Evaluation of α-Amylase Inhibitory Activity, Molecular Modeling, Total Antioxidant and Theoretical Studies of Novel Schiff Base Transition Metal Complexes

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By condensing pyrene-1-carbaldehyde and 4-aminoantipyrine, a Schiff base ligand, (*Z*)-1,5-dimethyl-2-phenyl-4-((pyren-1-ylmethylene)-amino)-1*H*-pyrazol-3(2*H*)-one and its Cu(II), Ni(II), Co(II) and Zn(II) complexes have been synthesized. The ligand and its metal complexes were characterized by FT-IR, UV-visible, ¹H & ¹³C NMR, ESI-mass spectra and elemental analysis. The antidiabetic and antioxidant activities of the synthesized Schiff base ligand and its metal complexes were studied. The molecular docking study of human pancreatic α-amylase (PDB: 1HNY). Furthermore, Theoretical analysis of geometry optimization and frontier molecular orbital analysis (HOMO-LUMO) was accomplished by density functional theory using B3LYP/3-21G*++ basis sets to understand the chemical stability of the synthesized ligand and their metal(II) complexes.

Keywords: Biological studies, Molecular docking, Geometry optimization, Density functional theory.

INTRODUCTION

Schiff base compounds containing -N=CHR group due to their ability to form stable and strong coloured metal complexes with transition metal ions with different oxidation states [1]. Schiff bases and their metal complexes from a choice of aldehydes and amines have been investigated in various biological fields were recently established to have significant antitumor and biological activity *viz*. anti-inflammatory, anticonvulsant agents, *etc*. and greater DNA binding ability [2-15]. Moreover, antipyrines are also widely used in medicines and some of them have been shown to reveal attractive chemical, physical, analytical and biological properties and it is believed that its amino derivative are equally used in medicine possibly as intermediates in anti-pyretic and analgesic drugs [16-20].

This prompted us to synthesize a novel Schiff base containing antipyrinyl moiety and its metal complexes. The objective of the present study was to investigate the antimicrobial, antidiabetic, antioxidant, molecular docking, geometry optimization and DFT studies of synthesized Schiff base ligand and its transition metal(II) complexes. Therefore, various methods and analytical tools are employed for antioxidant content it is desirable to establish methods that can directly measure the total antioxidant capacity (phosphomolybdenum methods) compared with that of the classical antioxidants, vitamin C [21]. As α-amylase inhibitor significantly decreases the post-prandial hyperglycemia in the treatment of type-II diabetes.

In view of this, we designed and synthesized a Schiff base ligand, (*Z*)-1,5-dimethyl-2-phenyl-4-((pyren-1-ylmethylene)-amino)-1*H*-pyrazol-3(2*H*)-one and its its Cu(II), Ni(II), Co(II) and Zn(II) complexes complexes, which were evaluated for *in vitro* α-amylase inhibitory activity with reference standard acarbose. Putative binding mode of the significant compounds with the target receptor was also predicted using the docking studies [22,23]. The geometries of metal complexes were optimized based on density functional theory (DFT) using the B3LYP/LACVP++ basis set. Computational methods have been used to gain more information about the structural and chemical properties of this compounds [24,25].

EXPERIMENTAL

Chemicals *viz*. 4-aminoantipyrine (E. Merck), pyrene-1-carbaldehyde (SRL) and metal(II) chlorides (Alfa) for the

synthesis of Schiff base were procured of the highest available purity. The solvents used for the synthesis were carefully distilled and dried by standard procedure. The HPLC grade solvents were used for spectroscopic studies. Elemental analyses (CHN) of complexes were analyzed by using a Perkin-Elmer 2400 elemental analyzer. Infrared spectra were recorded on the Perkin-Elmer ATR-FTIR type spectrophotometer in the range between 4000 and 400 cm^{-1}. The UV-visible spectra of complexes were analyzed in HPLC grade methanol on a Perkin-Elmer Lambda-25 spectrophotometer in the range between 200-900 nm. The ESI mass spectra of complexes were recorded on Q-TOF-Mass Spectrometer. The ^{1}H & ^{13}C NMR spectrum of the ligand was recorded in DMSO-d_6 on 400MHz Bruker FT-NMR. The chemical shift values are given in ppm using tetramethylsilane (TMS) as an internal reference.

