

Biological, electrochemical, molecular docking and DFT studies of the asymmetric Schiff base: synthesis of 2-hydroxy-6-methyl-3-((*E*)-1-((4-methyl-3-((*E*)-(pyridin-3-ylmethylene)amino)phenyl)imino)ethyl)-4*H*-pyran-4-one

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Abstract

The asymmetric Schiff base 2-hydroxy-6-methyl-3-((*E*)-1-((4-methyl-3-((*E*)-(pyridin-3-ylmethylene)amino)phenyl)imino)ethyl)-4*H*-pyran-4-one (AL) was synthesized, and characterized by LC-MS, FT-IR, UV-Vis, ¹H and ¹³C NMR techniques as well as cyclic voltammetry. The optimized molecular structures, IR and UV-Vis spectral modeling, stability, reactivity, and specific quantum chemical properties of the synthesized AL were examined using Density Functional Theory (DFT). The theoretical findings were consistent with the experimental results. The results show that compound AL has good antioxidant and anti-inflammatory activity. The electrochemical behavior of AL and BHT in the presence of superoxide radicals shows that the radical reaction is spontaneous. Apro-AL calculations indicated the ability of the AL compound to inhibit the primary protease (4GCA). Finally, the docking studies and ADME-T results showed that the AL compound under investigation could be developed as a therapeutic agent.

Keywords: Synthesis; Schiff base; DFT; Cyclic voltammetry; Antioxidant activity

1. Introduction

The discoverer of "Schiff bases" is known as Hugo Schiff.¹ Schiff bases have an imine function (C=N) and are formed when primary amines condense with carbonyl compounds.^{2–4} Schiff bases, also known as azomethines, are widely used in biology and medicine as antioxidants, antimicrobials, antibacterials, antifungals and anti-inflammatory agents.^{5–10} Antioxidants can be divided into two groups: those that transfer electrons or hydrogen atoms, mainly phenolic compounds. They are used to assess the ability to scavenge free radicals.^{11,12} The most widely used organic molecules among synthetic drugs are Schiff bases, which, in addition to their other functions, contain elec-

trons in the nitrogen atom, the π bond and phenolic groups, and these components are important of living things due to their antioxidant action, which aids in the prevention of harmful diseases caused by free radicals.^{13–19}

The antioxidant activity of all compounds with one or two hydroxyl groups is higher than that of those with methoxy groups. The HOMO and LUMO energies of molecular orbitals, chemical softness and electronegativity of the compounds are useful in explaining their antioxidant activities according to quantum chemical calculations.²⁰

Numerous studies have shown how incredibly effective Schiff bases are at scavenging free radicals. "Oxidative stress" refers to the harmful consequences of free radicals, which have the ability to damage living cells. The composi-

tion of human body cells is altered by free radicals, which can cause harm and other illnesses, including diabetes, cancer, autoimmune diseases, neurological problems and Alzheimer's illnesses.^{21–23}

The antioxidant activities of two Schiff base compounds obtained by condensation of anisaldehyde with hydrazine (ASB1) and 3,5-dichloroaniline (ASB2) were evaluated. These compounds performed a very poor of scavenging the DPPH radical, but they demonstrated significant activity in scavenging the ABTS radical, with the ASB1 compound being less active than ASB2, although ASB1 presents a larger total antioxidant capacity (TAC) than ASB2. As urease and acetylcholinesterase enzyme inhibitors, ASB1 and ASB2 appear to have acceptable pharmacokinetic properties.²⁴

The synthesis, characterization and antioxidant activity of two Schiff bases were studied: 2,2'-((1*E*,1'*E*)-((4-methyl-1,3-phenylene)bis(azanylidene))bis(methanylylidene))bis(4-methoxyphenol) (L),²⁵ and 2,4-bis(2-hydroxy-3-methoxybenzaldehyde)diiminotoluene (SB).²⁶ The antioxidant activity of L and SB was examined using a series of chemical tests, including reducing power, hydroxyl radical scavenging, DPPH, ABTS, and β -carotene bleaching. The findings indicate that these two chemical compounds exhibit strong antioxidant activity. Superoxide anion radical scavenging demonstrated a robust interaction between $O_2^{\cdot -}$ and the compounds. The high K_b value confirms this. The spontaneity of the anti-free radical reaction is demonstrated by the negative value of ΔG° .

In this work, the Schiff base 2-hydroxyl-6-methyl-3-((*E*)-1((4-methyl-3-((*E*)-(pyridin-3-ylmethylene)amino)phenyl)imino)ethyl)-4*H*-pyran-4-one (AL) has been synthesized and its mass spectrum has been analyzed. The synthesized compound was characterized by spectroscopy methods (UV-Vis, FT-IR), 1H and ^{13}C NMR, and electrochemistry (cyclic voltammetry). DFT was used to determine the HOMO and LUMO states and to assess the stability, reactivity and other quantum chemical properties of the examined molecule. The optimized molecular structure was assessed by cyclic voltammetry to analyze the electrochemical properties. The biological activity of the synthesized compound was evaluated using several *in vitro* methods.

2. Experimental

2.1. Products, materials and methods used

The following solvents and compounds were employed without further purification: 2,4-diaminotoluene,

3-acetyl-2-hydroxy-6-methyl-4*H*-pyran-4-one, 3-pyridinecarboxaldehyde, diethyl ether, acetonitrile, ethanol, methanol, and DMF. These were all purchased from Merck, Sigma-Aldrich, or Fluka commercial sources.

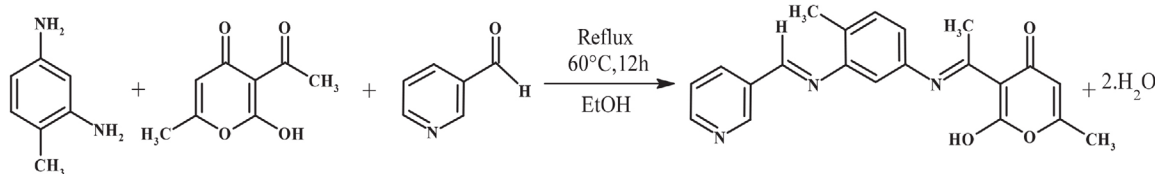
Measurement of UV and visible light absorption was performed using a Shimadzu UV-vis 1800 spectrophotometer. Absorption spectra in the UV-visible range from 190 to 1100 nm were registered with a spectrophotometer using DMF solutions and quartz cells (1 cm).

Infrared Fourier Transform (IR-FT) spectroscopy (Shimadzu QATR-S) was used to acquire spectra in the range 400 cm^{-1} to 4000 cm^{-1} . The melting point was determined using the Büchi Melting Point B-540 apparatus. 1H NMR and ^{13}C NMR spectra were recorded on Bruker spectrometer (working frequency 400 MHz and 100 MHz). The mass spectrum of the compound was acquired at a retention time of 2.283 minutes using the LC/MSD iQ instrument. On aluminium plates, thin-layer chromatography (TLC) was carried out. (Schleicher and Schüll GmbH). The eluent was dichloromethane.

2.2. Preparation of a schiff base 2-Hydroxyl-6-methyl-3-((*E*)-1((4-methyl-3-((*E*)-(pyridin-3-ylmethylene)amino)phenyl)imino)ethyl)-4*H*-pyran-4-one (AL)

The asymmetric compound 2-hydroxyl-6-methyl-3-((*E*)-1((4-methyl-3-((*E*)-(pyridin-3-ylmethylene)amino)phenyl)imino)ethyl)-4*H*-pyran-4-one was prepared as documented in the literature.²⁷ Scheme 1 shows that 1.0 mmol of 2,4-diaminotoluene is dissolved in ethanol with two different aldehydes, 1.0 mmol of 3-acetyl-2-hydroxyl-6-methyl-4*H*-pyran-4-one and 1.0 mmol of 3-pyridinecarboxaldehyde. The mixture is refluxed for twelve hours at 60°C under a nitrogen atmosphere. The compound precipitates only after the solution is concentrated under vacuum. Diethyl ether is used to wash the dark orange precipitate obtained from filtration. Thin-layer chromatography (TLC) was used to confirm the purity of the final compound. Dichloromethane/ethanol was employed as the eluent. A yield of 95 % was obtained for the ligand, and its melting point is 176°C . The compound is stable at ambient temperature and requires no special storage precautions.

IR (cm^{-1}): 3354 $\nu(\text{OH})$, 3225 $\nu(\text{CHAr})$, 2976 $\nu(\text{CHAlph})$, 1691 $\nu(\text{C=O})$, 1552 $\nu(\text{C=N})$, 1467 $\nu(\text{C=C})$, 1251 $\nu(\text{C-O})$, 1155 $\delta(\text{O-H})$. UV-Vis (λ_{max} , nm, DMF as solvent): 321. LC-MS (g/mol): 361. 1H NMR (400 MHz; $\text{DMSO}-d_6$) δ 15.35 (s, 1H, -OH), 9.09 (s, 1H, -CH=N-), 8.89 (t, 1H, H16), 8.64 (dt, 1H, H18), 8.17 (dt, 1H, H20),



Scheme 1. Scheme of reaction of the asymmetric Schiff base AL.

7.48 (t, 1H, H19), 7.02 (d, 1H, H3), 6.55 (dd, 1H, H1), 6.47 (d, 1H, H6), 5.81 (s, 1H, H24), 2.13 (s, 3H, -CH₃), 2.01 (s, 3H, H₃C-C=C-), 2.52 (s, 3H, H₃C-C=N-). ¹³C NMR (100 MHz; DMSO-*d*₆) δ 17.81 (-CH₃), 19.73 (-C=C-CH₃), 20.18 (H₃C-C=N-), 96.77, 107.17, 110.17, 112.80, 121.88, 123.85, 124.36, 131.10, 131.72, 137.35, 146.63, 150.88, 158.98 (13 aromatic carbons), 163.03 (-CH=N-), 163.60 (H₃C-C=N-), 175.72 (HO-C-O), 163.91 (H₃C-C-O), 184.39 (C=O).

2. 3. Computations using quantum chemistry

DFT calculations are currently considered the most widely used computational methods. In this case, Gaussian 09 W was the program used for all quantum chemistry calculations. In addition, the optimized molecular structures were determined by applying the DFT approach at the B3LYP/6-31G'(d,p) level.²⁸ Moreover, the computed vibrational frequencies were provided by the optimized molecule structures. However, the electronic spectra of the investigated AL derivatives in ethanol as solvent were predicted using DFT at the B3LYP/6-31G'(d,p) level. Chemical potential (μ), energy gap (ΔE_{gap}), Electrophilicity index (ω), chemical hardness (η), electronegativity (χ), and chemical softness (σ) were calculated utilizing HOMO and LUMO orbital energies that were determined. These equations were employed to determine each of these parameters.^{29,30}

$$\text{Ionization Energy } I = -E_{\text{HOMO}} \quad (1)$$

$$\text{Electron Affinity } A = -E_{\text{LUMO}} \quad (2)$$

$$\eta = (E_{\text{LUMO}} - E_{\text{HOMO}})/2 \quad (3)$$

$$\sigma = 1/\eta \quad (4)$$

$$\omega = \mu^2/2\eta \quad (5)$$

$$\chi = (I + A)/2 \quad (6)$$

$$\mu = -\chi \quad (7)$$

$$\Delta E_{\text{gap}} = E_{\text{LUMO}} - E_{\text{HOMO}} \quad (8)$$

2. 4. Antioxidant activity

2. 4. 1. ABTS scavenging test for cation radicals

With some slight adjustments, the ABTS scavenging assay was used to assess antioxidant activity with minimal deviations from the methodology of Re *et al.*³¹ The ABTS⁺ solution was obtained by combining 2.45 mM of K₂S₂O₈ and 7 mM ABTS in H₂O. The mixture was incubated at room temperature for 12 hours to initiate the ABTS oxidation. A 96-well microplate was filled with a combination of 160 μ L of the ABTS (2,2-azinobis-(3-ethylbenzthiazoline-6-sulfonic)

solution and varying amounts of the sample prepared in methanol (40 μ L). Optical density was quantified at 734 nm following a 10-minute incubation period. The percentage of inhibition for each concentration was determined by reading the optical density against a blank (methanol). Ascorbic acid, BHA, BHT, quercetine and α -tocopherol were served as reference standards. The following formula was used to express the results as a percentage of inhibition:

$$I (\%) = \frac{A_{\text{Control}} - A_{\text{Sample}}}{A_{\text{Control}}} \times 100 \quad (9)$$

where: A_{Sample} and A_{Control} represent the absorbances of the sample and the negative control, respectively.

2. 4. 2. *ortho*-phenanthroline assay

The Szydłowska-Czerniaka technique was employed to identify the antioxidant capacity of the *ortho*-phenanthroline assay.³² For each dilution, 50 μ L of ferric chloride (0.2%), 30 mL of *ortho*-phenanthroline (0.5%) and 110 μ L of methanol were added to each microplate well in triplicate. Ascorbic acid, BHT and BHA were selected as antioxidant standards, and methanol as a negative control. The plate was incubated in the dark at 30 °C for 20 minutes. Absorbance was quantified at 510 nm. Absorbance values were reported as the results.

2. 4. 3. Reducing power

With a few minor adjustments, the decreasing power test was calculated using the Oyaizu method.³³ 10 μ L of the methanol-solubilized sample, 40 μ L of phosphate buffer (pH 6.6), and 50 μ L of 1% of K₃Fe(CN)₆ were combined. After 20 minutes at 50 °C, 10 μ L of 0.1% of ferric chloride, 40 μ L of purified H₂O and 50 μ L of 10% trichloroacetic acid were introduced to the mixture. Ascorbic acid, BHA, BHT, and α -tocopherol were employed as antioxidant standards, and the optical density was measured at 700 nm.

2. 4. 4. Silver nanoparticle (SNP) assay

Ozyurek *et al.*³⁴ state that the silver (Ag⁺) reduction method was used to evaluate the antioxidant activity. A mixture of 20 μ L at different concentrations of sample dissolved in methanol was added to approximately 130 mL of SNP solution (1 mM AgNO₃, 1% citrate solution) and 50 mL of distilled water. Following 30 minutes of incubation at 25 °C, the optical density of the combination was observed at 423 nm. Ascorbic acid and BHA were used as antioxidant standards.

