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SYNTHESIS, DFT STUDY AND ANTIMICROBIAL ACTIVITY OF SCHIFF BASES DERIVED FROM BENZALDEHYDES AND AMINO ACIDS

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ABSTRACT

Three Schiff bases were synthesized by reaction of different benzaldehydes with amino acids. The characterization of these compounds was performed using IR spectroscopy, molecular calculations, thin-layer chromatography, determining the melting point and other physical characteristics. IR spectra for imino groups (C=N), which are characteristic of Schiff bases, show stretching frequency from 1629 to 1654 cm^{-1}. The obtained spectral results were confirmed by molecular calculations using the density functional theory (DFT) and were performed before experimental work. The DFT global chemical reactivity descriptors were calculated and used to predict their relative stability and reactivity of synthesized compounds. The antimicrobial assay of all compounds were screened for Gram-positive bacteria species: *Staphylococcus aureus* ATCC 25923; *Methicillin-resistant Staphylococcus aureus*: MRSA ATCC 33591; *Bacillus subtilis* ATCC 6633; and *Enterococcus faecalis* ATCC 29212, Gram-negative: *Salmonella enterica* ATCC 31194; *Pseudomonas aeruginosa* ATCC 9027; *Escherichia coli* ATCC 25922; Extended Spectrum Beta-Lactamase producing E. *coli*: ESBL E. *coli* ATCC 35218, and one yeast *Candida albicans* ATCC 1023.The highest values of inhibition zones were recorded for compound1, followed by the compound 3, while compound 2 performed inhibitory effect just in case of MRSA. DFT calculations show that antimicrobial activity has a good correlation with chemical reactivity descriptors obtained Schiff bases.

Keywords: Schiff bases; L-cysteine; L-asparagine; DFT; FT-IR; antimicrobial activity.

INTRODUCTION

Schiff compounds have received much attention in the wide variety of fields due to their characteristic properties such as preparative accessibility, structural stability and biological activities such as anti-fungal, anti-bacterial, antitumor and antioxidant activity.[1-5] Bacterial resistance to currently available antibiotics is rapidly increasing, therefore there is a clear need for the development of new and effective antimicrobial agents. Hospital-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) has become an important problem to deal with owing to their multidrug resistance.[6,7]

Schiff bases and their metal complexes are of major interest because of their ability to bind oxygen to redox systems exerting their ability to oxidize DNA. They showed significant antimicrobial activity due to the free radical scavenging ability of their metal complexes.[8] Schiff bases which are derived from the condensation reaction of amino acids and aldehyde are considered as an important class of ligands that

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coordinate to metal ions *via* nitrogen from azomethine group.[9,10] Coordination bond can be achieved also through other atoms with free electron pairs as phenolate oxygen, sulfhydryl sulphur and carboxylate oxygen.[11] Schiff base ligands are easily synthesized and form complexes with almost all metal ions.[12] Their activity generally increases by complexation with different metal ions, consequently understanding the characteristics of ligands and metal can lead to the synthesis of highly active compounds.[13,14]
DFT is a reliable and efficient computation method for calculating molecular structures, vibration frequency, and energy of chemical reactions.[15] Many studies have shown that descriptors of DFT studies are widely used to calculate molecular structures. The results obtained are in good correlation with the experimental data.[16,17] Some investigations of DFT have been carried out on Schiff bases complexes[18,19] but very little investigations of DFT study was on Schiff bases. The aim of this study is to synthesize the new Schiff bases, perform their characterization, make a DFT study and examine their antimicrobial activity.

EXPERIMENTAL

Material and Methods

All of the used chemicals have the highest purity and were obtained from the commercial sources. Aldehydes (2,3-dihydroxybenzaldehyde and3-nitrobenzaldehyde) and L amino acids (asparagine and cysteine) were respectively obtained from Sigma–Aldrich (St Louis, MO, USA) and Merck (Darmstadt, Germany). To record the FT-IR spectra of synthesized products of Schiff bases it was used spectrometer Spectrum BX FT-IR (Perkin Elmer) in the range 4000-450 cm^{-1}, at a resolution of 2 cm^{-1} and room temperature (~ 25 °C). For that procedure, KBr disc method was applied. To form KBr pastille, 1.50 mg of the sample and 150 mg of KBr were taken, and the mixture was homogenized and further pressed with a hydraulic press in a special matrix. The melting point was measured by a Melting point meter (Kruss; A. Kruss Optronic, Germany).The purity of the synthesized compounds was tested by TLC on Silica-TLC Alu foils (Fluka, Germany) plates and spots were visualized by using a UV lamp.