Synthesis of Schiff base ligand (HL): Schiff base was synthesized according to the reported procedure [26]. An ethanolic solution of pyrene-1-carbaldehyde (0.1 mol in 25 mL) was added to an ethanolic solution of 4-aminoantipyrine (0.1 mol in 25 mL) and refluxed for 5 h. On cooling the solution, the precipitate was separated and recrystallized with ethanol The obtained ligand was stable in air and light. Yield: 87%; colour: bright yellow. m.p.: > 250 °C (dec.); Anal. calcd. (found) % for $C_{28}H_{21}N_3O$: C, 78.46 (80.94); H, 5.12 (5.09); N, 10.11 (9.66); ^{1}H NMR (DMSO-d_6, δ ppm): 2.50 (s, 1H, C-CH$_3$), 3.26 (s, 1H, N-CH$_3$), 7.42-8.82 (m, 1H, Ar-H), 10.76 (s, 1H, N=CH); ^{13}C NMR (DMSO-d_6, δ ppm): 35.81(N-CH3), 10.41 (C-CH$_3$), 117.65-134.99 (Ar-C), 160.18 (C=O), 152.66 (C=N); Positive-ion ESI-MS (MeOH) *m/z* (%): 415. IR (v_{max}, cm^{-1}): 1554 (CH=N); 1618 (C=O); 1491 (C=C); $λ_{max}$ (nm) in MeOH: 407, 399 and 234.

Synthesis of metal(II) complexes

Synthesis of [Cu(HL)] (1a): A hot methanolic solution of (*Z*)-1,5-dimethyl-2-phenyl-4-((pyren-1-ylmethylene)amino)-1*H*-pyrazol-3(2*H*)-one ligand (HL) (0.1 mol) was added slowly with a constant stirring of CuCl$_2$·2H$_2$O (0.1 mol) and the mixture was refluxed for about 8 h. On cooling at room temperature, the solid product was precipitated out, filtered and washed several times with cold methanol and dried in a vacuum over P$_4$O$_{10}$. Yield: 74%; colour: brown. m.p.: > 300 °C (dec.); Anal. calcd. (found) % for $C_{28}H_{25}N_3O_3Cl_2Cu$: C, 57.39 (56.39); H, 4.30 (4.29); N, 7.17 (7.17); Positive-ion ESI-MS (MeOH) *m/z* (%): 585. IR (v_{max}, cm^{-1}): 1593 (C=N); 1672 (C=O); 3331 (OH); 584 (Cu-N); 499 (Cu-Cl); $λ_{max}$ (nm) in MeOH: 661 (d-d), 394, 361 and 275.

Synthesis of [Ni(HL)] (1b): Complex **1b** was synthesized with NiCl$_2$·6H$_2$O (0.1 mol) by the following procedure described from complex **1a**. Yield: 72%, colour: brown. m.p.: > 300 °C (dec.); Anal. calcd. (found) % for $C_{28}H_{25}N_3O_3Cl_2Ni$: C, 57.87 (57.85); H, 4.34 (4.34); N, 7.23 (7.22); Positive-ion ESI-MS (MeOH) *m/z* (%): 582. IR (v_{max}, cm^{-1}): 1572 (C=N); 1586 (C=O); 3348 (OH); 583 (Ni-N); 498 (Ni-Cl); $λ_{max}$ (nm) in MeOH: 682 (d-d), 383, 288 and 211.

Synthesis of [Co(HL)] (1c): Complex **1c** was synthesized with CoCl$_2$·6H$_2$O (0.1 mol) by the following procedure described from complex **1a**. Yield: 74%, colour: dark yellow. m.p.: > 300 °C (dec.); Anal. calcd. (found) % for $C_{28}H_{25}N_3O_3Cl_2Co$: C, 57.85 (57.01); H, 4.33 (4.31); N, 7.23 (7.21); Positive-ion ESI-MS (MeOH) *m/z* (%): 581. IR (v_{max}, cm^{-1}): 1572 (C=N); 1590 (C=O); 3417 (OH); 583 (Co-N); 475 (Co-Cl); $λ_{max}$ (nm) in MeOH: 683 (d-d), 383, 287 and 233.

Synthesis of [Zn(HL)] (1d): Complex **1d** was synthesized with ZnCl$_2$ (0.1 mol) by the following procedure described from complex **1a**. Yield: 67%, colour: red. m.p.: > 300 °C (dec.); Anal. calcd. (found) % for $C_{28}H_{21}N_3OCl_2Zn$: C, 60.95 (60.86); H, 3.84 (3.79); N, 7.62 (7.85); Positive-ion ESI-MS (MeOH) *m/z* (%): 553. IR (v_{max}, cm^{-1}): 1570 (C=N); 1592 (C=O); 519 (Zn-N); 476 (Zn-Cl); $λ_{max}$ (nm) in MeOH: 383, 287 and 207.