2. 4. 5. Superoxide radical scavenging

The method of Chung Pin Liang *et al.*³⁵ was utilized to measure the superoxide radical scavenging activity. For

this assay, 20 μL of each extract at various concentrations were combined with 20 μL of pyrogallol (0.025 M) and 140 μL of Tris-HCl buffer (0.05 M, pH 8.2). The combination was incubated at 25 $^{\circ}\text{C}$ for five minutes. After the incubation period, 20 μL of HCl (8 mM) was introduced. The absorbance of the final solution was evaluated at 420 nm with a spectrophotometer. Ascorbic acid and BHT were used as reference standards, the percentage of Superoxide radical scavenging activity was determined according to the formula.

$$\text{SRS activity (\%)} = \frac{A_{\text{Control}} - A_{\text{Sample}}}{A_{\text{Control}}} \times 100 \quad (10)$$

where A_{control} : control absorbance, A_{Sample} : sample absorbance.

The results were determined as the 50% inhibitory concentration (IC_{50}) and expressed in $\mu\text{g/mL}$.

2. 4. 6. Inhibition of Albumin Denaturation

The protein denaturation approach was established by Karthik *et al.*³⁶ for the *in vitro* determination of the anti-inflammatory activity. For the assay, 1 mL of each sample and 1 mL (0.2%) bovine serum albumin were combined in 50 mM Tris-HCl buffer (pH 6.6). Following incubation at 37 $^{\circ}\text{C}$ for 15 minutes, the mixture was heated to 72 $^{\circ}\text{C}$ for five minutes. After cooling, spectrophotometric turbidity measurements were performed at 660 nm. Distilled water served as the blank, while diclofenac, a common medication, served as the reference. Three replicates of the experiment were performed. The relationship (11) was applied to calculate the percentage inhibition of protein denaturation:

$$I(\%) = \frac{A_b - A_s}{A_b} \times 100 \quad (11)$$

I: Inhibition denaturation, A_b : Absorbance control, A_s : Absorbance sample.

2. 4. 7. Superoxide radical scavenging assay ($\text{RSAO}_2^{\bullet-}$)

Electrochemical measurements were performed with a potentiostat under the control of AUTOLAB software and connected to a computer.

Electrochemical studies using cyclic voltammetry were carried out in a cylindrical glass cell containing three electrodes. The reference electrode was a saturated calomel electrode (SCE); the counter-electrode was made of carbon graphite; and the working electrode was a glassy carbon electrode with a surface area of 7 mm^2 . The supporting electrolyte was lithium perchlorate (LiClO_4) and the solvent was acetonitrile. Voltammograms were recorded in a nitrogen atmosphere at room temperature and at a scan rate of 100 mV/s within a potential range of -2500 to $+1800$ mV/SCE.

The Ferrocene/Ferrocenium (Fc/Fc^+) system was considered the international standard. Scavenging of superoxide radicals was investigated using methods reported in the literature.^{25,37}

Cyclic voltammograms (CVs) were recorded in solutions containing 0.1 M acetonitrile/ LiClO_4 at a rate of 100 mV/s, using a scan potential range of $+600$ to -1200 mV/SCE, and the solutions were then allowed to saturate with O_2 for 20 minutes. The chemical compound AL and standard BHT were added in increasing amounts. The formula (12) was used to determine the percentage of superoxide radical removal:

$$\text{RSAO}_2^{\bullet-} (\%) = \frac{(i_{pa}^0 - i_{pa})}{i_{pa}^0} \times 100 \quad (12)$$

where i_{pa}^0 and i_{pa} represent the anodic current densities in the absence and presence of the tested samples.

The following equations,³⁸ (13 and 14) were used to calculate the binding constant (K_b) and the Gibbs free energy (ΔG°):

$$\log\left(\frac{1}{C_{\text{test}}}\right) = \log K_b + \log\left(\frac{i_{pa}}{(i_{pa}^0 - i_{pa})}\right) \quad (13)$$

$$\Delta G^{\circ} = -RT \ln (C_s \times K_b) \quad (14)$$

where T is the temperature, the gas constant is R (8.314 $\text{J.K}^{-1}.\text{mol}^{-1}$) and the concentration of acetonitrile (C_s) is $19.147 \text{ mol.l}^{-1}$.

2. 5. Docking of Molecules

Molecular docking is one of the most potent methodologies for understanding the binding interactions between proteins and ligands in the pharmaceutical design sector. Molecular docking is an exemplary modeling technique for assessing complex drug-target interactions

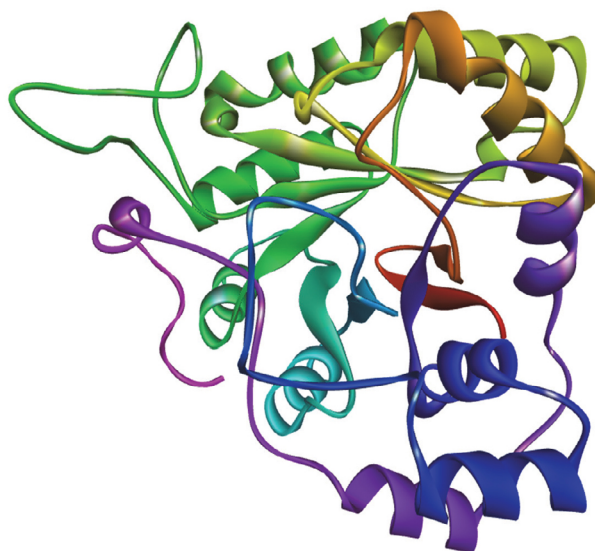


Figure 1. Crystal structure of the 4GCA major protease.

through the calculation of energy minimization and binding energy.^{39,40} The final step in verifying molecular docking is to determine the extent to which the compounds bind to the protease. The Protein Data Bank (PDB) provided the crystal structure of Apro Aldose reductase (protein) with the code 4GCA (Figure 1). In addition, molecular docking simulations used the optimized AL geometry at the B3LYP/6-31G'(d,p) level obtained using the DFT approach. Therefore, PyRx 0.8 virtual screening tool was utilized to perform the molecular docking process. The Accelry Discovery Studio Visualizer, version 24.1.0, was utilized to visualize the resulting AL/Apro complex.⁴¹

3. Results and discussion

3. 1. Spectral analysis

3. 1. 1. UV-Vis spectrum analysis

Experimental spectra of the synthesized compound (AL), recorded in DMF solution in the range of 200 to 600 nm at ambient temperature, present two bands in the ultraviolet spectrum. The first one at 264 nm is attributed to the $\pi \rightarrow \pi^*$ transitions of the aromatic rings,⁴² while the second one, at 321 nm is attributed to the $n \rightarrow \pi^*$ transition of the azomethine group (C=N) (Figure 2). Compound is transparent above 450 nm.^{43,44}

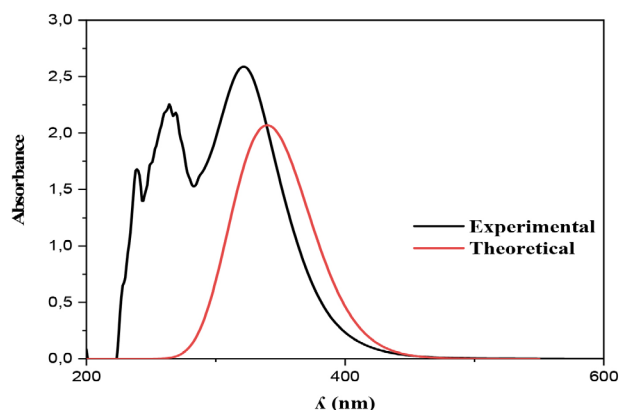


Figure 2. Theoretical and experimental UV-Vis spectra of compound AL.

3. 1. 2. Analyzing vibrational spectra

Figure 3 illustrates the infrared spectrum of the synthesized Schiff base (AL), which was measured in the region of 500–4000 cm^{-1} . A prominent band at 1552 cm^{-1} in the infrared spectrum of AL is ascribed to the azomethine (C=N).⁴⁵ The stretching vibrations of the aromatic rings of (C=C) are observed at 1467 cm^{-1} .^{46,47} $\nu(\text{C-O})$ is the contributor to the band at 1251 cm^{-1} .⁴⁸ Moreover, the (O–H) band of the phenolic group is observed at 3354 cm^{-1} .^{49,50} The asymmetric and symmetric elongations of $-\text{CH}_3$ are

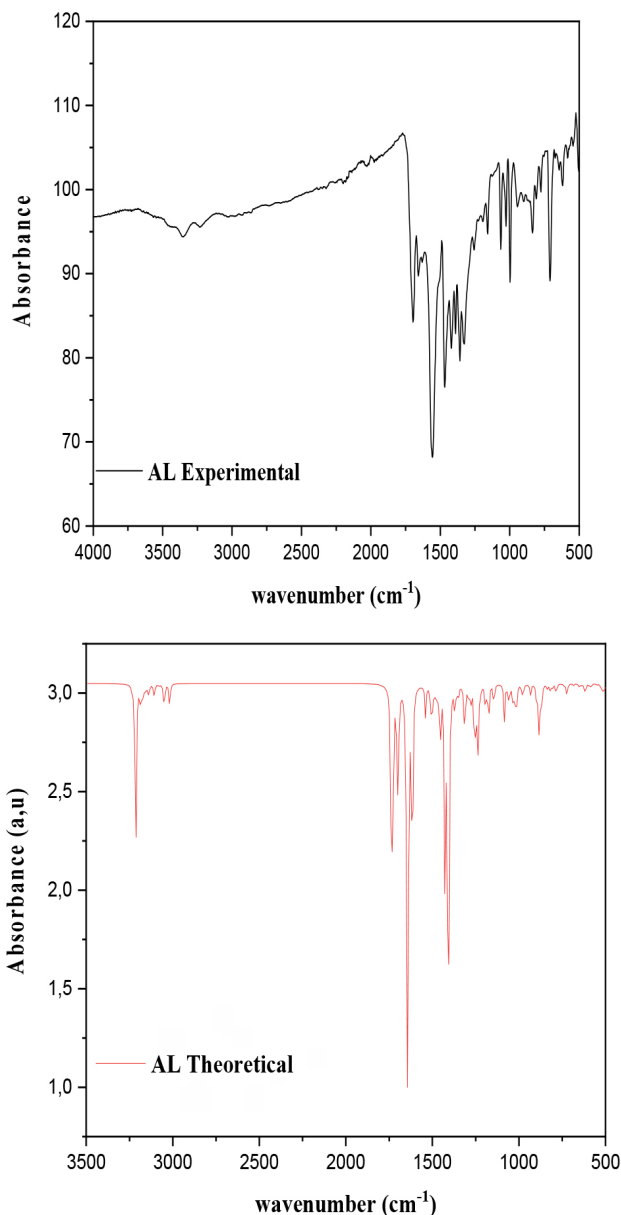


Figure 3. Experimental and Theoretical IR spectrum of compound AL.

responsible for the absorption bands in the 2932–3008 cm^{-1} region.^{51,52} Deformation of the phenolic group $\delta(\text{O-H})$ is observed at 1155 cm^{-1} .⁴⁸

The IR and UV spectra were compared and elucidated by DFT. The experimental identification of these bands provides evidence for the synthesis of the new Schiff base compound (AL). A strong consistency and favorable alignment with the DFT results is confirmed by the spectroscopic study IR and UV.

3. 1. 3. Liquid chromatography coupled to mass spectrometry (LC-MS)

The mass spectrum of compound AL was acquired by the LC/MSD iQ instrument with a retention time of

2.283 min,^{53–55} as illustrated in Figure 4. The molecular ion peak [m/z] of the free compound was detected at 360, corresponding to the exact molecular weight ($M - 1$). Consequently, we conclude that the molar mass of compound AL is 361 g·mol⁻¹.

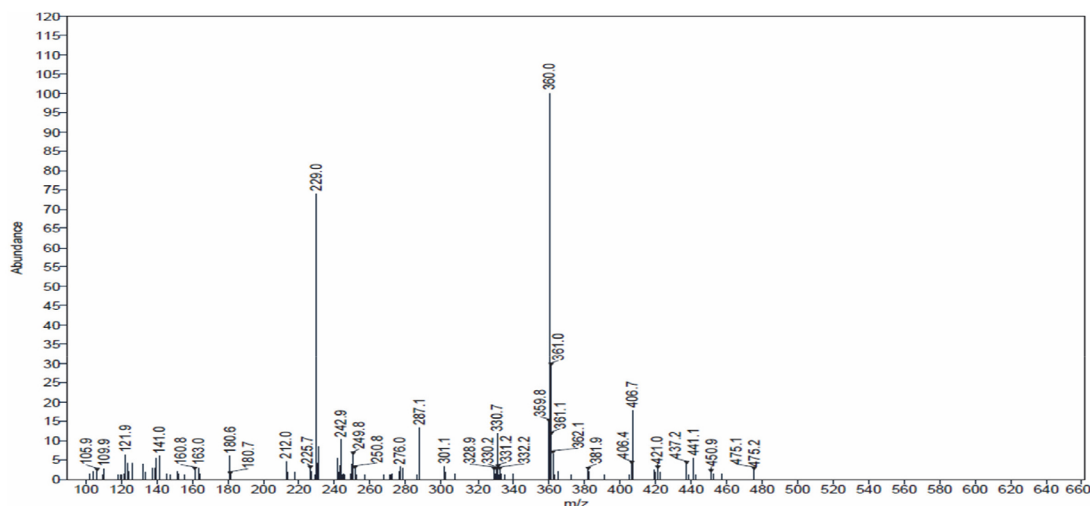


Figure 4. Mass spectrum of compound AL.