Procedure for Preparation Compounds 1 to 3

For compound **1** [(E)-4-amino-2-((2,3-dihydroxybenzylidene)amino)-4-oxobutanoic acid] L-asparagine (26.0 mg, 0.2 mmol) and 2,3-dihydroxybenzaldehyde (28.0 mg, 0.2 mmol), for compound **2** [(E)-3-mercapto-2-((3-nitrobenzylidene)amino)propanoic acid] L-cysteine (24.3 mg 0.2 mmol) and 3-nitrobenzaldehyde (30.2 mg, 0.2 mmol), for compound **3** [(E)-2-((2,3-dihydroxybenzylidene)amino)-3-mercaptopropanoic acid] L-cysteine and 2,3-dihydroxybenzaldehyde (0.2 mmol) were each dissolved in 100 mL of methanol (Scheme-1). The methanol solutions of benzaldehydes were added dropwise to a solution of amino acids. The mixtures were stirred for 8 h at room temperature. The resulting yellow solutions were heated for an hour at 40°C and then cooled to 0°C for 24 h and then evaporated to dryness. Recrystallization from methanol yielded yellow crystals.

Microbiological Procedures

Bacterial Culture

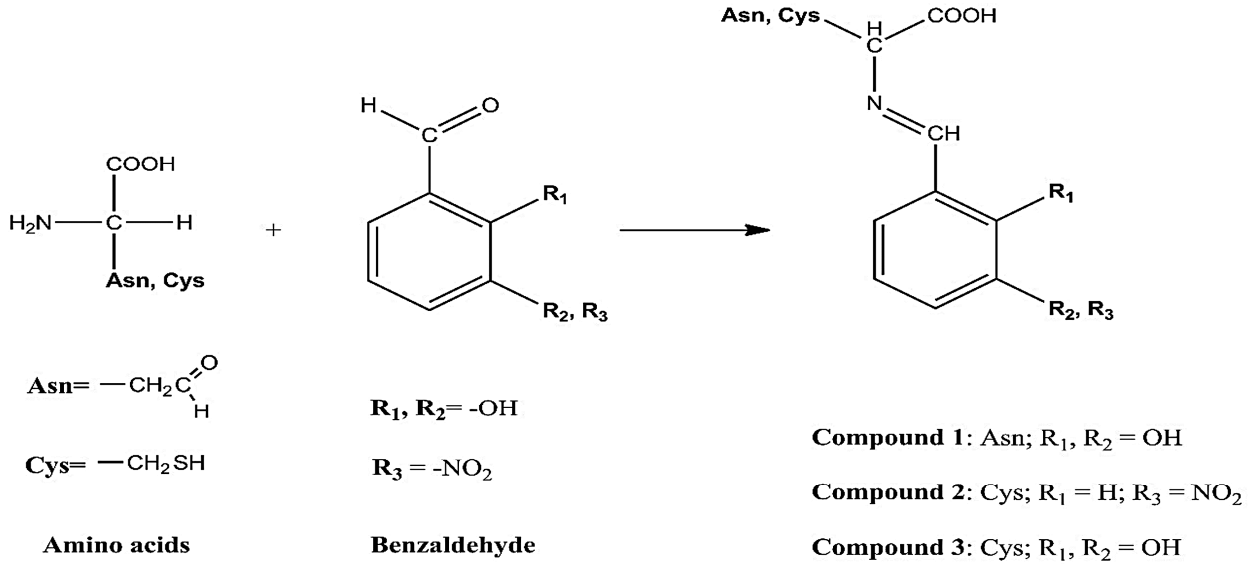
In vitro antimicrobial activity of synthesized compounds was evaluated using four Gram-positive (*Staphylococcus aureus* ATCC 25923; *Methicillin-resistant Staphylococcus aureus*: MRSA ATCC 33591; *Bacillus subtilis* ATCC 6633; and *Enterococcus faecalis* ATCC 29212), four Gram-negative bacteria species (*Salmonella enterica* ATCC 31194; *Pseudomonas aeruginosa* ATCC 9027; *Escherichia coli* ATCC 25922; Extended Spectrum Beta-Lactamase producing E. *coli*: ESBL E. *coli* ATCC 35218), and one yeast *Candida albicans* ATCC 1023. For antimicrobial testing, investigated compounds were dissolved in 80% methanol to the final concentration of 1 mg/mL. Antimicrobial effects of tested compounds were determined by agar well diffusion method.[20]