Antioxidant activity: The antioxidant potential of Schiff base ligand and metal(II) complexes were evaluated by using the phosphomolybdenum method. Total antioxidant capacity was based on the reduction of Mo(VI) to Mo(V) by accepting an electron from an antioxidant at acidic pH. About 3 mL of antioxidant reagent (0.6 M H$_2$SO$_4$, 28 mM Na$_3$PO$_4$ and 4 mM ammonium molybdate) were added to the test samples with various concentrations (10, 50, 100, 250 and 500 µg/mL). The test mixture to accomplish proper diffusion with phospho-molybdenum reagent was incubated at 95 °C for 90 min in a water-bath. The total antioxidant activity of extracts and vitamin C standard drug were measured and determined their absorbance at 695 nm [27-29] using the following formula:

$$TOA = \frac{A_t - A_c}{A_t} \times 100$$

where A_t: Absorbance of test and A_c: Absorbance of control

Antidiabetic activity: The synthesized compounds were tested for their inhibitory potential against α-amylase enzyme. A different concentration of the test compounds 10, 50,100, 250 and 500 µg/mL was used for the assay [30,31]. Briefly, α-amylase (0.5 mg/mL) was incubated with and without extract and standard for 10 min at 25 °C. This experiment was performed in 20 mM sodium phosphate buffer (pH 6.9). After pre-incubation, 1% starch solution (1mL) was added and the reaction mixture was incubated for 30 min at 25 °C. In order to stop the enzymatic reaction, DNSA reagent (1mL) was added as colour reagent and then incubated in a boiling water-bath for 15 min. After cooling down to the room temperature, the absorbance measured at 540 nm and the concentrations were plotted against % inhibition The percentage of inhibition was calculated using eqn. 2:

$$Inhibition\ (\%) = 100 \times \frac{A_t - A_c}{A_t}$$

where A_t: absorbance of test and A_c: absorbance of control.

Molecular docking studies: Exploration of mechanism of action and molecular interaction of synthesized derivatives with α-amylase was performed by molecular docking studies using Maestro-V10.2 software integrated into the Schrodinger 2015-2 molecular modeling package. To study the molecular interaction of compounds, crystallographic data of human pancreatic α-amylase (PDB: 1HNY) were retrieved from Protein Data Bank. Retrieved crystal structure of α-amylase was cleaned and hydrogen atoms were added. All the heteroatoms were removed

before docking study [32]. The 2D structures were sketched using Chem Draw-ultra v14.0 followed by 3D structure conversion and energy minimization by ChemBio Office modelling software (Cambridge soft, UK). The outputs were visualized by PyMol console for virtual examination of various binding modes.

Molecular orbital analysis: All the theoretical orbital analysis were performed using Jaguar V8.8 program as incorporated in Schrodinger suite 2015-2 [33].

RESULTS AND DISCUSSION

The synthesis of (Z)-1,5-dimethyl-2-phenyl-4-((pyren-1-ylmethylene)amino)-1H-pyrazol-3(2H)-one Schiff base ligand and its metal complexes have been synthesized and characterized by spectral and elemental analytical data. All the complexes are stable at room temperature, soluble in most of the organic solvents such as methanol, ethanol, acetonitrile, DMF and DMSO but insoluble in water.

NMR analysis: The ^1H NMR spectrum of ligand shows the following signals. Aromatic hydrogen multiplet around δ 7.42-8.82, =C-CH$_3$ at δ 2.50 , -N-CH$_3$ at δ 3.26 and azomethine proton (HC=N) at δ 10.76. In ^{13}C NMR spectra of Schiff base ligand (**HL**), azomethine carbon signal has appeared at δ 152.66 ppm. The signals due to C-CH$_3$ and N-CH$_3$ present in the pyrazolone ring are observed in the expected range at δ 10.41 ppm and 35.81 ppm. The aromatic carbon signals are observed at δ 117.65-160.18 ppm range depending on their electronic environment.