3. 1. 4. ¹H NMR and ¹³C NMR analysis

The ¹H-NMR spectrum of the ligand AL in DM-SO-*d*₆ shows the phenolic OH group in the offset region at 15.35 ppm (singlet),⁵⁶ and the azomethine proton at 9.09 ppm (singlet).^{51,52} The methyl group of the azomethine is situated at 2.52 ppm (singlet).^{56,57} The aromatic protons of the ligand AL are observed in the region between 5.82 and 8.89 ppm: H24 (s, 5.81 ppm, 1H), H6 (d, 6.47 ppm, 1H), H1 (dd, 6.55 ppm, 1H), H3 (d, 7.02 ppm, 1H), H19 (t, 7.48 ppm, 1H), H20 (dt, 8.17 ppm, 1H), H18 (dt, 8.64 ppm, 1H), H16 (t, 8.89 ppm, 1H).^{26,56} An additional peak at 2.13 ppm is attributed to -CH₃ protons.^{49,56} The signal relating to the methyl group of the pyranone ring is observed at 2.01 ppm.⁵⁶

The ¹³C NMR spectrum of AL shows two peaks appearing at 163.03, 163.60 ppm, which are attributed to the imine carbon atoms (C10, C11).⁵⁸ The aromatic carbons of AL are observed between 96.77 to 158.98 ppm: C14 (96.77 ppm), C24 (107.17 ppm), C3 (110.17 ppm), C1 (112.80

ppm), C19 (121.88 ppm), C5 (123.85 ppm), C15 (124.36 ppm), C6 (131.10 ppm), C20 (131.72 ppm), C2 (137.35 ppm), C4 (146.63 ppm), C16 (150.88 ppm), C4 (158.98 ppm).²⁶ The spectrum also shows three peaks corresponding to C21, C23 and C25 of the pyranone ring which appear further downfield due to the presence of electronegative groups ((HO-C-O), (H₃C-C-O), and (C=O)). Their peaks are observed at 175.72, 163.91, and 184.39 ppm, respectively.^{57,44} The C12 of the methyl group of the azomethine (H₃C-C=N-) is detected at 20.18 ppm and the C27 of the methyl group of the pyranone ring is observed at 19.73 ppm.⁵⁷ On the other hand, the C7 of the methyl group (CH₃) of the toluene is detected at 17.81 ppm.⁵⁰ The NMR data are collected in Table 1, 2.

Table 1. Experimental results of ¹H-NMR of AL

Comp	(OH)	(-CH ₃)	(H ₃ C-C=C-)	(H ₃ C-C=N-)	(-CH=N-)	(H _(1,3,6,16,18,19,20,24))
AL	15.35 (s, 1H)	2.13 (s, 3H)	2.01 (s, 3H)	2.52 (s, 3H)	9.09 (s, 1H)	5.82 to 8.89 (m, 8H)

(AL)

Table 2. Experimental results of ¹³C-NMR of AL

Comp	(-C=C-CH ₃)	(H ₃ C-C=N-)	(-CH=N-)	(H ₃ C-C=N-)	(CH ₃)	(HO-C-O)	(H ₃ C-C-O)	(C=O)	(C _{Aromatic carbons})
AL	19.73	163.60	163.03	20.18	17.81	175.72	163.91	184.39	96.77 to 158.98 (C _(1-6,14-16,18-20,24))

3. 2. Characterization by cyclic voltammetry

The cyclic redox voltammogram of a solution of compound AL at a concentration of 0.003 mol/L in acetonitrile in the presence of lithium perchlorate LiClO_4 0.1 mol/L on a glassy carbon electrode was studied between potentials from +1.8 to -2.5 V/SCE, in a nitrogen atmosphere at a rate of 0.1 V/s. Figure 5 shows an anodic peak at $E_{\text{pa}} = 1.491$ V/SCE, corresponding to the oxidation of the OH group.²⁶ During the cathodic scan, a peak is observed at $E_{\text{pc1}} = -1.494$ V/SCE corresponding to the reduction of the imine function ($\text{C}=\text{N}$), confirming the Schiff base compound. Under the same conditions, ferrocene has also been studied by means of cyclic voltammetry, showing reversible behavior ($\text{OxFc}/\text{RedFc}^+$) at 362.9/261.8 mV/SCE potentials with $E_{1/2} = 291.8$ mV/SCE (Figure 5).²⁵

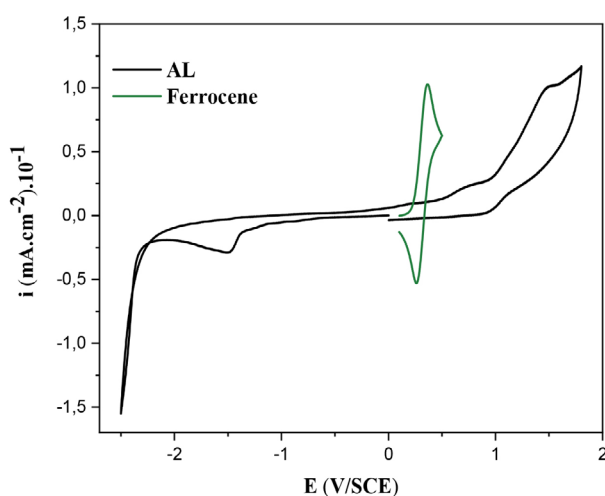


Figure 5. Cyclic voltammograms of the ligand AL and ferrocene in acetonitrile/ LiClO_4 0.1 M at a scan rate of 0.1 V/s.

3. 2. 1. Calculating the energies E_{HOMO} , E_{LUMO} and ΔE_{gap} of the ligand AL

A relationship between theoretical orbital energies and oxidation-reduction potentials can be established between the theoretical DFT calculation and the electrochemical behavior. The E_{HOMO} , E_{LUMO} and ΔE_{gap} energies of the AL ligand were calculated utilizing the oxidation and reduction potentials based on the subsequent relationships:

$$E_{\text{HOMO}} = -[E_{\text{ox}} - E_1(\text{ferrocene}) + 4.8] \quad (15)$$

$$E_{\text{LUMO}} = -[E_{\text{red}} - E_1(\text{ferrocene}) + 4.8] \quad (16)$$

$$\Delta E_{\text{gap}} = E_{\text{LUMO}} - E_{\text{HOMO}} \quad (17)$$

The calculated experimental values are $E_{\text{HOMO}} = -5.999$ eV, $E_{\text{LUMO}} = -3.014$ eV and the energy gap ($\Delta E_{\text{gap}} = 2.985$ eV) of the AL ligand.

3. 2. 2. Frontier molecular orbitals analysis

Understanding molecular reactivity and electronic characteristics largely depends on the lowest unoccupied molecular orbitals (LUMOs) and the highest occupied molecular orbitals (HOMOs).⁵⁹ The molecular frontier orbitals of the compound AL and their related energies are shown in Figure 6.

The way a molecule interacts with other species is largely determined by these frontier orbitals. The capacity to donate an electron is denoted by the HOMO and the capacity to accept an electron is denoted by the LUMO.⁶⁰ The reactivity of the compound under investigation is established by FMO analysis.^{61–64}

The reactivity of the molecule can be clarified through the LUMO and HOMO molecular orbitals. ΔE_{gap} is determined as the energy difference between the E_{HOMO} and E_{LUMO} . The decrease of the value of ΔE_{gap} , the more reactive the molecule.^{65,66} The values of the E_{HOMO} , E_{LUMO} , $E_{\text{HOMO}-1}$, $E_{\text{LUMO}+1}$ energies of the ligand AL found are -5.99; -2.07; -6.24; -1.6 eV, respectively. The energy gap $\Delta E_{\text{gap1}} = E_{\text{LUMO}} - E_{\text{HOMO}}$ equal to 3.92 eV on the other hand $\Delta E_{\text{gap2}} = E_{\text{LUMO}+1} - E_{\text{HOMO}-1}$ equal to 4.64 eV.

The theoretical results obtained show that the optimal ΔE_{gap} value of AL is 3.92 eV, which occurs between the HOMO and LUMO.

We note that the experimental value of ΔE_{gap} for AL is 2.985 eV. This aligns well with the theoretical values. We conclude that the chemical reactivity of the studied compound AL is high.⁶⁷

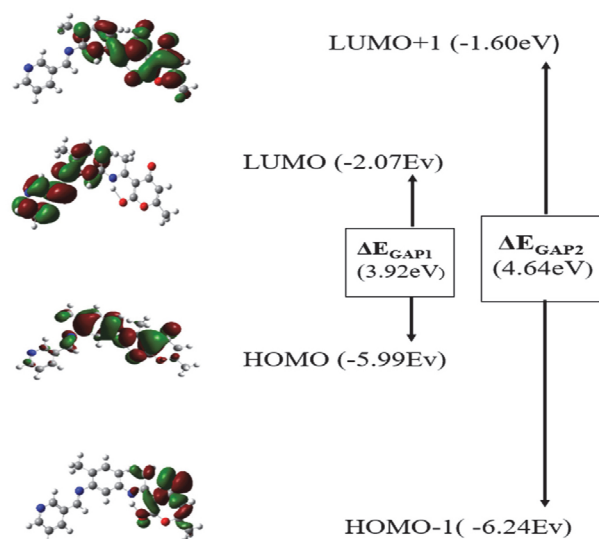


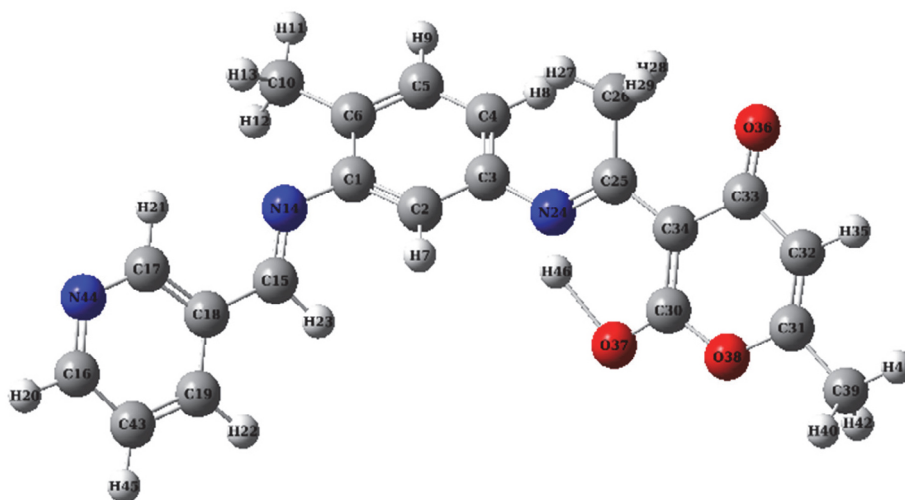
Figure 6. The ligand AL's frontier orbital molecules and the associated energies.

According to the Figure 6, the frontier molecular orbitals (HOMO, HOMO-1, LUMO and LUMO+1) of the ligand AL under study show the distribution of energy levels.

- The energy distribution of the HOMO for the ligand AL extends over the whole molecule, except for the pyridine group, the CH₃ group attached to C=N and the CH₃ group of the aromatic ring, as well as some of their carbon atoms.
- The energy level of HOMO-1 covers only the molecule iminoethyl-2-hydroxy-6-methyl-4H-pyran-4-one.
- The LUMO energy covers the molecule with the exception of the CH₃ groups of the aromatic ring and of iminoethyl-2-hydroxy-6-methyl-4H-pyran-4-one.
- The LUMO+1 energy covers the molecule with the exception of the CH₃ group of the aromatic ring and pyridin-3-ylmethylene-amino.

3. 3. Density functional theory (DFT) study

Gaussian 09W software were used to create the theoretical chemical structures of AL in order to predict their activities. Including the atomic labels, Figure 7 shows the optimized geometries of AL.



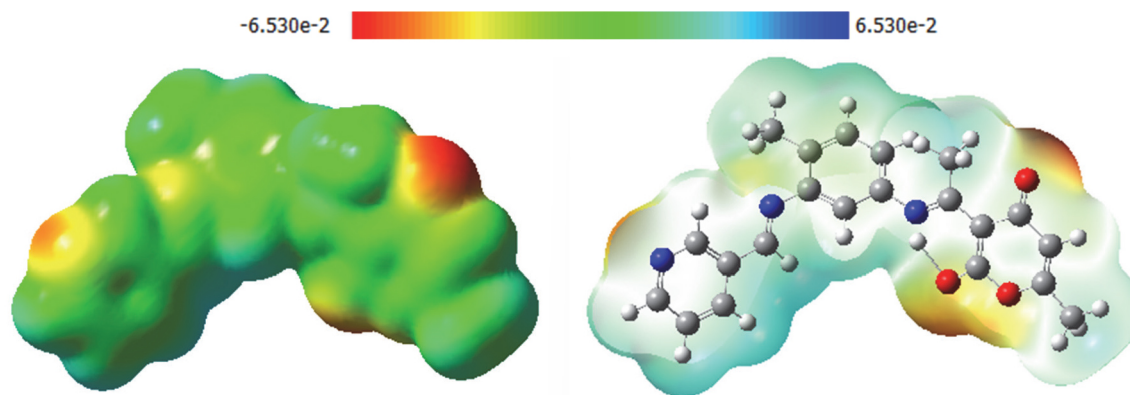


Figure 8. Molecular Electrostatic Potential (MEP) of Schiff base AL.

ferred to a large extent from the charge distribution on its surface.^{68,69} The oxygen and nitrogen atoms, along with the hydroxyl group of compound AL serve as the nucleophilic centers.