Antimicrobial Activity

Agar Well Diffusion Method

Bacterial strains were cultured overnight at 37 °C in Mueller Hinton medium (beef infusion solids 2 g, starch 1.5 g, casein hydrolysate 17.5 g, agar 17 g, distilled water 1000 mL; FlukaBiochemica; Buchs, Switzerland) and *Candida albicans* in Sabouraund Glucose Agar (D glucose 40 g, peptone 10 g, , agar 15

g, distilled water 1000 mL; Fluka Biochemica; Buchs, Switzerland). The inoculum was adjusted according to CLSI (Clinical and Laboratory Standards Institute)[21] using a sterile saline solution to the final density of 0.5 McFarland standard (~1.5 x 10^8 CFU/mL). Microbial inoculums were spread over the entire surface of plates with growth medium and left for 15 minutes at room temperature to achieve a total absorption. Holes with a diameter of 8 mm have punched aseptically in inoculated plates using the sterile cork borer, and the well is filled with 100 µl of the investigated compound. After that, agar plates containing bacteria were incubated at 37 °C for 18-24 hours, while plates with *C. albicans* were incubated at 37 °C for 24-48 hours. Antimicrobial action of investigated compounds was evaluated based on diameter (mm) of inhibition zones that occur as the result of Schiff bases diffusion in the medium and inhibition of the microbial growth. Ampicillin (10 µg; HiMedia Laboratories Pvt. Ltd., India) and Nystatin (100 units; Oxoid Ltd., England) were used as positive control for bacteria and yeast respectively, while 80% methanol was used as negative control. All the tests were performed in triplicate, and the mean values (±SD) were calculated.



Scheme-1**:** Synthesis of Compounds 1 to 3

Computational Methods: Structural and Electronic Properties

The computations were performed using Spartan 14. The geometry optimizations of synthesized compounds **1** to **3** (Fig.-3) were calculated at the DFT level and the 6-31G* basis set. The calculations were carried out with the B3LYP functional, in which Becke's non-local exchange and the Lee-Yang-Parr correlation functionals were applied.[22]

RESULTS AND DISCUSSION

Chemistry

The compounds **1** to **3** were prepared from methanolic solutions of different benzaldehydes and L-amino acids, in a molar ratio of 1:1 at room temperature. The target compounds **1**, **2** and **3** were obtained in excellent yields (51%, 45% and 70%, respectively). The synthesized compounds were checked for purity and R_F values were determined by TLC silica gel F254 as the stationary phase and chloroform: methanol as mobile phase. For the novel compounds **1**-**3**, melting points were determined by capillary methods. The obtained results of melting points and R_F values of compounds **1** to **3** are shown in Table-1.

The structures of the prepared compounds **1** to **3** were confirmed by IR spectra. The IR spectra of the compounds **1** to **3** are recorded in the solid state using the KBr disc technique. Selected stretching frequencies which are due to a key feature of Schiff bases and structural parameters were calculated and listed in Tables-2, 3 and 4.

Table-1: Physico-analytical Data of the Schiff Base

Compounds	Empirical formula	Color	Melting point (°C)	RF
1	$C_{11}H_{12}N_2O_5$	yellow	113.5	0.03
2	$C_{10}H_{10}N_2O_4S$	pale yellow powder	149.1	0.55
3	$C_{10}H_{11}NO_4S$	light yellow	191.5	0.12

Table-2: Experimental and Theoretical FT-IR Frequencies of Compound **1**.

Assignment	2,3-Dihydroxybenz -aldehyde [cm^{-1}]		L-Asparagine [cm^{-1}]		Compound 1. [cm^{-1}]	
	Exp.	Theo.	Exp.	Theo.	Exp.	Theo.
υ(OH)	3414	3306	3383	3307	3550	3440
υ(C=O)	1735	1731	2000	1870	2085	1847
υ(NH_2)	-	-	3400	3445	3356	3548
υ(C=N)	-	-	-	-	1653	1650
υ(C-H)	3276	3221	3028	3038	3068	3176
υ(C=C)	1598	1539	-	-	1499	1525

Table-3: Experimental and Theoretical FT-IR Frequencies of Compound 2.

Assignment	3-Nitrobenzaldehyde[cm^{-1}]		L-Cysteine[cm^{-1}]		Compound 2. [cm^{-1}]	
	Exp.	Theo.	Exp.	Theo.	Exp.	Theo.
υ(OH)	-	-	3855	3684	3432	3578
υ(C=O)	1853	1804	2078	1854	1721	1708
υ(N-O)	1352	1399	-	-	1480	1470
υ(NH_2)	-	-	3525	3555	-	-
υ(SH)	-	-	2638	2700	2800	2736
υ(C=N)	-	-	-	-	1623	1625
υ(C-H)	3241	3212	3180	3133	3250	3230
υ(C=C)	1527	1524	-	-	1531	1520

Table-4: Experimental and Theoretical FT-IR Frequencies of Compound 3.