The electrospray ionization (ESI) mass spectra of Schiff base and its metal complexes were used to compare the stoichiometric composition. The Schiff base ligand (**HL**) shows a molecular ion peak M$^+$ at m/z 415. The molecular ion peak for the metal (II) complexes (**1a-d**) were observed at [C$_{28}$H$_{25}$N$_3$O$_3$Cl$_2$Cu] m/z 585, [C$_{28}$H$_{25}$N$_3$O$_3$Cl$_2$Ni] m/z 580, [C$_{28}$H$_{25}$N$_3$O$_3$Cl$_2$Co] m/z 581, [C$_{22}$H$_{16}$N$_3$O$_3$BrZn] m/z 553. The elemental analysis values were in close agreement with the values calculated from molecular formula assigned to these complexes, which is also supported by the ESI-mass studies of complexes.

The infrared spectra and UV-visible spectral data of Schiff base ligand (**HL**) metal(II) complexes (**1a-d**) are summarized in Table-1. The IR spectra of copper complexes exhibited a broad band at 3331-3417 cm^{-1}, which is attributed due to the presence of water molecule. The peak shows 3095-2850 cm^{-1} attributed to –CH stretching both in ligand and corresponding complexes. The ligand exhibited sharp band in 1554 cm^{-1} for -C=N azomethine vibrations. The shifting of the band to higher frequencies 1593-1570 cm^{-1} indicates complexation.

The bands that appeared below 650 cm^{-1} are assigned to the metal-nitrogen to ν(M-N), metal-oxygen ν(M-O) and metal chlorine ν(M-Cl) bonds. A weak band observed in the visible range 661-683 nm was due to the d-d transition, which is usually absent in the Zn(II) complex due to the completely filled d^{10} electronic configuration. A moderate intense band was found in the ultraviolet range 370-400 nm was due to ligand to metal charge transfer transition (LMCT) and a strong band in the range 361-211 nm was due to an intraligand charge transfer transition.

Antimicrobial activity: The results of antimicrobial activity of Schiff base ligand (**HL**) and its metal(II) complexes (**1a-d**) were screened for their antibacterial activity against various human pathogenic bacteria as such as E. coli, P. aeruginosa, S. aureus, B. subtilis and antifungal activity against C. albicans. Ciprofloxacin and amphotericin were used as the standard drugs for bacterial and fungal studies, respectively and the zones of inhibition are given in Table-2. The synthesized complexes shows moderate activity compared to the specific standard.

Antioxidant activity: The total antioxidant capacity of Schiff base ligand (**HL**) and its metal complexes (**1a-d**) showed a good inhibitory potential compared to the standard (Table-3). Among the tested compounds, Cu(II) complex shows the maximum antioxidant activity.

TABLE-1
FT-IR SPECTRAL DATA (cm^{-1}) AND UV-VISIBLE SPECTRAL DATA λ$_{max}$ (nm) OF
SCHIFF BASE LIGAND (HL) AND ITS METAL(II) COMPLEXES (**1a-d**)

Compounds	ν(C=N)	ν(C=O)	ν(OH)	ν(M-Cl)	ν(M-N)	d-d	Charge transfer
HL	1555	1619	-	-	-	Not available	407, 399, 234
1a	1594	1673	3334	499	584	661	394, 361, 275
1b	1572	1586	3348	498	583	682	383, 288, 211
1c	1572	1590	3417	475	583	683	383, 287, 233
1d	1570	1592	-	476	587	Not available	383, 287, 207

TABLE-2
ANTIBACTERIAL ACTIVITY OF SCHIFF BASE LIGAND (HL) AND ITS METAL(II) COMPLEXES (**1a-d**)
AGAINST PATHOGENIC BACTERIA TESTED BY A DISC DIFFUSION METHOD

Compounds	Inhibition zone (mm)				
	E. coli	S. aureus	P. aeruginosa	B. subtilis	C. albicans
HL	8	11	14	13	8
1a	7	9	11	14	9
1b	9	11	16	20	5
1c	9	8	11	15	8
1d	6	12	13	17	6
Ciprofloxacin	12	13	17	24	–
Amphotericin	–	–	–	–	21

TABLE-3
ANTIOXIDANT ACTIVITY OF SCHIFF BASE LIGAND (HL) AND ITS METAL(II) COMPLEXES (1a-d) BY TOTAL ANTIOXIDANT METHOD OF VARIOUS CONCENTRATIONS

Compounds	Concentration				
	10	50	100	250	500
HL	15.56	21.83	59.39	70.72	84.56
1a	17.89	23.49	61.28	73.48	85.38
1b	27.81	23.45	61.23	73.41	85.34
1c	17.88	23.48	61.27	73.44	85.43
1d	17.52	22.96	60.91	73.18	85.01
Vitamin C	22.43	32.11	69.78	82.23	94.55

Antidiabetic activity: Schiff base ligand and its metal(II) complexes revealed an inhibitory action similar to the widely used commercial drug (acarbose) against pancreatic α-amylase are summarized in Table-4. All complexes showed good to excellent inhibitory potential compared to the standard among that Co(II) complex showed the maximum activity.