3. 3. 2. Mulliken charge and natural bond orbital (NBO) analysis

Mulliken charges and natural bond orbital studies are employed to ascertain the charge distribution in the molecular structure and to locate active sites. Natural bond orbital charge analysis is the most efficient technique for

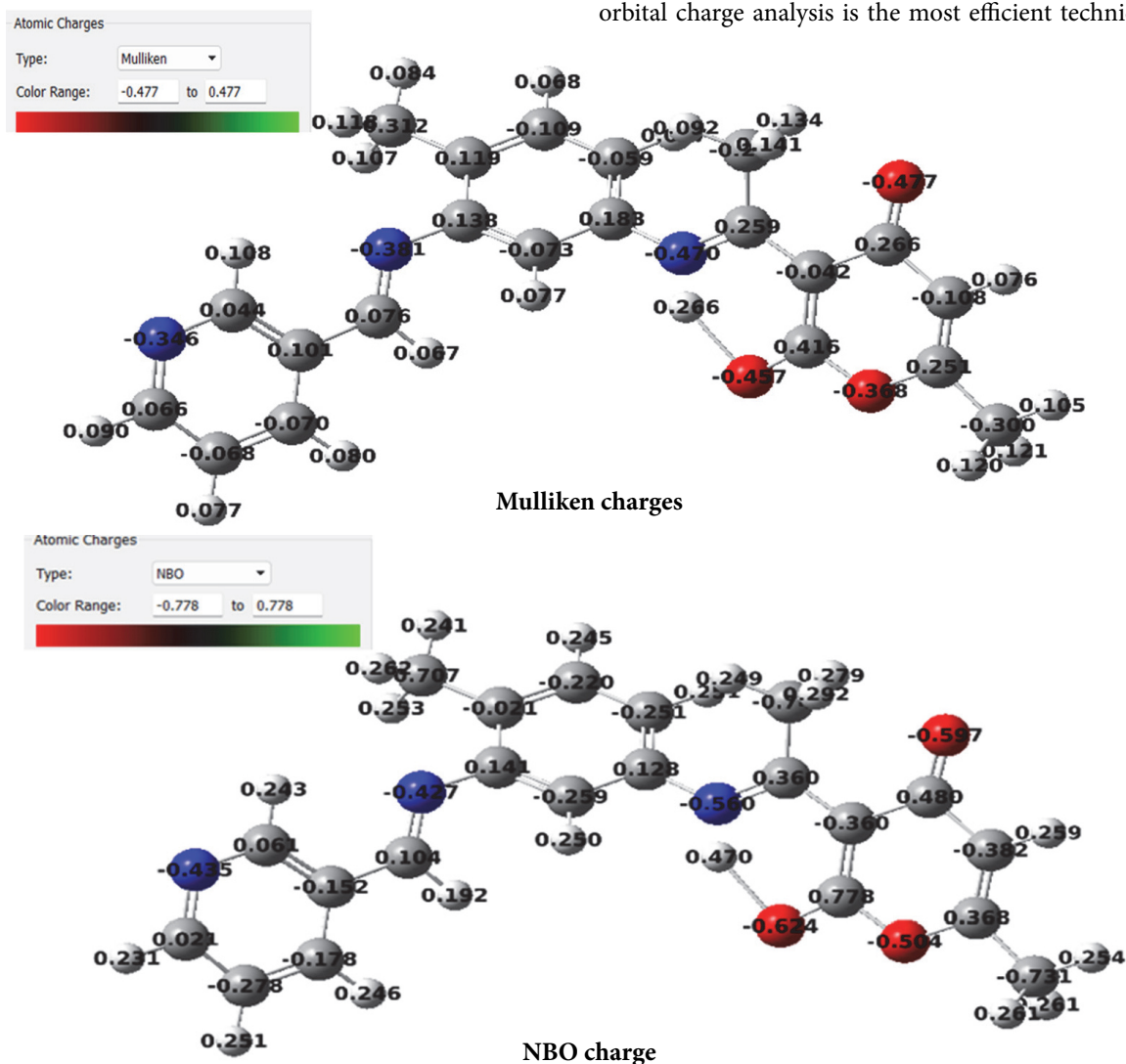


Figure 9. Mulliken charge density and NBO atomic charge of the AL ligand.

examining intramolecular and intermolecular bonding and atomic interactions. It additionally offers insights into charge transfer within molecular systems.²⁶ For the investigated Schiff base (AL), the natural distribution of atomic charges for all atoms is shown in Figure 9. The results show that nitrogen and oxygen atoms possess the highest negative charges, which are attributable to molecular relaxation.⁴¹ In addition, the hydrogen atoms have most of the positive charges. Negative charges are located at O36, O37, N38 and N14, N24, N44 for the ligand AL, which can lead to electronic interactions with the free radical.

3. 4. Evaluation of the antioxidant activity

Antioxidants come into contact with free radicals by Hydrogen Atom Transfer (HAT), where the free radical extracts a hydrogen atom from the antioxidant, and by single electron transfer (SET), where the antioxidant donates an electron to reduce radicals, metals and carbonyls. An antioxidant response can involve both mechanisms (HAT and SET).⁸⁰ Due to the involvement of many processes in the neutralization of free radicals, the use of a single experiment is insufficient to evaluate the entire antioxidant capacity.⁸¹ To accurately assess the overall antioxidant efficacy of compound AL, nine separate studies were conducted. The IC₅₀ and A_{0.5} values of the compound AL and the standards were determined.

3. 4. 1. ABTS Scavenging assay for cation radicals

The antioxidant response is accompanied by faster reaction kinetics, making the ABTS test one of the most sensitive methods for assessing antioxidant activity.⁸² The foundation of this technique is the antioxidant's capacity to stabilize the colored cationic radical ABTS, which is initially formed when an oxidant oxidizes ABTS. Spectro-

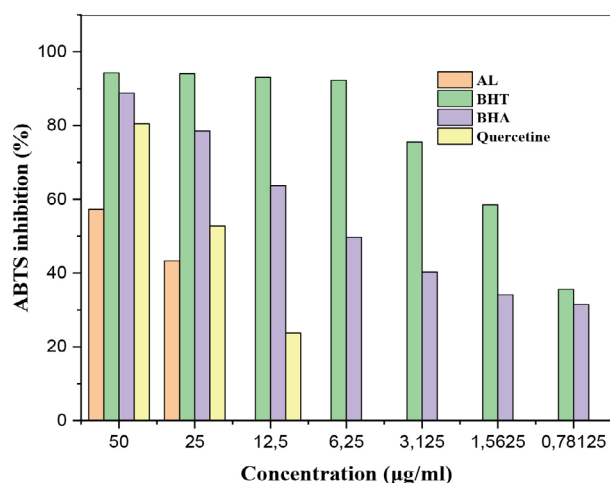


Figure 10. Percentage of inhibition in ABTS⁺ radical scavenging activity of AL at varying doses.

photometric monitoring is employed to track how the antioxidants in the compound AL reduce this radical.

The results indicate that the inhibition rate of ABTS is directly related to the concentration of the synthesized product AL and the standards used. When the concentration of the studied compound increases in the reaction medium, the inhibition rate gradually rises. The antioxidant activity of the compound AL was considerable. The IC₅₀ value was 37.15 µg/mL, demonstrating a remarkable capacity to scavenge ABTS radicals (Figure 10).

These results are notable in comparison to the standards. The compound AL showed a good free radical scavenging activity. ABTS is soluble in both organic and aqueous solvents.

3. 4. 2. *ortho*-Phenanthroline test

The reductive capacity of compound AL was examined using the phenanthroline test. With an A_{0.5} value of 30.54 µg/mL, close to the standards, it can be observed that the absorbance of phenanthroline inhibition increases with the concentration of the synthesized compound (AL) (Figure 11). The phenanthroline test, which measures the reduction of metallic iron, confirmed the antioxidant potential of compound AL and demonstrated its good antioxidant activity in comparison to the standards.

In this activity, Fe³⁺ can be reduced to Fe²⁺ thanks to the reducing agents in the Schiff base AL. The latter combines with orange-red phenanthroline to form a stable complex.⁸³

Polyphenols antioxidant capacity depends on the degree of hydroxylation and conjugation of phenolic compounds.⁸⁴

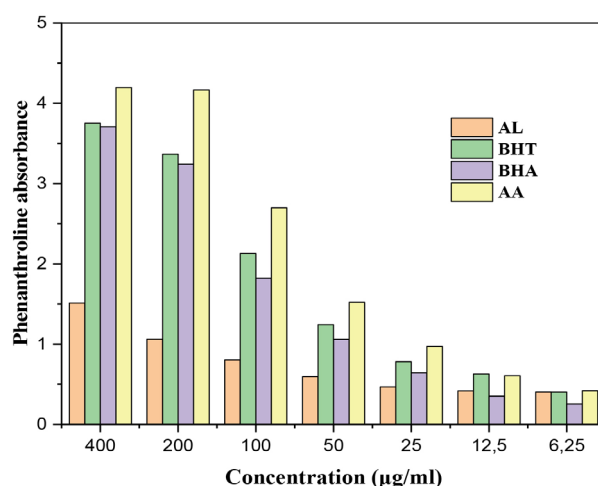


Figure 11. Percentage of inhibition in *ortho*-phenanthroline assay of AL at varying doses.

3. 4. 3. Reducing Power (FRAP)

Another significant antioxidant process is the reduction of metals (copper and iron). This characteristic is frequently used to investigate a substance's capacity to interact

with metals in order to reduce them, from complexes, and transform them into more stable and non-reactive compounds.⁸⁵ The absorbance of the metal complexes produced is typically used to measure the reducing power of antioxidants on metals. The antioxidant constituent in the iron-reducing power assay converts potassium ferricyanide to potassium ferrocyanide, which combines with ferric chloride to form a colored complex.⁸⁶ The reducing ability of the synthesized compound AL was observed to be directly proportional to its concentration. The value of $A_{0.5}$ represents the iron and copper reduction capacity results of compound AL (Figure 12), according to Table 4. The copper reducing ability of compound AL is low, as shown by its $A_{0.5}$ value of 270.56 $\mu\text{g/mL}$ in comparison to the standards.

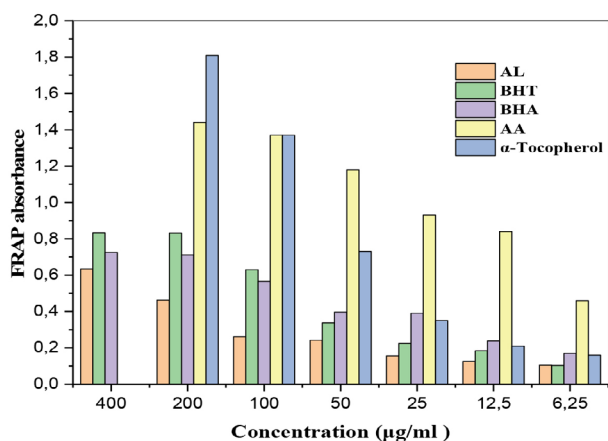


Figure 12. Percentage of inhibition in reducing power activity of AL at varying doses.

3. 4. 4. Silver nanoparticle (SNP) assay

In the silver nanoparticle test, silver salts are converted into Ag^0 silver nanoparticles (SNPs) by the reduction of Ag^+ ions. The compound AL showed good antioxidant activity, as indicated by a value of 19.54 $\mu\text{g/mL}$, surpassing the efficacy of BHA and ascorbic acid (Figure 13).

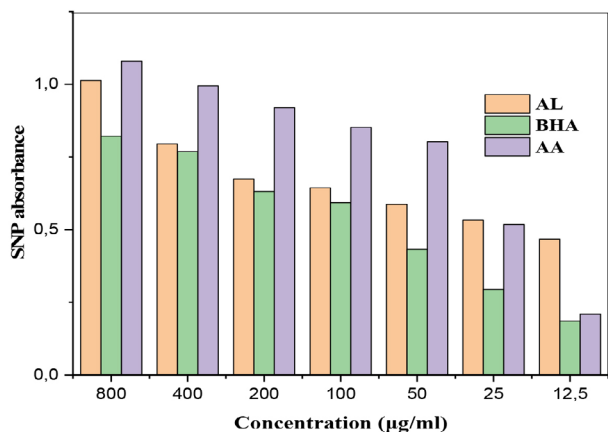


Figure 13. Percentage of inhibition in silver nanoparticle (SNP) assay of AL at varying doses.

According to Figure 13, it is observed that the inhibition rate of AL, ascorbic acid and BHT increases with increasing concentration.

3. 4. 5. Superoxide radical scavenging (SRS)

Our Schiff base AL has good antioxidant activity with IC_{50} 86.65 $\mu\text{g/mL}$, which is lower than that of standard ascorbic acid, according to the superoxide radical scavenging study (Figure 14). It is observed that when the concentration of the studied compound increases in the reaction medium, the inhibition rate progressively rises.

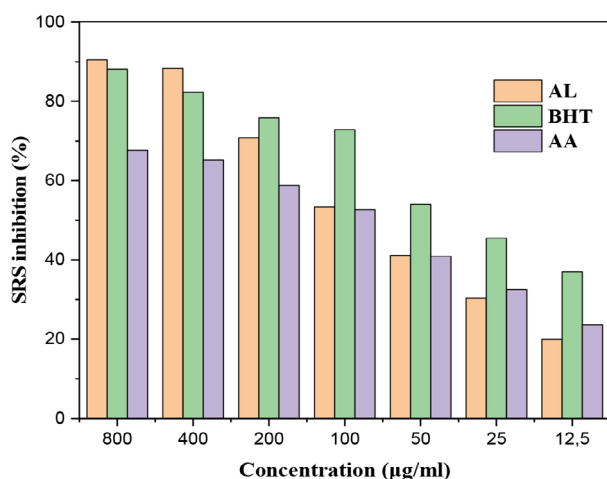


Figure 14. Percentage of inhibition in superoxide radical scavenging activity of AL at varying doses.

In conclusion, the results of the antioxidant evaluation of the tested assays (ABTS, phenanthroline, FRAP, SNP, and superoxide radical scavenging) showed good antioxidant activity for the ABTS, phenanthroline, superoxide radical scavenging and SNP tests for Schiff base AL. However, the FRAP assay showed lower activity (Table 4).

3. 4. 6. Electrochemical behavior of the superoxide radical in the presence of AL and BHT

The electrochemical properties of the superoxide radical were studied *via* cyclic voltammetry at a concentration of 10^{-3} M for the compounds AL and BHT in acetonitrile medium, in the presence of LiClO_4 (0.1 M). According to the results obtained for compound AL in the Figure 5 ($E_{\text{pa}} = 1.491$ V/SCE, $E_{\text{pc}} = -1.494$ V/SCE), it can be seen that the compound is inactive in the range -1.2 to 0.6 V/SCE. This allowed us to study the electrochemical behavior of compound AL with the superoxide radical within this range of potentials (-1.2 to 0.6 V/SCE).