Assignment	2,3-Dihydroxybenz -aldehyde [cm^{-1}]		L-Cysteine[cm^{-1}]		Compound 3[cm^{-1}]	
	Exp.	Theo.	Exp.	Theo.	Exp.	Theo.
υ(OH)	3414	3306	3855	3684	3750	3700
υ(C=O)	1735	1731	2078	1854	1850	1834
υ(NH_2)	-	-	3525	3555	-	-
υ(SH)	-	-	2638	2700	2699	2690
υ(C=N)	-	-	-	-	1626	1653
υ(C-H)	3414	3306	3180	3133	3164	3174
υ(C=C)	1598	1598	-	-	1479	1479

Table-5: The Correlation Factors of Compared Stretching Frequencies for Compounds **1**-**3**

Compounds	R^2 for Assignment
1	0.9776
2	0.9954
3	0.9995

Comparison of the experimentally measured and theoretically computed stretching frequencies of IR spectra can be utilized to eliminate the uncertainties in the fundamental assignments of the spectra. The calculated and experimental values stretching frequencies show good correspondence. The correlation factors of the linear regression used to compare the experimentally measured and theoretically computed IR specters for compounds **1**, **2** and **3** are presented in Table-5.

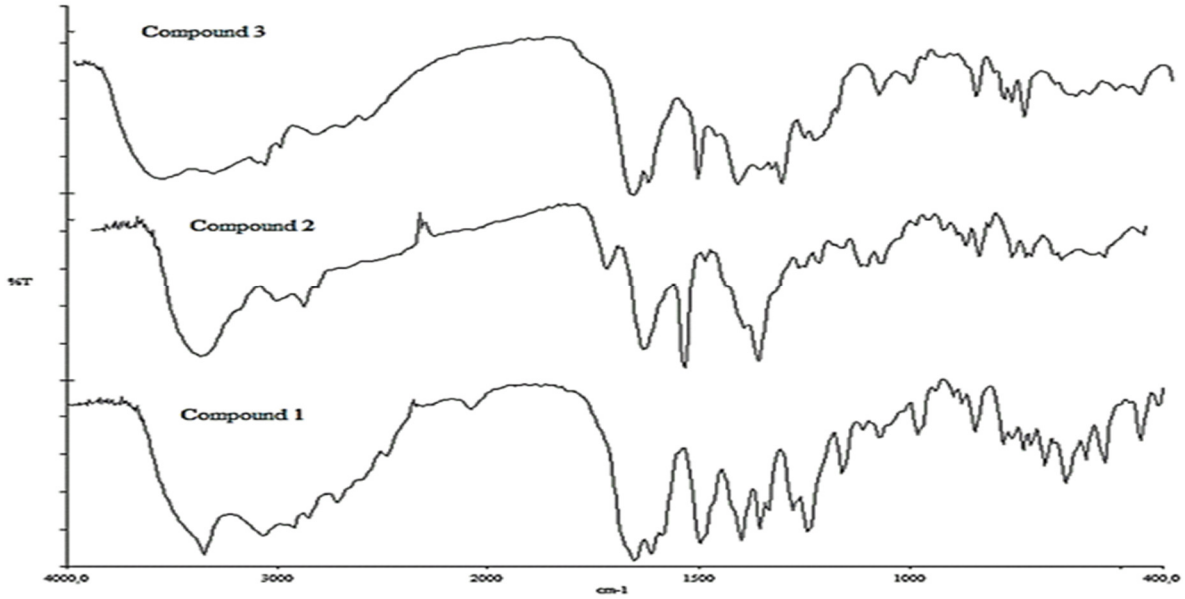


Fig.-1: IR Spectra of Compounds **1** to **3**

The IR spectrum experimental and theoretical of compounds **1** to **3** are shown in Fig.-1 and 2. The IR spectrum of each compound (**1**-**3**) showed bands within the 1623-1653 cm^{-1} region, which is due to C=N groups stretching frequency, and this is a key characteristic of Schiff bases. All of the vibrational frequencies of the fundamental modes of Schiff bases agree with the simulated IR frequencies. These spectrums confirm the suggested structure.