TABLE-4
ANTIDIABETIC ACTIVITY OF SCHIFF BASE LIGAND (HL) AND ITS METAL(II) COMPLEXES (1a-d) TESTED BY α-AMYLASE INHIBITION TECHNIQUE OF VARIOUS CONCENTRATIONS

Compounds	Concentration				
	10	50	100	250	500
HL	14.32	22.48	41.26	60.21	74.33
1a	15.73	24.56	43.95	63.55	76.49
1b	14.92	23.43	42.82	62.89	75.11
1c	15.66	24.38	43.74	63.19	76.08
1d	14.67	23.03	42.61	62.34	74.83
Acarbose	18.22	26.33	44.69	63.29	81.52

Molecular docking studies: The effective binding energy value of Schiff base and its metal (II) complexes **(1a-d)** with human pancreatic α-amylase were found to be -4.36, -3.37, -2.18, -4.04 and -2.63 kcal mol^{-1}, respectively, which makes favourable stacking interaction between a receptor and complexes, leads to hydrogen bond interaction and hydrophobic contacts. The observed best docking poses and 2D interaction

sites for all the complexes are shown in Figs. 1-3. Moreover, the ligand and complexes showed hydrophobic contacts with PHE 222, PHE 223, ALA 224, TRP 221, PRO 223, PRO 4, PRO 332, TYR 2, TYR 333 and TYR 221 (Table-5). The docking score value of complex **1c** has good agreement with its anti-diabetic activity.

TABLE-5
in vitro **ANTIDIABETIC ACTIVITY OF SCHIFF BASE LIGAND (HL) AND ITS METAL(II) COMPLEXES (1a-d) AGAINST HUMAN PANCREATIC α-AMYLASE**

Compd.	Docking score (kcal mol^{-1})	Active sites with a mode of interaction hydrophobic contacts
HL	-4.36	PRO 223, PHE 222, ALA 224, TRP 221
1a	-3.37	PRO 223, PHE 222, ALA 224, TRP 221
1b	-2.18	PRO 223, PHE 222, PRO 4, TYR 2
1c	-4.04	PRO 332, PRO 4, TYR 333
1d	-2.63	PRO 332, PRO 4

Molecular orbital analysis: The HOMO and LUMO energy for Schiff base ligand and its metal(II) complexes calculated by density functional theory (DFT) using B3LYP/321G* ++ basis set are shown in Figs. 4 and 5. The smaller the value of ΔE, the reactivity of the compound is more [34-37]. The important quantum parameters such as HOMO-LUMO energy gap (ΔE), chemical potentials (pi), absolute electro-negativities (χ), absolute softness (σ), absolute hardness (η), global electro-philicity (ω), global softness (S) and additional electronic charge (ΔN$_{max}$) were calculated and the values are tabulated in Table-6.

The resulting ΔE values of Schiff base ligand and its metal (II) complexes **(1a-d)** showed 3.46, 3.03, 1.83, 2.93 and 3.11 eV, respectively. The response of an energy band gap ΔE values of complexes were of the following order **1b < 1c < 1a < 1d**. The observed values showed that complex Ni(II) **(1b)** exhibits a small band gap.