In the absence of molecular oxygen, the cyclic voltammogram showed no electrochemical response (Figure 15). However, in the presence of oxygen, the superox-

Table 4. Antioxidant activity of compound AL.

Substances	ABTS IC ₅₀ mM ^a	Phenanthroline A _{0.50} mM ^a	FRAP A _{0.50} mM ^a	SNP A _{0.50} mM ^a	SRS IC ₅₀ mM ^a
AL	37.15 ± 0.68	30.54 ± 0.27	270.56 ± 2.93	19.54 ± 0.86	86.65 ± 5.51
BHT ^b	1.55 ± 0.26	9.10 ± 0.17	76.80 ± 0.60	N.T.	39.46 ± 0.94
BHA ^b	7.54 ± 0.67	18.54 ± 0.25	78.61 ± 1.76	73.46 ± 0.13	N.T.
AA ^b	N.T.	8.96 ± 0.1	6.77 ± 1.15	24.73 ± 0.16	88.43 ± 0.83
EDTA [*]	N.T.	N.T.	N.T.	N.T.	N.T.
Quercetine [*]	24.31 ± 0.32	N.T.	N.T.	N.T.	N.T.
α-Tocopherol [*]	N.T.	N.T.	34.93 ± 2.38	N.T.	N.T.

^a The values are the means ± S.D. of three measurements taken in parallel. ($p < 0.05$). N.T.: not tested.

^b References compounds.

ide radical showed a reduction peak at -0.931 V/SCE and an oxidation peak at 0.312 V/SCE, the latter attributed to oxygen reoxidation (Figure 15). The redox couple ($O_2 / O_2^{\bullet -}$) is irreversible.⁸⁷

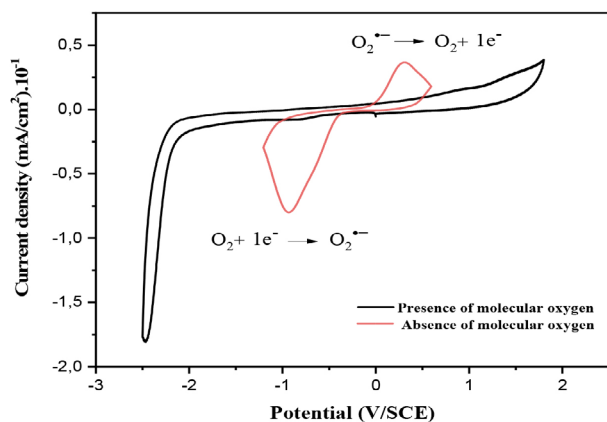


Figure 15. Cyclic voltammograms in acetonitrile and 0.1 M LiClO₄, both absence and presence of molecular oxygen.

A study of the electrochemical behavior of the $O_2^{\bullet -}$ radical in the absence and presence of the BHT and AL samples (concentration of 10^{-3} M) shows a decrease in the anodic and cathodic current (Figure 16). This indicates that BHT and compound AL interact with the $O_2^{\bullet -}$ radical. The reaction mechanism has been delineated theoretically.³⁸

The $O_2^{\bullet -}$ is produced by the reduction of an electron with molecular oxygen dissolved in the solution:



The antioxidant (BH) undergoes an electrochemical reaction with the superoxide anion radical as follows:

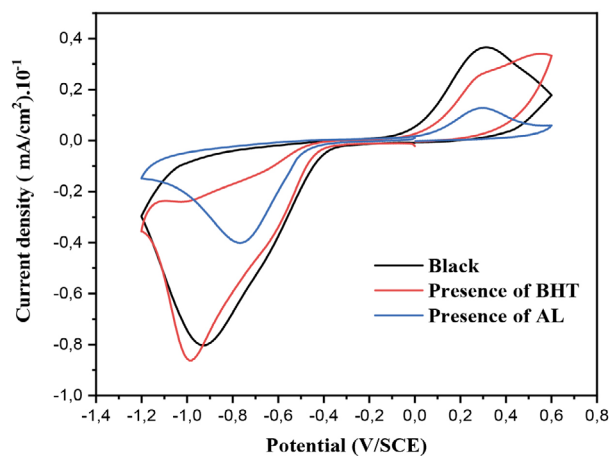
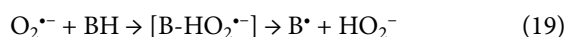


Figure 16. Cyclic voltammograms of 0.1 M acetonitrile/LiClO₄ with $O_2^{\bullet -}$, in the absence and presence of AL and BHT compounds.

Effect of Concentration

The electrochemical study of the superoxide anion radical in the presence of the AL compound and the BHT standard indicates a diminution in anodic current densities with increase in concentration (Figure 17).⁸⁸ To determine the $RSO_2^{\bullet -}$ %, the binding constant (K_b) and the Gibbs free energy (ΔG°), we studied the effect of the concentration of compound AL and BHT.

The binding constant (K_b) was determined by plotting the logarithmic curves $\log(1/C_{\text{test}}) = f(\log(i_{\text{pa}}/i_{\text{pa}}^\circ))$ from equation (13) (Figure 18). Extrapolation of these curves allowed the determination of the constant K_b of AL and BHT.

Equation (12) was utilized to calculate the $RSO_2^{\bullet -}$ % of the tested compound AL and BHT (Table 5). An increase in the concentration of the tested products corresponds with a rise in the $RSO_2^{\bullet -}$ %.

– The Gibbs free energy values (ΔG°) were derived from equation (14).

– The results for the binding constant and Gibbs free energy are summarized in Table 6.

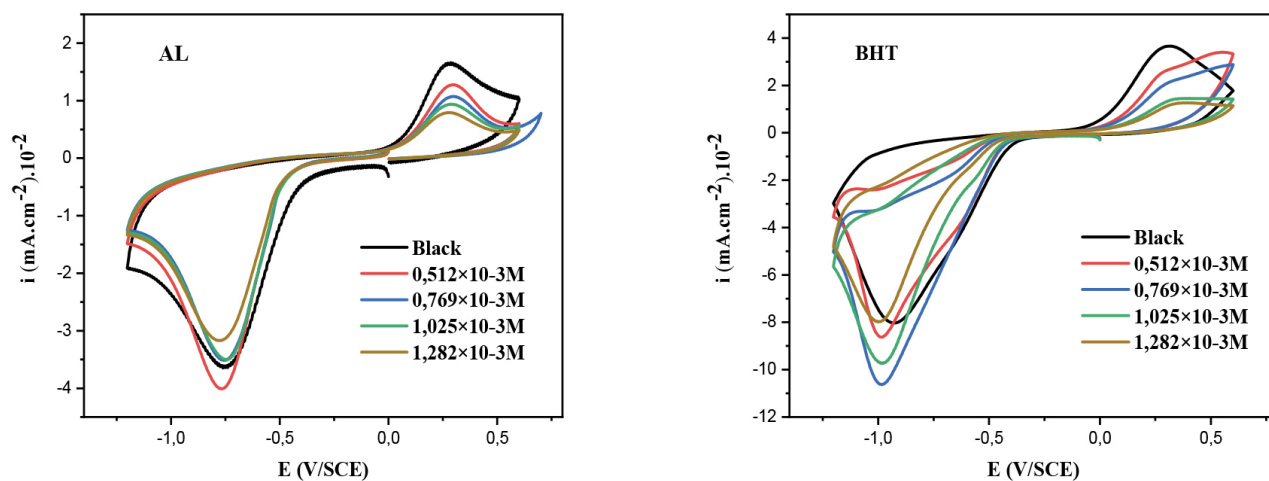


Figure 17. Cyclic voltammograms of $O_2^{\bullet-}$ with varying concentrations of AL and BHT in acetonitrile/LiClO₄ 0.1 M medium.

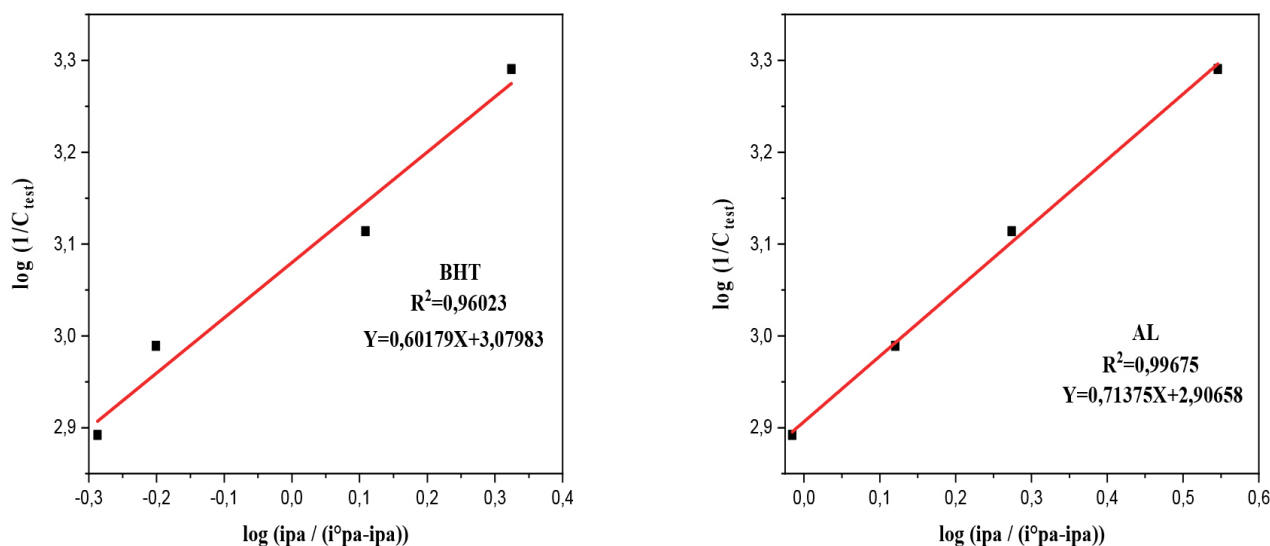


Figure 18. Plots of $\log (1/C_{\text{test}})$ versus $\log (i_{\text{pa}} / (i^{\circ}_{\text{pa}} - i_{\text{pa}}))$ for AL and BHT.

Table 5. Values of concentration, current density and RSAO₂^{•-} (%) of AL and BHT compounds.

Compounds C. 10 ⁻³ (M)	BHT		AL	
	$i_{\text{pa}} \cdot 10^{-1}$ (mA/cm ²)	RSAO ₂ ^{•-} (%)	$i_{\text{pa}} \cdot 10^{-1}$ (mA/cm ²)	RSAO ₂ ^{•-} (%)
Blank	0.370	–	0.167	–
0.512	0.251	32.16	0.130	40.44
0.769	0.208	43.78	0.109	61.79
1.025	0.143	61.35	0.095	64.04
1.282	0.126	65.94	0.082	67.41

The compound with a high K_b constant shows a powerful interaction with the radical.⁸⁹ This ensures a robust interaction between the antioxidant and the superoxide radical. Negative ΔG° values demonstrate the spontaneity of the free radical reaction.

Table 6. Thermodynamic parameters of the AL and BHT compounds.

Compounds	BHT	AL
K_b (M ⁻¹)	1201.8	806.4
$-\Delta G^{\circ}$ (kJ·mol ⁻¹)	24.872	23.88

3. 4. 7. Anti-inflammatory activity

Protein denaturation is indeed one of the fundamental characteristics of inflammation, which occurs when proteins undergo denaturation of their tertiary and secondary structures due to external stresses or substances like ROS.

Denatured proteins frequently lose their biological role and cause dysregulation of the inflammatory response, which can lead to rheumatic and inflammatory illnesses.⁹⁰

According to Figure 19, the percentage of inhibition in albumin denaturation activity increases with the increase in concentration. We investigated the anti-inflammatory potential of compound AL by evaluating its influence on protein denaturation *in vitro*. The compound AL was observed to have a good anti-inflammatory activity ($IC_{50} = 2.67 \pm 0.10 \mu\text{g/mL}$) compared to the standard diclofenac ($IC_{50} = 1.21 \pm 0.12 \mu\text{g/mL}$) (Figure 19).

The anti-inflammatory effect noted in this study is due to the phenolic compounds abundant in compound AL.⁹¹

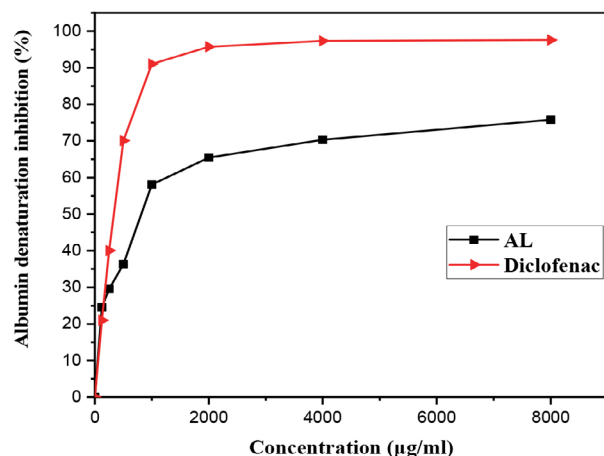


Figure 19. Percentage of inhibition in albumin denaturation activity of AL at varying doses.

3. 5. Docking of molecules

3. 5. 1. Assessment of the ADME-T activity

The drug-likeness of the synthesized compounds was assessed in comparison to the standards BHA, BHT, and quercetin in accordance with Lipinski's rule. Generally, an orally active drug fulfils the following criteria: a molecular weight (MW) under 500 D, a maximum of ten hydrogen bond acceptors (n-ONs), no more than five hydrogen bond donors (n-OH and n-NH), a single permissible violation, and an octanol-water partition coefficient (milogP) not above 5.⁹²

According to Table 7, the results illustrate that compound AL adheres to Lipinski's principles, demonstrating

favorable solubility, whereas quercetin shows one violation, which presents potential concerns of mutagenicity and irritation. Conversely, in the toxicity profile, AL was categorized as a relatively safe compound, with the exception of the standards, which indicated a potential risk of toxicity. The assessed compound demonstrated no toxicity risk. Consequently, it does not induce any tumorigenic, irritation, reproductive or mutagenic effects. The study results suggest that the synthesized Schiff base AL possesses favorable ADME-T characteristics and may serve as a potential therapeutic candidate.