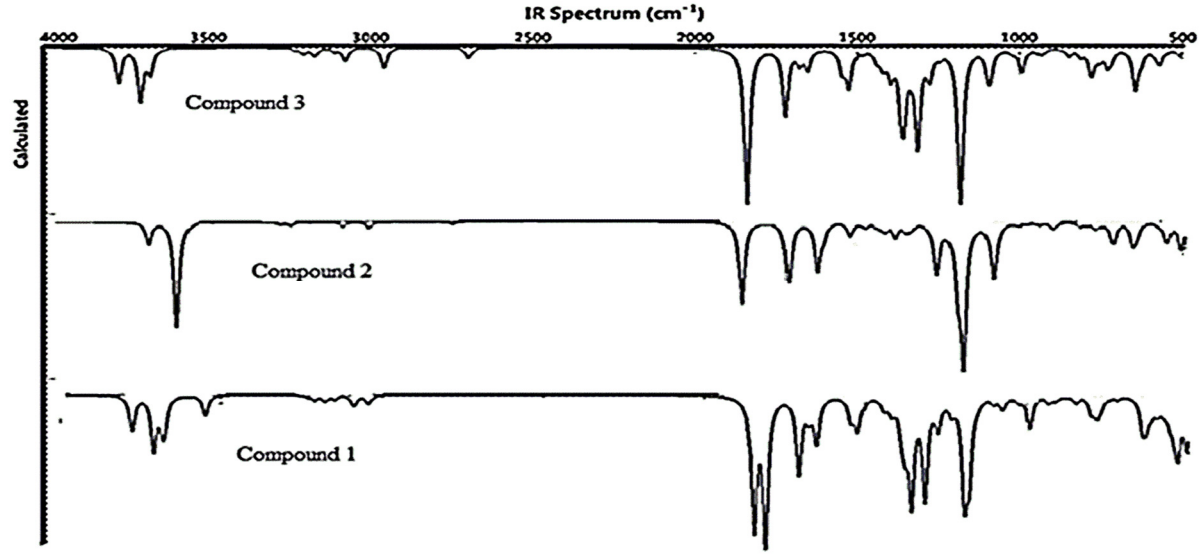


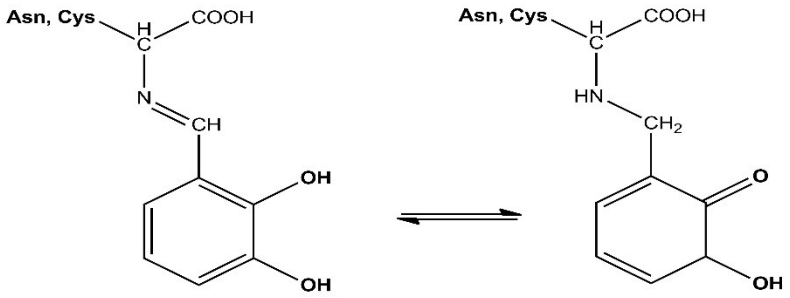
Fig.-2: Theoretical IR Spectrum of Compounds **1** to **3**

Calculations of Molecular Orbital

The atom superposition and electron delocalization molecular orbital (ASED-MO) method are used to investigate the geometric and electronic structures[22] as well as the types of electronic transitions[23] in the compounds **1** to **3**, which is shown at Fig.-3.

The Schiff bases formation is confirmed by the values of bond lengths and bond orders (Mulliken and Löwdin) for Compound **1**: C7-N1, C6-C7, and C5-C6 bonds which are equal to 1.281Å (1.72, 1.98), 1.467Å (1.05, 1.12) and 1.403Å (1.38, 1.36), respectively, with the double bond character for N1-C7 bond.

For Compound **2**: C7-N2, C6-C7, and C5-C6 bonds which are equal to 1.271Å (1.78, 2.02), 1.479Å (1.01, 1.09) and 1.387Å (1.45, 1.50), respectively, with the double bond character for the N2-C7 bond.
For Compound **3**: C7-N1, C6-C7, and C5-C6 bonds which are equal to 1.278Å (1.75, 1.99), 1.468Å (1.05, 1.11) and 1.402Å (1.38, 1.36), respectively, with the double bond character for the N1-C7 bond. The proposed keto-enol tautomerism for compounds **1** and **3** (Scheme-2) is supported by the partial double bond character of C5-O4 and C5-O2 with a good contribution of the enolic form.