Geometry optimization: Geometry optimization is a technique to predict the 3D arrangement of atoms in a molecule and also provide information regarding geometry *via* minimization of energy. It involves a sequence of iterations accomp-
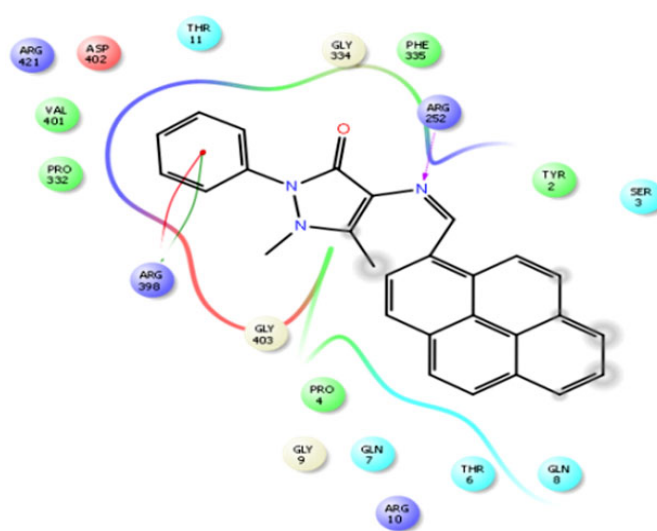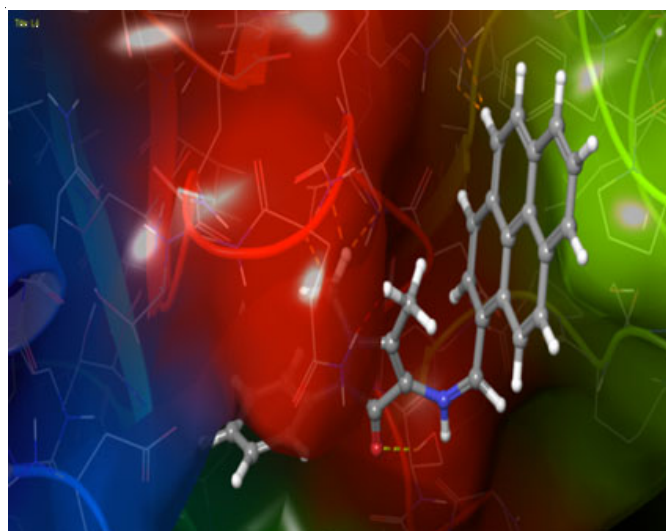

Fig. 1. Molecular docked model of Schiff base ligand **(HL)** located in the active site of the human pancreatic α-amylase (3D and 2D interaction)
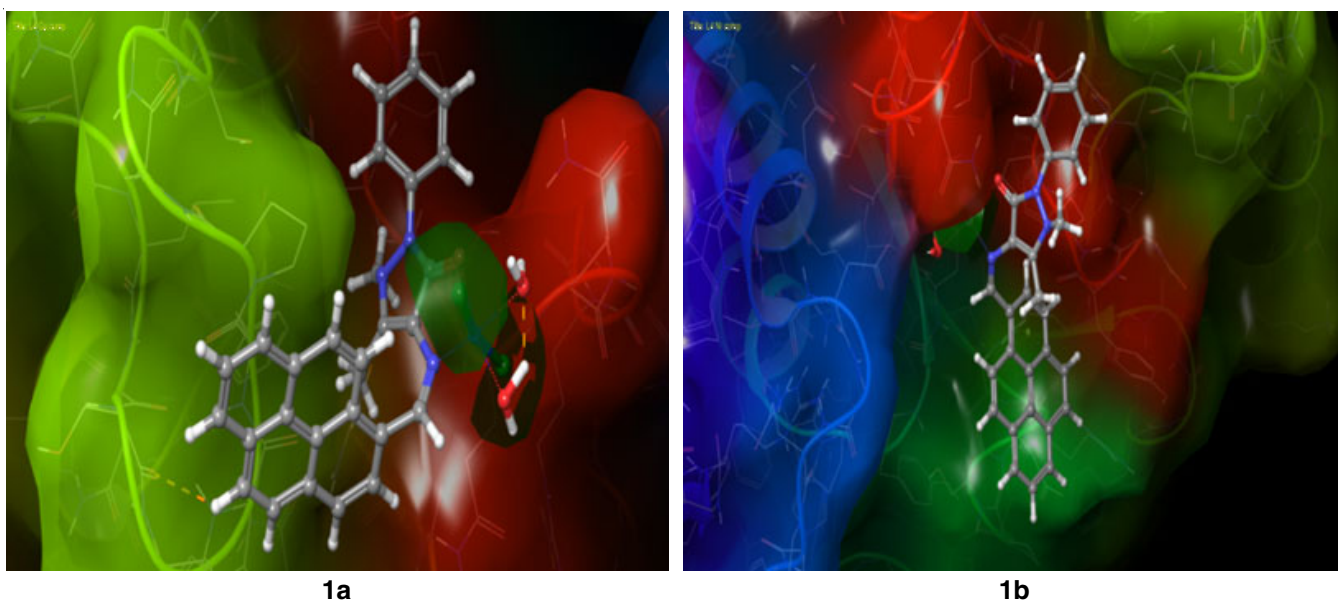
1a　　　　　　　　　　　　　　　　　**1b**