3.5.2. Molecular docking analysis

Molecular docking simulations have elucidated the various interactions and their energies between amino acids and an inhibitor within the active sites of enzymes. This analysis illustrates the energy distribution of the various interactions between Apro and the ligand AL. Table 8 summarizes the interactions between the active amino acids of the target receptor (Apro) and AL.⁹³

Table 8. Comparison of the affinity of AL with selected standards.

Compounds	Binding energy (Kcal/mol)
AL	-10.6
BHA*	-7.1
BHT*	-7.1
Quercetine*	-8.2

*: Drugs Reference.

The crystal structure of the optimal docked poses for the Apro-AL complex is depicted in Figure 20. The tested ligand predominantly interacts with the exterior region of Apro.⁴¹ The binding interaction diagrams of AL in both 3D and 2D formats with the major 4GCA protease are presented in Figure 21. Hydrogen bonds are crucial for the interaction between inhibitors and receptors. Analysis of the 3D and 2D interaction diagrams indicates the presence of the following types of interactions:

Table 9 demonstrates that the AL ligand forms five hydrogen bonds with Ile260 (1.77 Å), Lys262 (2.16 Å), and Lys21 (1.95 Å) *via* hydrogen and oxygen atoms, carbonyl

Table 7. Computed pharmacokinetic and physicochemical properties (ADME-T) of the synthesized compounds, crucial for oral bioavailability.

Compounds	solubility	n-rotb	miLog P < 5	MW < 500	TPSA (oA)	nOHNH < 5	nON < 10	vio	MV	Toxicity risks			
										Tumo	Irr	R,E	Mut
AL	-4.96	4	2.50	361.40	88.05	1	6	0	376.46	No	No	No	No
BHA*	-2.50	2	2.83	180.25	29.46	1	2	0	199.93	Yes	No	No	No
BHT*	-3.98	2	4.82	220.35	20.23	1	1	0	260.32	Yes	Yes	Yes	Yes
Quercetine*	-2.49	1	1.49	302.24	131.36	5	7	0	282.77	Yes	No	No	Yes

*: Drugs Reference, Number of rotatable bonds (n-rotb); Topological polar surface area (TPSA); Logarithm of partition coefficient between n-octanol and water (miLogP); Molecular weight (MW); Number of hydrogen bond acceptors (n-ON); Number of hydrogen bond donors (n-OH/NH); Lipinski's violation (vio); Molecular volume (MV) (Tumo): tumorigenic (Irr): irritant (R,E): reproductive effective. (Mut): mutagenic.

group respectively, and with Ser210 (2.80 Å), Cys298 (3.63 Å) *via* the nitrogen of the imine groups, it also exhibits four π -alkyl interactions with Lys262 (4.35 Å) and Cys298 (4.97 Å), acting on the pyran and pyridine rings respectively, and His110 (4.09 Å), Tyr209 (4.48 Å), which interact with methyl group, an alkyl type interactions are observed with Leu212 (3.82 Å), Pro215 (4.76 Å), and Lys77 (5.44 Å) *via* methyl groups, a π - π T-shaped type of Trp111 (5.03 Å) with pyridine group, a carbon hydrogen bond with Pro211 (3.44 Å) *via* OH function, a π - π stacked interaction of Tyr209 (3.76 Å) with the benzene group.

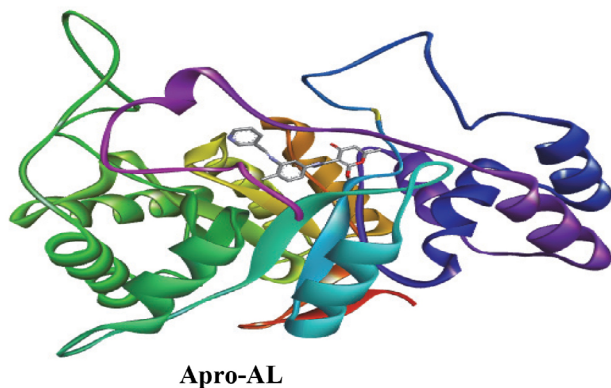


Figure 20. Optimal visualization of the docked poses of AL with the 4GCA main protease.

For the standard BHA, there are two hydrogen bonds with Gln193 (1.91 Å) and Tyr48 (1.98 Å) *via* OH function. π -Alkyl of Tyr209 (4.05 Å) and Trp20 (4.77 Å) reacts with *tert*-butyl group, and Trp20 (5.03 Å) with methyl group, a π - σ interaction occurs with Tyr209 (3.64 Å) and Tyr209 (3.66 Å) *via* methyl groups and Tyr209 (3.68 Å) react with the benzene group, a carbon hydrogen bond with Ser214 (3.59 Å) which interacts with methyl group, and a π -donor hydrogen bond with Ser210 (3.23 Å), interacting with the benzene group.

For BHT, it was found to interact with a six π -alkyl of Trp20 (4.13 Å), His110 (5.15 Å), Tyr48 (5.19 Å) with methyl group and Trp20 (4.91 Å), Trp219 (5.19 Å), Trp111 (5.23 Å) with the *tert*-butyl groups, alkyl interaction with Val47 (5.53 Å) *via* the *tert*-butyl group, and a π - π stacked interaction occurs between of Trp20 (4.44 Å) and the benzene group.

For quercetine, there are three hydrogen bonds of Val47 (2.06 Å), Cys298 (2.42 Å) and Gln183 (2.49 Å) with OH functions, a π -cation interaction with His110 (2.78 Å) *via* the benzene group, two π -sulfur interactions with Cys298 (4.40 Å) and Cys298 (5.60 Å) involving the benzene and benzopyran rings respectively, a π - π stacked with Trp20 (4.08 Å), Trp20 (4.95 Å) involving the benzopyran ring, a π - π T-shaped interaction with Trp20 (4.79 Å) involving the benzene ring, and a π -alkyl interaction occurs between Val47 (4.76 Å) and the benzopyran ring.

Table 9. Results of molecular docking, outlining interactions and distances of the analyzed AL with the major protease of 4GCA.

Substances	Interactions of Amino Acids	Distance (Å)	Type of the interaction
AL	– Ile260, Lys21, Lys262	1.77, 1.95, 2.16	Conventional Hydrogen Bond
	Ser210, Cys298	2.80, 3.63	Conventional Hydrogen Bond
	– His110, Lys262, Tyr209	4.09, 4.35, 4.48	π -Alkyl
	Cys298	4.97	π -Alkyl
	– Leu212, Pro215, Lys77	3.82, 4.76, 5.44	Alkyl
	– Trp111	5.03	π - π T-shaped
	– Pro211	3.44	Carbon Hydrogen Bond
	– Tyr209	3.76	π - π Stacked
BHA*	– Gln193, Tyr48	1.91, 1.98	Conventional Hydrogen Bond
	– Tyr209, Trp20, Trp20	4.05, 4.77, 5.03	π -Alkyl
	– Tyr209, Tyr209, Tyr209	3.64, 3.66, 3.68	π -Sigma
	– Ser214	3.59	Carbon Hydrogen Bond
	– Ser210	3.23	π -Donor Hydrogen Bond
BHT*	– Trp20, Trp20, His110	4.13, 4.91, 5.15	π -Alkyl
	Tyr48, Trp219, Trp111	5.19, 5.19, 5.23	π -Alkyl
	– Val47	4.53	Alkyl
	– Trp20	4.44	π - π Stacked
Quercetine*	– Val47, Cys298, Gln183	2.06, 2.42, 2.49	Conventional Hydrogen Bond
	– His110	2.78	π -Cation
	– Cys298, Cys298	4.40, 5.60	π -Sulfur
	– Trp20, Trp20	4.08, 4.95	π - π Stacked
	– Trp20	4.79	π - π T-shaped
	– Val47	4.76	π -Alkyl

*: Drugs Reference.

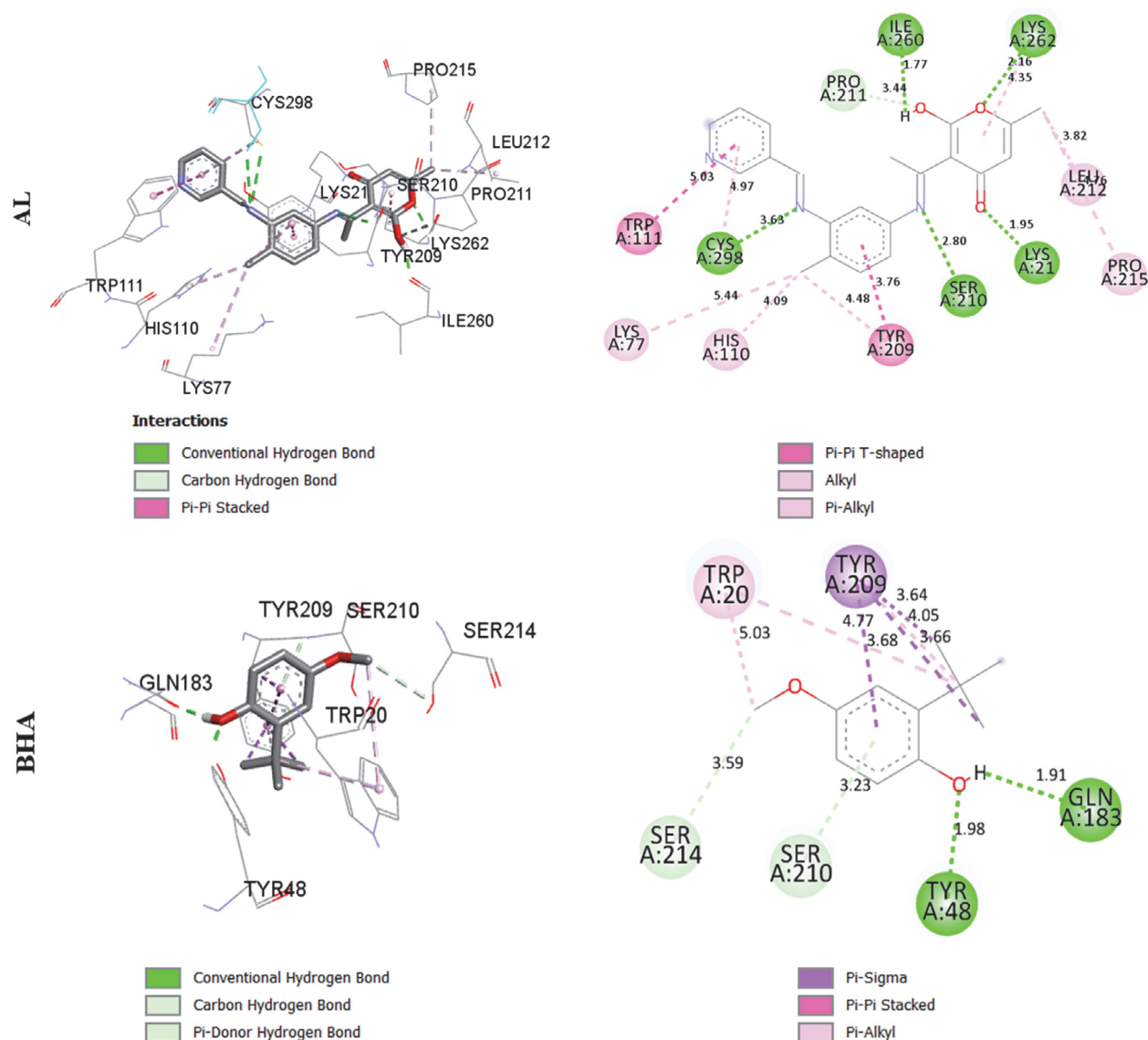


Figure 21. Three-dimensional and two-dimensional binding interaction diagrams of AL, BHA, BHT, and quercetin with the 4GCA main protease.

π - π cation and π -alkyl interactions are classified as hydrophobic van der Waals forces, whereas hydrophilic interactions involve hydrogen bonding forces.^{41,94} The presence of hydrogen bonds is crucial for the interaction between the inhibitor and the receptor. The theoretically computed interactions of the inhibitor-receptor complex have yielded highly favorable results. Thus, we may assert that the chemical AL exhibits significant inhibitory activity.

Table 8 compiles comparative values of binding energies of the substances in the following sequence: AL > quercetin > BHA and BHT. As a result, the examined ligand exhibited superior inhibitory efficacy against the 4GCA main protease compared to the standard compounds.

The amino acids demonstrated a more significant reaction at the nucleophilic sites (methyl groups). Figure 22 displays the interactions with the molecular surface adja-

cent to the examined ligands at the binding site of Apro. Consequently, the green area signifies the electron acceptor zone, whereas the pink area denotes the electron donor region. The assessed interactions between the inhibitor and receptor complex yielded highly favorable results.⁹⁵

4. Conclusion

This study describes the synthesis of a novel bioactive Schiff base. The resulting compound exhibited an elevated melting point, and its structure was elucidated utilizing LC-MS, IR, UV-Vis, ¹H and ¹³C NMR, and electrochemical analysis by cyclic voltammetry techniques.

