynamic stability and difficulty in spontaneous decomposition, meaning that the compound is stable under standard conditions. This may be due to the thiazole ring and electron density distribution in STZ causing extra stability in STZ over the pyrimidine ring in SDZ.

Table 8: Infrared vibration frequencies and intensities of sulphathiazole

Number	Frequency (cm ⁻¹)	Intensity	Number	Frequency (cm ⁻¹)	Intensity
1	14.4861	0.8506	36	868.1659	23.3752
2	22.5966	0.4270	37	922.5251	1.4074
3	39.2486	1.5724	38	964.9921	60.9531
4	43.1941	0.3501	39	996.5898	1.0164
5	103.2953	1.1588	40	1001.2010	0.3729
6	139.0057	0.3526	41	1032.2630	4.8596
7	154.9871	1.1480	42	1060.09500	112.2669
8	196.8316	65.3557	43	1068.0780	1.5080
9	216.3990	12.6801	44	1092.1790	65.7827
10	222.8693	29.3692	45	1128.2730	64.5092
11	239.1638	18.6268	46	1179.4900	9.6504
12	281.0824	3.6963	47	1233.4520	59.5125
13	311.5366	26.5563	48	1260.3000	16.9774
14	352.4308	8.1686	49	1327.6510	5.4762
15	403.8890	12.0312	50	1364.9610	7.7393
16	416.0250	0.0468	51	1371.5790	176.6026
17	423.4377	0.6637	52	1388.8910	154.2985
18	434.7412	1.7844	53	1400.6310	1.16520
19	441.0282	131.4247	54	1487.7760	6.2146
20	469.0126	434.7034	55	1550.2100	36.6287
21	528.0930	5.9148	56	1555.5350	84.3038
22	529.5475	3.4110	57	1622.3820	563.8857
23	552.4375	4.0536	58	1630.1700	7.3513
24	609.5361	28.8136	59	1656.6530	167.1346
25	630.3341	2.5893	60	1714.8290	188.2641
26	649.6898	153.2358	61	3205.1110	13.0729
27	659.6279	0.3624	62	3206.0750	13.3179
28	684.4054	35.2926	63	3234.3250	1.5487
29	717.6890	34.9539	64	3235.5410	9.6952
30	730.8232	14.1428	65	3273.0060	7.5437
31	774.1028	30.4892	66	3319.5690	1.8731
32	830.8016	60.7234	67	3637.0450	105.1861
33	844.7852	1.2530	68	3642.1210	54.5648
34	847.6055	48.9647	69	3761.8340	27.3523
35	862.2920	70.9028			

**Figure 2:** Infrared spectrum of sulphadiazine

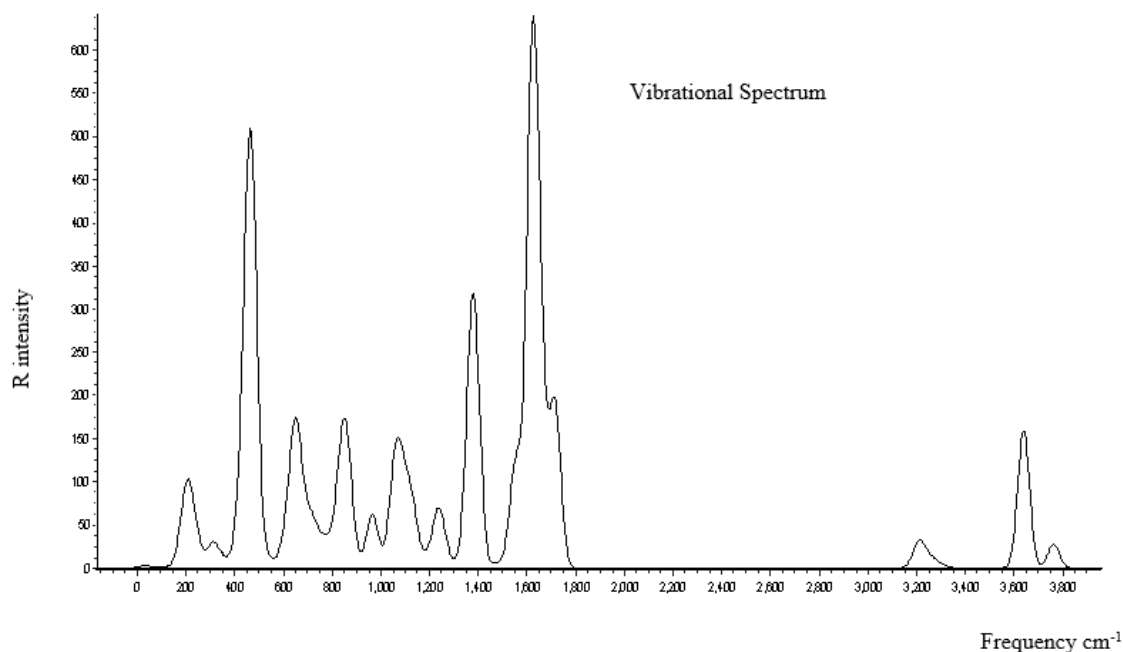


Figure 3: Infrared spectrum of sulphathiazole

Simultaneously, the study showed low thermodynamic values for STZ in the isolated state. This means that the system has reached a state of low internal energy or high entropy stability. Thus, STZ combines the qualities of high reactivity and effectiveness.

The infrared analysis may facilitate the identification of the structural changes of these compounds when they bind to bacterial receptors. The higher theoretical values for the vibrational frequencies could be due to the neglect of hydrogen bonds. Furthermore, the differences in the theoretical values between the two sulphonamides could be due to the type of heterocyclic ring attached to the 4-aminobenzenesulphonamide moiety. Sulphadiazine has a pyrimidine ring, while sulphathiazole has a thiazole ring, causing a difference in electron density, which explains the variation in the strength of the two compounds in targeting bacterial cells as well as their rate of absorption.

CONCLUSION

The present study used a quantum mechanical model based on density function theory to study the electronic structure of two sulphonamide derivatives: sulphadiazine and sulphathiazole. The findings provided a chemical explanation for the observed differences in the efficacy and stability of the two drugs. Sulphathiazole features a smaller energy gap than sulphadiazine due to its sulphur- and nitrogen-containing thiazole ring,

which enhances its electronic reactivity and binding affinity toward bacterial enzymes. Despite the better biological activity of sulphathiazole, its high reactivity increases the risk of formation of toxic metabolites or renal crystals. This limits the clinical use of sulphathiazole, while the safer sulphadiazine is preferred. This study has highlighted the pivotal role of theoretical chemistry in modern drug discovery. It facilitates the design of safer, greener, and more effective drugs for future healthcare needs.

DECLARATIONS

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None.

Conflict of Interest

No conflict of interest is associated with this study.

Contribution of Author

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. N. A. Jasim and T. G. Mjeed were equally responsible for the design and execution of the study, and both authors read and approved the final manuscript for publication.

Ethical approval

Not applicable

Availability of data and materials

All data used during the current study are available from the corresponding author.

Use of Artificial intelligence/Large language models

The authors confirm that AI-based tools were used solely for language editing and manuscript polishing purposes (e.g., grammar, phrasing, and clarity). No AI tools were used to generate content, interpret data, or influence study design, results, or conclusions. All intellectual contributions, study analyses, and interpretations reported in the manuscript are the original work of the authors.

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