Fig. 2. Molecular docked model of Schiff base metal complexes Cu(II) (**1a**) and Ni(II) (**1b**) located in the active site of the human pancreatic α-amylase (3D interaction)
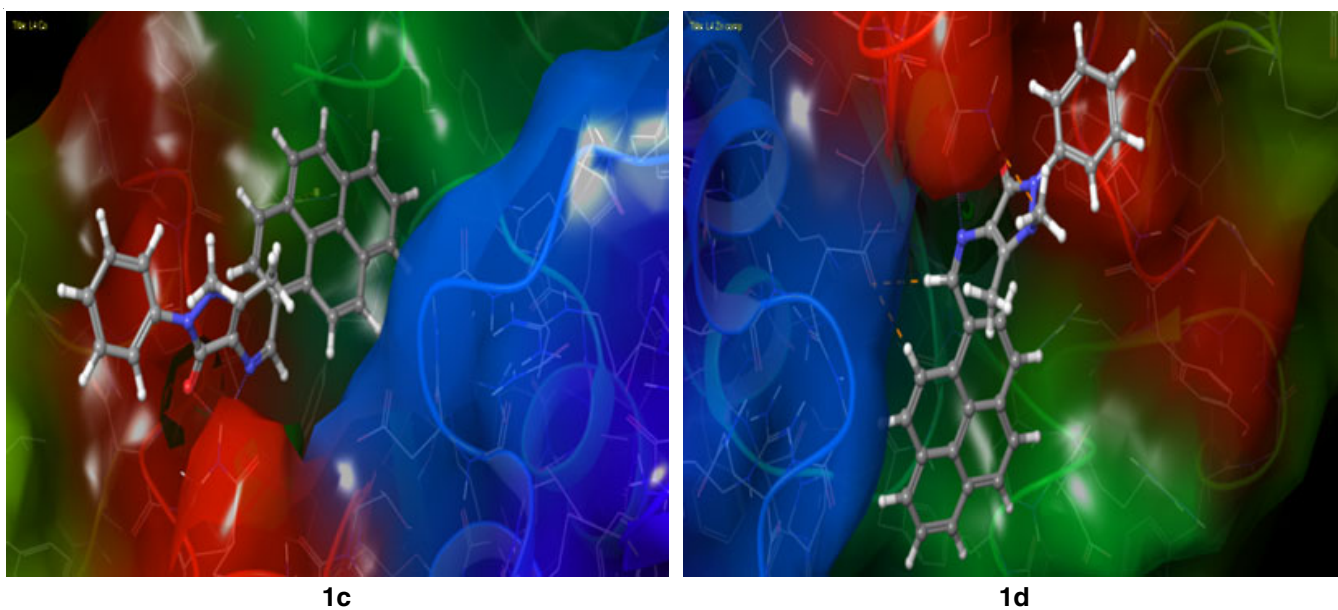

1c　　　　　　　　　　　　　　　　　**1d**

Fig. 3. Molecular docked model of Schiff base metal complexes Co(II) (**1c**) and Zn(II) (**1d**) located in the active site of the human pancreatic α-amylase (3D interaction)
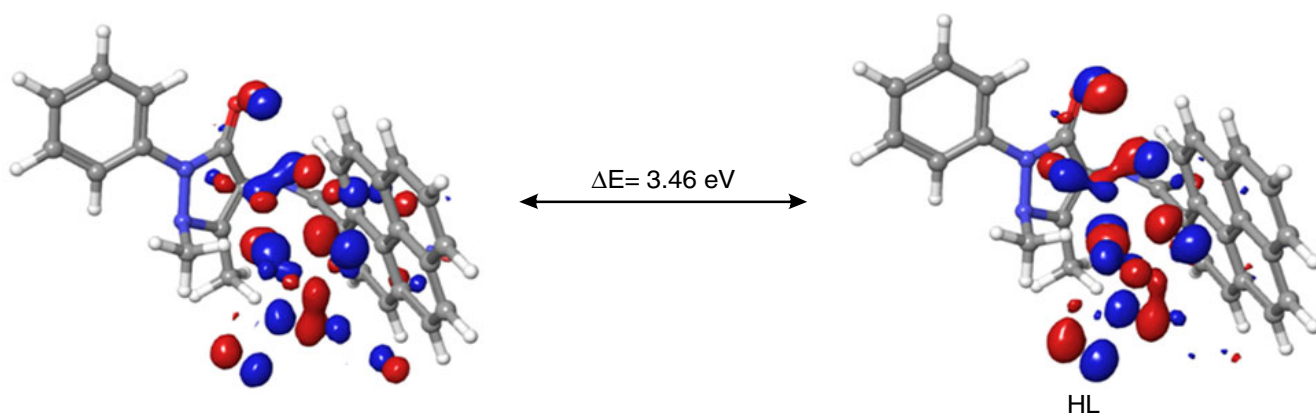