In addition, a quantum chemical analysis of the Schiff base AL was performed using the DFT approach with the B3LYP/6-31G'(d,p) basis set. The theoretical re-

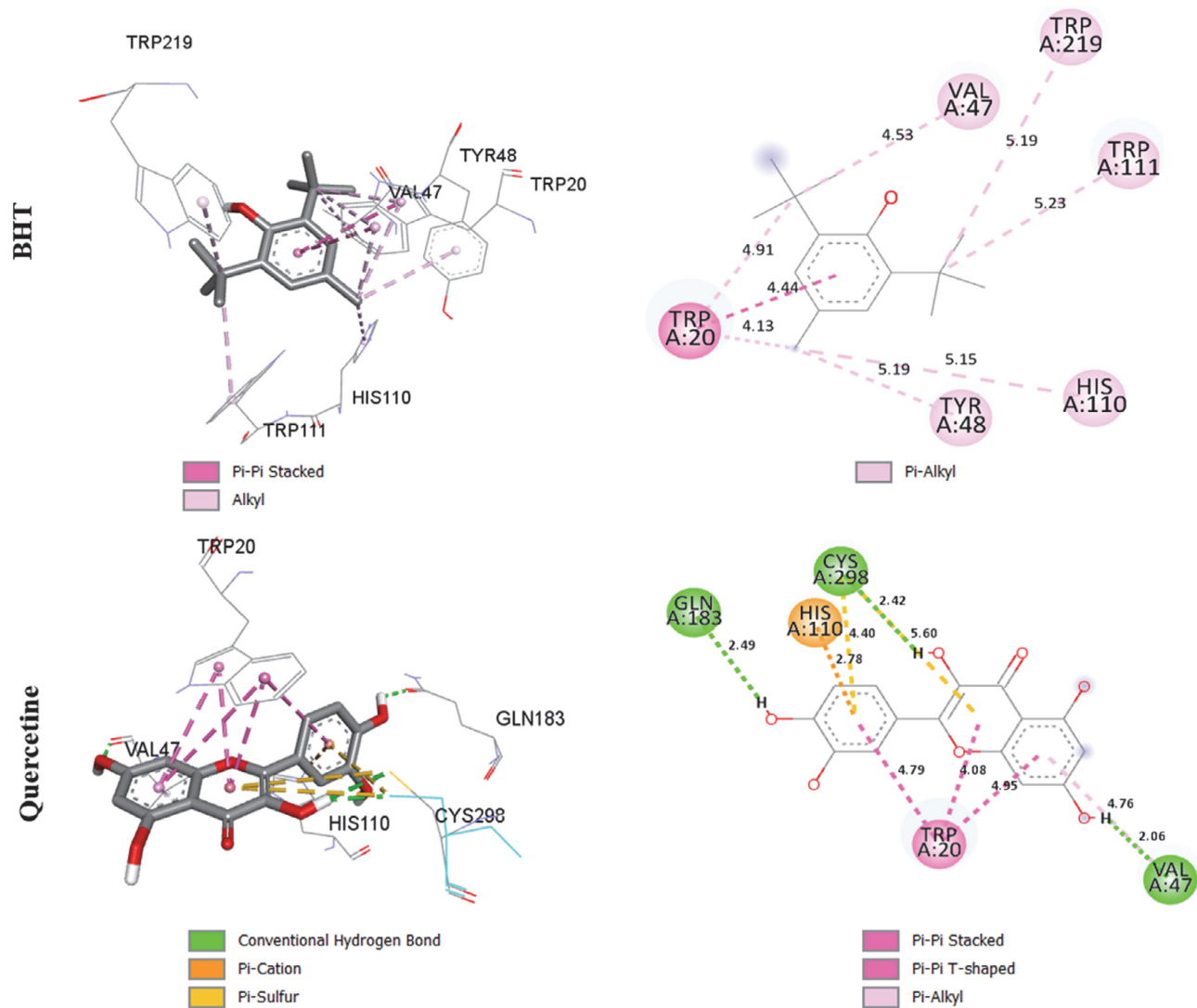


Figure 21. Continued.

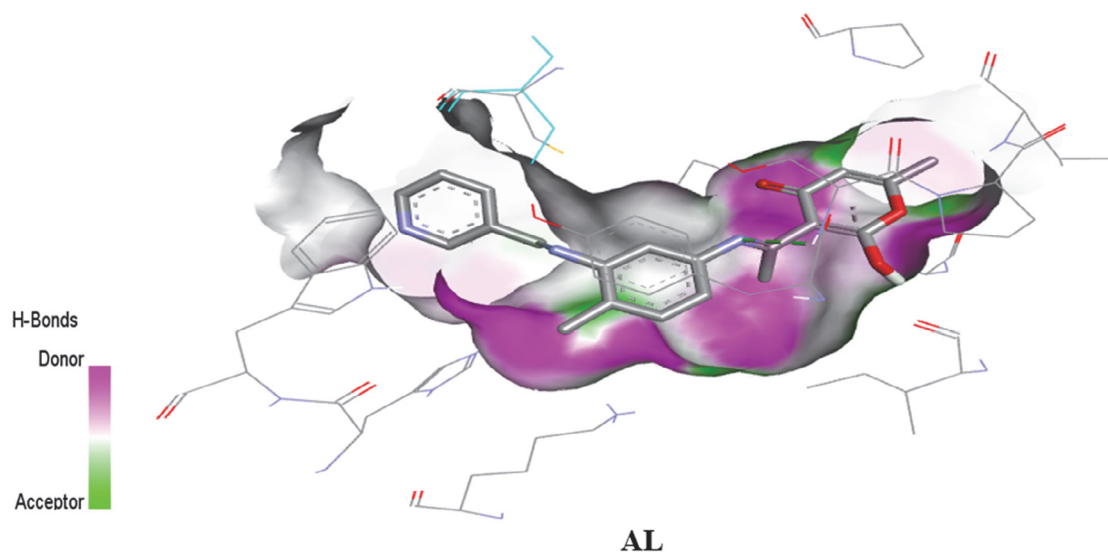


Figure 22. Interaction of the AL ligand with its molecular surface representation within the active site pocket.

sults from IR and UV-Vis correlated well with the experimental data. Furthermore, the E_{HOMO} values suggest that AL acts as an electron donor, facilitating electron transfer to the acceptor species. The derived value of ΔE_{gap} indicated the high reactivity of AL. The MEP analysis showed that the oxygen and nitrogen atoms, together with the hydroxyl group of compound AL, function as nucleophilic sites. The NBO charge analysis indicated that the oxygen and nitrogen atoms have the most negative charge.

In vitro investigation of the antioxidant efficacy of the tested compound AL revealed excellent activity in ABTS, phenanthroline, SNP and SRS assays and moderate activity in the FRAP assay compared to standards. AL showed good anti-inflammatory activity compared to diclofenac.

The cyclic voltammetry study allowed us to measure the scavenging effect on the superoxide anion radical and to indicate the significant interaction between $O_2^{\cdot -}$ and compound AL, which is quantified by the high K_b values obtained. The negative ΔG° value confirms the spontaneity of the antiradical reaction. The mechanism of the antiradical reaction involves the transfer of hydrogen atoms.

The anticipated ADME-T and pharmacokinetic properties suggest that this compound possesses favorable oral bioavailability and exhibits significant biological activity. The biological investigation indicated that AL may serve as a promising new class of radical scavengers and oxidative stress inhibitors, potentially leading to the development of effective and safe pharmaceuticals. On the other hand, the Apro-AL docking calculations demonstrated the ability of the AL compound to inhibit the main protease 4GCA. Finally, the docking results suggested that the AL compound under investigation could be developed as a therapeutic agent.

5. References

1. H. Schiff, *Justus Liebigs Ann. Chem.* **1864**, 131, 118–119. DOI:10.1002/jlac.18641310113
2. M. Tümer, *J. Coord. Chem.* **2007**, 60, 2051–2065. DOI:10.1080/00958970701236727
3. S. S. Sayed, S. Dawood, K. Ibrahim, A. Sajjad, A. Umar, R. ur Atiq, *Biointerface Res. Appl. Chem.* **2020**, 10, 6936–6963. DOI:10.33263/BRIAC106.69366963
4. S. Muhammad, A. Bashir, A. Saeed, *FUDMA J. Sci.* **2024**, 8, 343–348. DOI:10.33003/fjs-2024-0804-2704
5. G. Ceyhan, C. Çelik, S. Uruş, İ. Demirtaş, M. Elmastaş, M. Tümer, *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2011**, 81, 184–198. DOI:10.1016/j.saa.2011.05.106
6. C. M. Da Silva, D. L. Da Silva, L. V. Modolo, R. B. Alves, M. A. De Resende, C. V. B. Martins, Â. De Fátima, *J. Adv. Res.* **2011**, 2, 1–8. DOI:10.1016/j.jare.2010.05.004
7. A. Jarrahpour, M. Motamedifar, K. Pakshir, N. Hadi, M. Zarei, *Molecules* **2004**, 9, 815–24. DOI:10.3390/91000815
8. Y. Zhang, B. Zou, Z. Chen, Y. Pan, H. Wang, H. Liang, X. Yi, *Bioorg. Med. Chem. Lett.* **2011**, 21, 6811–6815. DOI:10.1016/j.bmcl.2011.09.029
9. K. N. Mohana, L. Mallesha, Doddahosur, M. Gurudatt, *Int. J. Drug Des. Discov.* **2024**, 2, 584–590. DOI:10.37285/ijddd.2.3.8
10. A. S. Alturiqi, A. M. A. Alaghaz, M. E. Zayed, R. A. Ammar, *J. Chin. Chem. Soc.* **2018**, 65, 1060–1074. DOI:10.1002/jccs.201800027
11. J. Pincemail, K. Bonjean, K. Cayeux, J.-O. Defraigne, *Nutr. Clin. Metab.* **2002**, 16, 233–239. DOI:10.1016/S0985-0562(02)00166-8
12. C. Sanchez-Moreno, *Food Sci. Technol. Int.* **2002**, 8, 121–137. DOI:10.1177/1082013202008003770
13. H. Kizilkaya, B. Dag, T. Aral, N. Genc, R. Erenler, *J. Chin. Chem. Soc.* **2020**, 67, 1696–1701. DOI:10.1002/jccs.202000161
14. A. Rauf, A. Shah, K. S. Munawar, A. A. Khan, R. Abbasi, M. A. Yameen, A. M. Khan, A. R. Khan, I. Z. Qureshi, H.-B. Kraatz, Zia-ur-Rehman, *J. Mol. Struct.* **2017**, 1145, 132–140. DOI:10.1016/j.molstruc.2017.05.098
15. A. Kajal, S. Bala, S. Kamboj, N. Sharma, V. Saini, *J. Catal.* **2013**, 2013, 1–14. DOI:10.1155/2013/893512
16. T. K. Bakır, J. B. Lawag, *Res. Chem. Intermed.* **2020**, 46, 2541–2557. DOI:10.1007/s11164-020-04105-y
17. A. G. Erturk, *J. Mol. Struct.* **2020**, 1202, 127299. DOI:10.1016/j.molstruc.2019.127299
18. A. Boussadia, A. Beghidja, L. Gali, C. Beghidja, M. Elhabiri, P. Rabu, G. Rogez, *Inorg. Chim. Acta.* **2020**, 508, 119656. DOI:10.1016/j.ica.2020.119656
19. Y. Tang, Z. Liu, *Cell Biochem. Funct.* **2008**, 26, 185–191. DOI:10.1002/cbf.1426
20. F. Sonmez, Z. Gunesli, B. Z. Kurt, I. Gazioglu, D. Avci, M. Kucukislamoglu, *Mol. Divers.* **2019**, 23, 829–844. DOI:10.1007/s11030-018-09910-7
21. R. P. Mason, *Redox Biol.* **2016**, 8, 422–429. DOI:10.1016/j.redox.2016.04.003
22. S. Rana, N. M. A. Rayhan, S. H. Emon, T. Islam, K. Rathry, M. Hasan, M. Islam Mansur, B. C. Sriyon, M. S. Islam, A. Ray, Md. A. Rakib, A. Islam, Kudrat-E-Zahan, F. Hossen, A. Asraf, *RSC Adv.* **2024**, 14, 33094–33123. DOI:10.1039/D4RA04375H
23. M. Valco, D. Leibfritz, M. T. D. Cronin, M. J. Mazur, *Int. J. Biochem. Cell Biol.* **2007**, 39, 44–84. DOI:10.1016/j.biocel.2006.07.001
24. A. J. Muhammad, D. Ahmed, S. Yousuf, N. Tabassum, M. T. Qamar, *Heliyon* **2019**, 5, e01758. DOI:10.1016/j.heliyon.2019.e01758
25. A. A. Madi, D. Haffar, F. Benghanem, S. Ghedjati, L. Toukal, V. Dorcet, R. Bourzami, *J. Mol. Struct.* **2021**, 1227, 129368. DOI:10.1016/j.molstruc.2020.129368
26. A. A. A. M. Abdallah, D. Haffar, F. Benghanem, S. Ghedjati, *J. Iran Chem. Soc.* **2023**, 20, 897–910. DOI:10.1007/s13738-022-02713-6
27. C. Chiter, A. Bouchama, T. N. Mouas, H. Allal, M. Yahiaoui, I. Warad, A. Zarrouk, A. Djedouani, *J. Mol. Struct.* **2020**, 1217, 128376. DOI:10.1016/j.molstruc.2020.128376