Scheme-2: Keto-enol Tautomerism in Compounds **1** and **3**

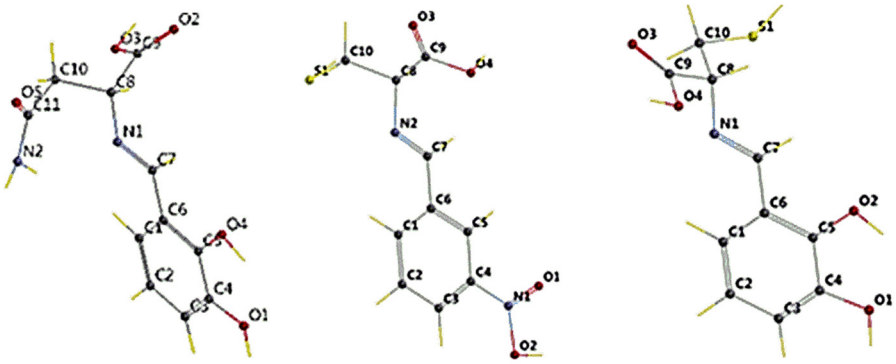


Fig.-3: The Optimized Geometry of Compounds **1** to **3**

Chemical Reactivity

The chemical reactivity descriptors calculated using DFT are total energy (E), chemical hardness (η), the electronic chemical potential (μ), and electrophilicity (ω). Chemical hardness is related to the stability and reactivity of a chemical system. In a molecule, it measures the resistance to change in the electron distribution or charge transfer.
Determination of chemical reactivity or chemical hardness of compounds is possible by calculating the gap between HOMO and LUMO orbitals.Chemical hardness is estimated using equation (1):

$$\eta = \frac{(\varepsilon LUMO - \varepsilon HOMO)}{2} \qquad (1)$$

Where εLUMO and εHOMO are the LUMO and HOMO energies.

The larger the HOMO–LUMO energy gap, the harder and more stable/less reactive the molecule.[24] The results indicate that compound **2** is harder and less reactive than **3** which is harder and less reactive than **1** (Table-7, Row 4). The electronic chemical potential is defined as the negative of electronegativity of a molecule and calculated using equation (2) [24]:

$$\mu = \frac{(\varepsilon HOMO + \varepsilon LUMO)}{2} \qquad (2)$$

Physically, μ describes the escaping tendency of electrons from an equilibrium system.[24] The greater the electronic chemical potential, the less stable or more reactive is the compound. Therefore, **2** is the most reactive and **1** is the least reactive of the compound (Table-7, row 5).

Global electrophilicity index (ω), introduced by Parr, is calculated using the electronic chemical potential and chemical hardness as shown in equation (3):

$$\omega = \frac{\mu 2}{2\eta} \qquad (3)$$

Electrophilicity index measures the propensity or capacity of a species to accept electrons.[24] It is a measure of the stabilization in energy after a system accepts an additional amount of electronic charge from the environment.[24] The electrophilicity values (Table-7, row 7) for the compounds are 2.079 eV for **1**, 5.850 eV for **2** and 2.724 eV for **3**. Among the compounds, **1** is the strongest nucleophile while **2** is the strongest electrophile.

Table-6: The Calculated Mulliken and Löwdin Bond Orders and Bond Lengths (Å) of Compounds **1** to **3** obtained from ASED-MO Theory

Compound 1				Compound 2				Compound 3			
Bond	Mulliken Bond Order	Löwdin Bond Order	Bond Length	Bond	Mulliken Bond Order	Löwdin Bond Order	Bond Length	Bond	Mulliken Bond Order	Löwdin Bond Order	Bond Length
C1-C2	1.47	1.55	1.386	C1-C2	1.38	1.47	1.400	C1-C2	1.47	1.55	1.386
C2-C3	1.38	1.44	1.403	C2-C3	1.47	1.55	1.385	C2-C3	1.38	1.44	1.403
C3-C4	1.43	1.47	1.387	C3-C4	1.27	1.31	1.415	C3-C4	1.43	1.47	1.387
C4-O1	0.90	1.23	1.377	C4-N1	0.93	1.19	1.396	C4-O1	0.89	1.22	1.379
C4-C5	1.28	1.31	1.407	N1-O1	1.55	2.01	1.204	C4-C5	1.28	1.31	1.407
C5-O4	1.00	1.30	1.361	N1-O2	1.04	1.30	1.357	C5-O2	1.00	1.29	1.363
C5-C6	1.38	1.36	1.403	C4-C5	1.24	1.30	1.414	C5-C6	1.38	1.36	1.402
C6-C7	1.05	1.12	1.467	C5-C6	1.45	1.50	1.387	C6-C7	1.05	1.11	1.468
C7-N1	1.72	1.98	1.281	C6-C7	1.01	1.09	1.479	C7-N1	1.75	1.99	1.278
N1-C8	0.94	1.10	1.463	C7-N2	1.78	2.02	1.271	N1-C8	0.97	1.12	1.451
C8-C9	0.91	0.96	1.532	N2-C8	0.94	1.11	1.449	C8-C9	0.91	0.96	1.535
C9-O2	1.89	2.17	1.210	C8-C9	0.90	0.96	1.537	C9-O3	1.87	2.17	1.211
C9-O3	1.08	1.36	1.353	C9-O3	1.88	2.19	1.207	C9-O4	1.09	1.37	1.351
C8-C10	0.96	1.03	1.546	C9-O4	1.10	1.38	1.348	C8-C10	0.95	1.03	1.537
C10-C11	0.94	1.00	1.530	C8-C10	0.94	1.02	1.544	C10-S1	1.00	1.14	1.838
C11-O5	1.86	2.09	1.222	C10-S1	1.00	1.14	1.836				
C11-N2	1.13	1.37	1.371								

Table-7: Global Chemical Reactivity Indices of Compounds **1**, **2** and **3**

	Compound 1	Compound 2	Compound 3
E (au)	-912.02	-1195.55	-1141.49
E_{HOMO} (eV)	-5.65	-6.40	-6.06
E_{LUMO} (eV)	-1.35	-1.50	-1.40
Energy gap (Δε) (eV)	4.30	4.90	4.66
μ(eV)	-3.195	-4.595	-3.635
η(eV)	1.805	2.455	2.425
ω(eV)	2.079	5.850	2.724

Biological Study

Antimicrobial Activity

The compounds **1** to **3** were tested for antimicrobial properties against Gram-positive, Gram-negative pathogenic bacteria species, and yeast *C. albicans*. Results of the inhibition zone values for the compounds are presented in Table-8.

Table-8: Inhibition Zones for Compounds **1** to **3** generated through the Agar Well Diffusion Method

Strain	Zones of Inhibition (mm)			
	Ampicillin (10 µg)	Compound 1	Compound 2	Compound 3
Staphylococcus aureus ATCC 25923	33.03±0.09	21.00±1.00	NI	24.26±0.64
MRSA ATCC 33591	NI	17.20±0.82	14.66±0.64	NI
Bacillus subtilis ATCC 6633	47.98±0.23	NI	NI	10.93±0.21
Enterococcus foecalis ATCC 29212	16.94±0.23	NI	NI	NI
*Salmonella entericaA*TCC 31194	16.03±0.07	21.00±1.00	NI	13.00±0.30
Pseudomonas aeruginosa ATCC 9027	13.02±0.09	24.96±0.25	NI	20.50±0.50
Escherichiacoli ATCC 25922	8.96±0.16	24.16±0.76	NI	18.00±1.00
ESBL *E. coli* ATCC 35218	NI	24.23±0.49	NI	19.00±0.20
Candida albicans ATCC	*21.12±0.24	44.96±0.35	23.50±0.50	42.03±0.15

The results are the mean ± SD (*n*=3)
*Inhibition zones generated by Nystatin (100 units) activity against *C. albicans*. NI = No inhibition zone; Methanol = NI.

Regarding the antibacterial activity, varying degree of inhibition is noted against all the investigated strains, except for *Enterococcus faecalis*. The highest values of inhibition zones were recorded for compound **1**, followed by the compound **3**, while compound **2** performed inhibitory effect only in the case of MRSA (Table-8, Fig.-4).

Compound **1** exhibited higher antibacterial activity against Gram-negative bacteria, especially against *Pseudomonas aeruginosa* and ESBL *E. coli*. Standard antibiotic (ampicillin) caused almost half smaller inhibition zones against *P. aeruginosa* (13.02±0.09 mm) compared to those made by compound **1** (24.96±0.25 mm). Furthermore, ampicillin did not have any inhibitory effect against ESBL *E. coli*, while compound **1** formed inhibition zones of 24.23±0.49 mm. These results are interesting, because Gram-negative bacteria are generally more resistant to antibacterial substances due to the low permeability barrier of the two-membrane cell and insufficient chemical diversity of compound libraries to probe this barrier.[25] In this investigation, Gram-positive *Bacillus subtilis* showed resistance to the compounds **1** and **2**, and sensitivity to the compound **3** with inhibition zones of 10.93±0.20 mm. Methicillin-resistant *Staphylococcus aureus*, MRSA was resistant to the commercial antibiotic, but showed sensitivity to the compounds **1** (17.20±0.81 mm) and 2 (14.66±0.64 mm). Since multidrug-resistant (MDR) bacteria are one of the most important current threats to public health,[26] obtained results are promising in terms of potential use of the analyzed compounds as antibacterial agents, especially considering their action against multidrug-resistant strains ESBL *E. coli* and MRSA. Tested compounds showed higher antifungal

comparing to the antibacterial activity. Antifungal activity of investigated compounds was tested through the inhibition of *Candida albicans*. All of the three samples have shown very strong antifungal properties. The strongest antifungal effect is observed in the case of the compound **1** (44.96±0.35 mm), followed by compound **3** (42.03±0.15 mm), and compound **2** (23.50±0.50 mm). All of the investigated compounds caused greater inhibition zones compared to the inhibition zones caused by standard antimycotic nystatin (20.97±0.24), (Fig.-4, Table-8). Compound **2**, which generally shows the minimal effect, unlike compounds **1** and **3**, does not have two hydroxyl groups on the benzene ring. The absence of these groups may be the reason for the reduced antimicrobial activity of the compound **2**.