28. H. Boulebd, Y. Zine, I. A. Khodja, A. Mermer, A. Demir, A. Debache, *J. Mol. Struct.* **2022**, 1249, 131546. DOI:10.1016/j.molstruc.2021.131546
29. A. Hellal, S. Chafaa, N. Chafai, L. Touafri, *J. Mol. Struct.* **2017**, 1134, 217–225. DOI:10.1016/j.molstruc.2016.12.079
30. M. Arivazhagan, V. P. Subhasini, *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2012**, 91, 402–410. DOI:10.1016/j.saa.2012.02.018
31. R. Re, N. Pellegrini, A. Proteggente, A. Pannala, M. Yang, C. Rice-Evans, *Free Radic. Biol. Med.* **1999**, 26, 1231–1237. DOI:10.1016/S0891-5849(98)00315-3
32. A. Szydłowski, C. Dianoczi, K. Recseg, G. Karlovits, E. Szlyk, *Talanta*. **2008**, 76, 899–905. DOI:10.1016/j.talanta.2008.04.055
33. M. Oyaizu, *Jpn. J. Nutr. Diet.* **1986**, 44, 307–315. DOI:10.5264/eiyogakuzashi.44.307
34. M. Özyürek, N. Güngör, S. Baki, K. Güçlü, R. Apak, *Anal. Chem.* **2012**, 84, 8052–8059. DOI:10.1021/ac301925b
35. C. Liang, C. Chang, C. Liang, K. Hung, C. Hsieh, *Molecules* **2014**, 19, 4681–4694. DOI:10.3390/molecules19044681
36. K. K. Kandikattu Karthik, P. B. R. Kumar, R. V. Priya, K. S. Kumar, R. S. B. Rathore, *Indian J. Res. Pharm. Biotechnol.* **2013**, 729–731.
37. L. V. Morris, C. Ortiz-Ledón, R. J. Hamers, *J. Electrochem. Soc.* **2024**, 171, 050501. DOI:10.1149/1945-7111/ad3eba
38. S. Ahmed, F. Shakeel, *Czech J. Food Sci.* **2012**, 30, 153–163. DOI:10.17221/447/2010-CJFS
39. P. Chowdhury, P. Pathak, *Chem. Phys. Lett.* **2020**, 761, 138057. DOI:10.1016/j.cplett.2020.138057
40. E. Yuriev, M. Agostino, P. A. Ramsland, *J. Mol. Recognit.* **2011**, 24, 149–164. DOI:10.1002/jmr.1077
41. K. Benbouguerra, N. Chafai, S. Chafaa, Y. I. Touahria, H. Tlidjane, *J. Mol. Struct.* **2021**, 1239, 130480. DOI:10.1016/j.molstruc.2021.130480
42. R. Hasan, M. A. Hossain, A. Salam, M. N. Uddin, *J. Taibah Univ. Sci.* **2016**, 10, 766–773. DOI:10.1016/j.jtusci.2015.11.007
43. E. Pahonțu, D.-C. Ilieș, S. Shova, C. Paraschivescu, M. Badea, A. Gulea, T. Roșu, *Molecules* **2015**, 20, 5771–5792. DOI:10.3390/molecules20045771
44. M. Sarigul, S. Erkan Kariper, P. Deveci, H. Atabey, D. Karakas, M. Kurtoglu, *J. Mol. Struct.* **2017**, 1149, 520–529. DOI:10.1016/j.molstruc.2017.08.016
45. V. Govindaraj, S. Ramanathan, *Turk. J. Chem.* **2014**, 38, 521–530. DOI:10.3906/kim-1301-83
46. S. A. Beyramabadi, B. Esmaeili, A. Gharib, M. Khorsandi-Chenarboo, A. Morsali, M. Khashi, R. Sanavi-Khoshnood, *J. Mol. Struct.* **2017**, 1146, 620–628. DOI:10.1016/j.molstruc.2017.06.050
47. Y. Bellal, S. Keraghel, F. Benghanem, T. Linda, G. Sığircık, B. Riadh, A. Ourari, *Int. J. Electrochem. Sci.* **2018**, 13, 7218–7245. DOI:10.20964/2018.07.91
48. J. Losada, I. Del Peso, L. Beyer, *Inorg. Chim. Acta.* **2001**, 321, 107–115. DOI:10.1016/S0020-1693(01)00511-4
49. I. Jirjees, S. A. Ali, H. A. Mahdi, *Int. J. Sci. Eng. Res.* **2015**, 6, 735–743.
50. T. Eren, M. Kose, K. Sayin, V. McKee, M. Kurtoglu, *J. Mol. Struct.* **2014**, 1065–1066, 191–198. DOI:10.1016/j.molstruc.2014.02.052
51. A. E. Şabik, M. Karabörk, G. Ceyhan, M. Tümer, M. Dıgırak, *Int. J. Inorg. Chem.* **2012**, 2012, 1–11. DOI:10.1155/2012/791219
52. A. Bhowmick, M. Islam, R. Bhowmick, A. Sarkar, D. Shibly, M. Hossain, *Am. J. Chem.* **2019**, 9, 21–25.
53. S. Kalkhoran, N. L. Benowitz, N. A. Rigotti, *J. Am. Coll. Cardiol.* **2018**, 72, 1030–1045. DOI:10.1016/j.jacc.2018.06.036
54. L. Li, F. Zhang, J. Zaia, R. J. Linhardt, *Anal. Chem.* **2012**, 84, 8822–8829. DOI:10.1021/ac302232c
55. M. Mazzarino, X. De La Torre, F. Botrè, N. Gray, D. Cowan, *Drug Test. Anal.* **2010**, 2, 311–322. DOI:10.1002/dta.148
56. A. H. A. S. Ahmed Hassan Abdel Salam, *J. Chem. Soc. Pak.* **2019**, 41, 1055–1055. DOI:10.52568/000823/JCSP/41.06.2019
57. J. Asegbeloyin, P. Ejikeme, L. Olasunkanmi, A. Adekunle, E. Ebenso, *Materials* **2015**, 8, 2918–2934. DOI:10.3390/ma8062918
58. C. Şenol, Z. Hayvali, H. Dal, T. Hökelek, *J. Mol. Struct.* **2011**, 997, 53–59. DOI:10.1016/j.molstruc.2011.04.037
59. M. S. Çavuş, H. Yakan, C. Başkan, H. Muğlu, A. A. Babacan, *J. Mol. Struct.* **2024**, 1304, 137655. DOI:10.1016/j.molstruc.2024.137655
60. M. A. Mumit, T. K. Pal, A. Alam, A.-A.-A.-A. Islam, S. Paul, C. Sheikh, *J. Mol. Struct.* **2020**, 1220, 128715. DOI:10.1016/j.molstruc.2020.128715
61. N. Nehra, R. K. Tittal, V. D. Ghule, *ACS Omega*. **2021**, 6, 27089–27100. DOI:10.1021/acsomega.1c03668
62. J. S. Singh, M. S. Khan, S. Uddin, *Polym. Bull.* **2023**, 80, 3055–3083. DOI:10.1007/s00289-022-04181-7
63. D. D. Li, M. L. Greenfield, *Fuel* **2014**, 115, 347–356. DOI:10.1016/j.fuel.2013.07.012
64. K. Merdja, C. K. Bendeddouche, M. Drissi, F. C. Kaouche, N. Medjahed, J. M. Padrón, M. Debdab, M. Rahmouni, E. H. Belarbi, *Indones. J. Chem.* **2023**, 23, 1722. DOI:10.22146/ijc.87476
65. V. Hadigheh Rezvan, *Results Chem.* **2024**, 7, 101437. DOI:10.1016/j.rechem.2024.101437
66. K. Sambathkumar, *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2015**, 147, 51–66. DOI:10.1016/j.saa.2015.03.052
67. A. M. Fahim, M. A. Shalaby, *J. Mol. Struct.* **2019**, 1176, 408–421. DOI:10.1016/j.molstruc.2018.08.087
68. M. Maria Julie, T. Prabhu, E. Elamuruguporchelvi, F. B. Asif, S. Muthu, A. Irfan, *J. Mol. Liq.* **2021**, 336, 116335. DOI:10.1016/j.molliq.2021.116335
69. J. K. Ojha, G. Ramesh, B. V. Reddy, *Chem. Phys. Impact.* **2023**, 7, 100280. DOI:10.1016/j.chphi.2023.100280
70. M. Miar, A. Shiroudi, K. Pourshamsian, A. R. Oliaey, F. Hatamjafari, *J. Chem. Res.* **2021**, 45, 147–158. DOI:10.1177/1747519820932091
71. R. Jayachitra, M. Padmavathy, A. Kanagavalli, G. Thilagavathi, N. Elangovan, S. Sowrirajan, R. Thomas, *J. Indian Chem. Soc.* **2023**, 100, 100824. DOI:10.1016/j.jics.2022.100824
72. S. Demir, F. Tinmaz, N. Dege, I. O. İlhan, *J. Mol. Struct.* **2016**,

- 1108, 637–648. DOI:10.1016/j.molstruc.2015.12.057
73. Y. Oueslati, S. Kansız, A. Valkonen, T. Sahbani, N. Dege, W. Smirani, *J. Mol. Struct.* **2019**, 1196, 499–507. DOI:10.1016/j.molstruc.2019.06.110
74. S. Kanchana, T. Kaviya, P. Rajkumar, M. D. Kumar, N. Elangovan, S. Sowrirajan, *Chem. Phys. Impact*. **2023**, 7, 100263. DOI:10.1016/j.chphi.2023.100263
75. Z. Ye, S. Xie, Z. Cao, L. Wang, D. Xu, H. Zhang, J. Matz, P. Dong, H. Fang, J. Shen, M. Ye, *Energy Stor. Mater.* **2021**, 37, 378–386. DOI:10.1016/j.ensm.2021.02.022
76. A. I. Aljameel, *Int. J. Electrochem. Sci.* **2022**, 17, 220524. DOI:10.20964/2022.05.39
77. K. Arulaabaranam, S. Muthu, G. Mani, A. S. Ben Geoffrey, *Heliyon* **2021**, 7, e07061. DOI:10.1016/j.heliyon.2021.e07061
78. J. da Cunha Xavier, F. W. D. Q. Almeida-Neto, P. T. da Silva, A. P. de Sousa, E. S. Marinho, M. M. Marinho, J. E. Rocha, P. R. Freitas, A. C. J. de Araújo, T. S. Freitas, C. E. S. Nogueira, P. de Lima-Neto, P. N. Bandeira, A. M. R. Teixeira, H. D. M. Coutinho, H. S. dos Santos, *J. Mol. Struct.* **2021**, 1227, 129692. DOI:10.1016/j.molstruc.2020.129692
79. T. K. Pal, M. A. Mumit, J. Hossen, S. Paul, A. Alam, A.-A.-A. Islam, C. Sheikh, *SSRN J.* **2021**. DOI:10.2139/ssrn.3929847
80. N. Bibi Sadeer, D. Montesano, S. Albrizio, G. Zengin, M. F. Mahomoodally, *Antioxidants*. **2020**, 9, 709. DOI:10.3390/antiox9080709
81. N. Zeghad, E. Ahmed, A. Belkhir, Y. V. Heyden, K. Demeyer, *Heliyon* **2019**, 5, e01575. DOI:10.1016/j.heliyon.2019.e01575
82. W. Chanput, N. Krueyes, P. Ritthiruangdej, *Int. Immunopharmacol.* **2016**, 40, 170–175. DOI:10.1016/j.intimp.2016.08.038
83. K. I. Berker, K. Güçlü, B. Demirata, R. Apak, *Anal. Methods*. **2010**, 2, 1770. DOI:10.1039/c0ay00245c
84. K. B. Pandey, S. I. Rizvi, *Int. J. Food Prop.* **2012**, 15, 702–708. DOI:10.1080/10942912.2010.498547
85. S. D. Oladipo, R. C. Luckay, K. A. Olofinisan, *Sci. Rep.* **2024**, 14, 27073. DOI:10.1038/s41598-024-78460-w
86. Z. Velez, M. Campinho, Â. Guerra, L. García, P. Ramos, O. Guerreiro, L. Felício, F. Schmitt, M. Duarte, *Agriculture* **2012**, 2, 472–492. DOI:10.3390/agriculture2040472
87. S. M. Kuzmin, S. A. Chulovskaya, V. I. Parfenyuk, *J. Electroanal. Chem.* **2016**, 772, 80–88. DOI:10.1016/j.jelechem.2016.04.024
88. A. René, M.-L. Abasq, D. Hauchard, P. Hapiot, *Anal. Chem.* **2010**, 82, 8703–8710. DOI:10.1021/ac101854w
89. S. Ahmed, F. Shakeel, *Czech J. Food Sci.* **2012**, 30, 153–163. DOI:10.17221/447/2010-CJFS
90. C. Mouffouk, S. Mouffouk, K. Oulmi, S. Mouffouk, H. Haba, *S. Afr. J. Bot.* **2020**, 130, 383–388. DOI:10.1016/j.sajb.2020.01.003
91. M. Serafini, I. Peluso, A. Raguzzini, *Proc. Nutr. Soc.* **2010**, 69, 273–278. DOI:10.1017/S002966511000162X
92. C. A. Lipinski, F. Lombardo, B. W. Dominy, P. J. Feeney, *Adv. Drug Deliv. Rev.* **1997**, 23, 3–25. DOI:10.1016/S0169-409X(96)00423-1
93. S. Gatfaoui, A. Sagaama, N. Issaoui, T. Roisnel, H. Marouani, *Solid State Sci.* **2020**, 106, 106326. DOI:10.1016/j.solidstatesciences.2020.106326
94. T. Topal, Y. Zorlu, N. Karapinar, *J. Mol. Struct.* **2021**, 1239, 130514. DOI:10.1016/j.molstruc.2021.130514
95. M. Venkateshan, M. Muthu, J. Suresh, R. Ranjith Kumar, *J. Mol. Struct.* **2020**, 1220, 128741. DOI:10.1016/j.molstruc.2020.128741

Povzetek

Sintetizirali smo asimetrično Schiffovo bazo 2-hidroksi-6-metil-3-((*E*)-1-((4-metil-3-((*E*)-(piridin-3-ilmetilen)amino)fenil)imino)etil)-4*H*-piran-4-on (AL) in jo karakterizirali z LC-MS, FT-IR, UV-Vis, ¹H ter ¹³C NMR metodami kot tudi s ciklično voltametrijjo. S pomočjo teorije gostotnega potenciala (DFT) smo optimizirali strukturo molekule, modelirali IR in UV-Vis spektra ter ocenili stabilnost, reaktivnost in specifične kvantno-kemijske lastnosti pripravljene spojine AL. Izsledki teoretičnih študij se skladajo z eksperimentalnimi rezultati. Rezultati kažejo, da ima AL dobre antioksidativne lastnosti in da deluje protivnetno. Elektrokemijsko obnašanje AL in BHT v prisotnosti superoksidnih radikalov kaže na spontanost radikalskih reakcij. Apro-AL izračuni nakazujejo sposobnost AL, da inhibira primarno proteazo (4GCA). Študije molekulskega sidranja in ADME-T analiza kažejo, da bi spojino AL lahko razvili v terapevtsko uporabno učinkovino.



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