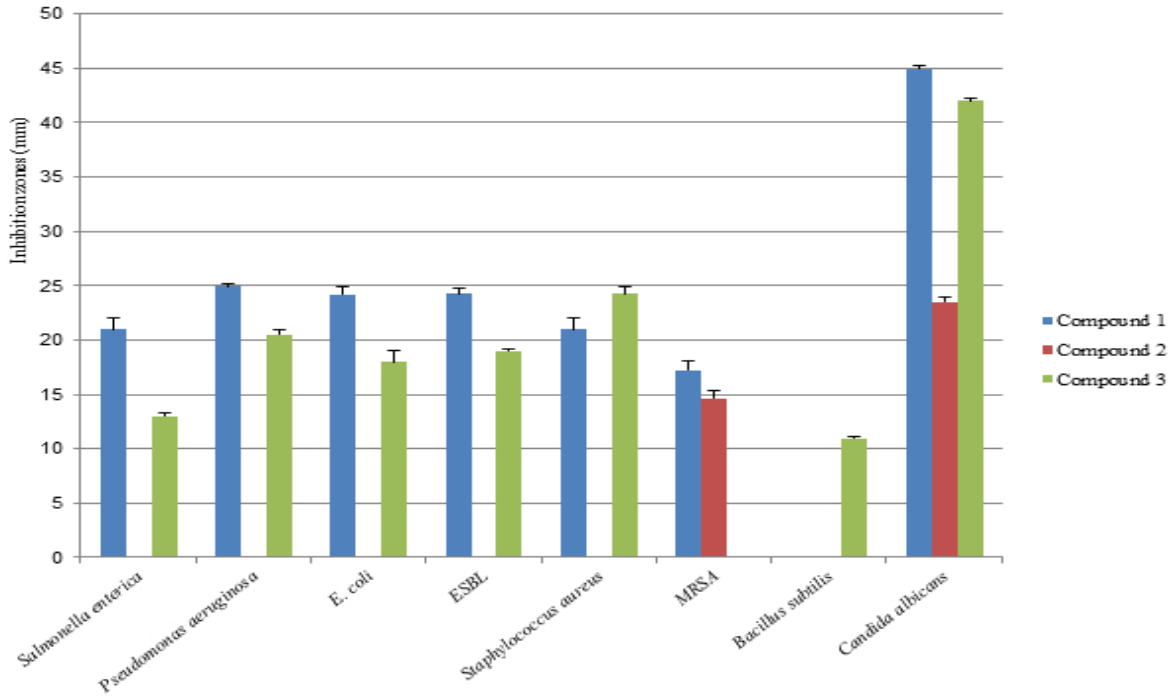


Fig.-4: Antimicrobial Properties of Investigated Compounds

Comparison of Antimicrobial Activity with Computational Calculations

The diffusion method showed that compounds **1**, **2** and **3** inhibit the growth of Gram-positive bacteria. The analyzed compounds showed different antimicrobial activity. The DFT analysis has been shown that compound **1** was the most reactive and compound **2** was the least reactive. (Table-7). Compound **1** has the best antimicrobial activity (Table-8 and Fig.-4). An examination of the mechanism of the antimicrobial action of these compounds remains for the future.

CONCLUSION

The Schiff bases were prepared from the reaction of L-asparagine with 2,3-dihydroxybenzaldehyde (compound **1**), L-cysteine with 3-nitrobenzaldehyde (compound **2**) and L-cysteine with 2,3-dihydroxybenzaldehyde (compound **3**). The structures of the prepared compounds were confirmed by FT-IR spectroscopic method and the antimicrobial activity was assessed. The conducted was DFT study of synthesized compounds. The antibacterial activity against the tested Gram positive and Gram negative organisms showed that the compound **1** had the highest activity compared to the compound **2** and **3**. All theoretical calculations were carried out by DFT method B3LYP at 6-31G* level. A comparative DFT study on compounds **1** to **3** has been accomplished. Comparison of the experimentally measured and theoretically computed stretching frequencies of IR spectra of Schiff bases show good correspondence. The calculated reactivity descriptors: E, μ,η, ω predict that compound **2** is most stable and compound **1** least stable. The most reactive compound **1**, showed the best antibacterial activity. The DFT calculations indicated that the calculated chemical reactivity descriptors of the molecules correlated well with antibacterial activity.

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