ΔE= 3.46 eV

HL

Fig. 4. Frontier molecular orbital's of Schiff base ligand (HL)

HOMO

Orbital energy (eV)

ΔE
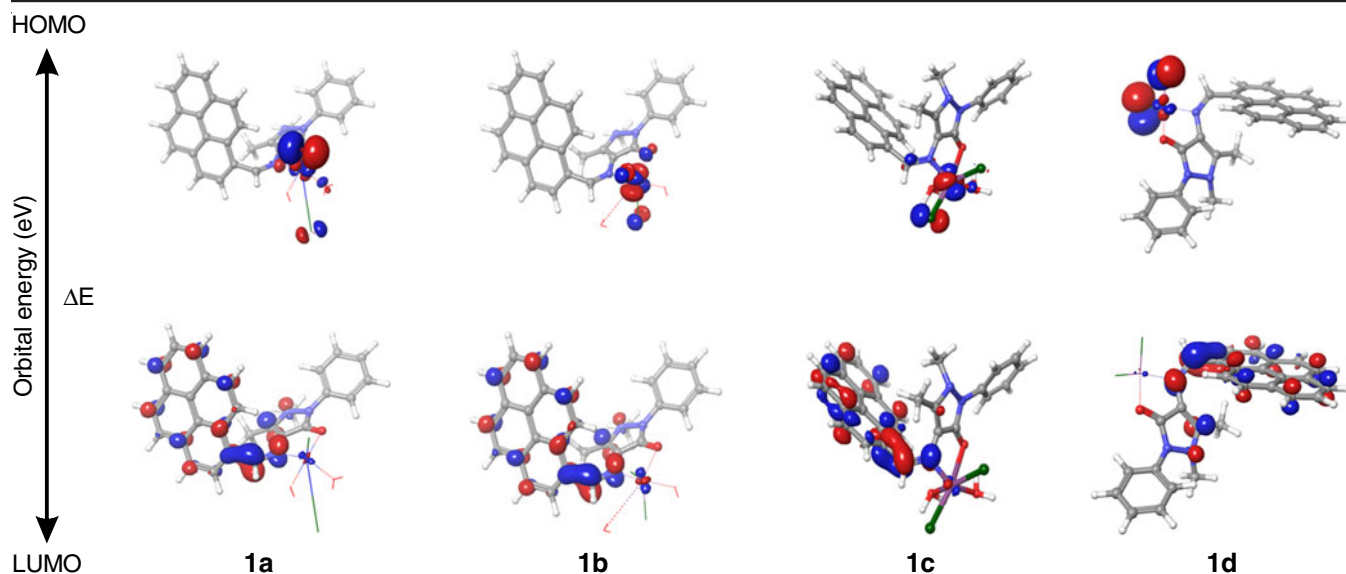
LUMO

1a **1b** **1c** **1d**

Fig. 5. Frontier molecular orbital's of Cu(II) (**1a**), Ni(II) (**1b**), Co(II) (**1c**) and Zn(II) (**1d**)

TABLE-6
ENERGIES OF HOMO-LUMO AND OTHER QUANTUM PARAMETERS OF
SCHIFF BASE LIGAND (HL) AND METAL(II) COMPLEXES (**1a–d**)

Compounds	HOMO (eV)	LUMO (eV)	ΔE (eV)	χ	η	σ	Pi	S	ω	ΔN max
HL	-5.42	-1.96	3.46	3.69	1.73	0.57	-3.69	0.28	3.93	2.13
1a	-5.69	-2.66	3.03	4.17	1.51	0.65	-4.17	0.32	5.75	2.75
1b	-4.17	-2.33	1.83	3.25	0.91	1.09	-3.25	0.54	5.77	3.54
1c	-5.36	-2.42	2.93	3.89	1.46	0.68	-3.89	0.34	5.17	2.65
1d	-5.86	-2.75	3.11	4.31	1.55	0.64	-4.31	0.32	5.95	2.76

lished until the energy of the molecule has attained a minimum. At the end of optimization, the molecules were attained a new geometry and energy. By this way, the geometry optimization for synthesized Schiff base ligand and its metal(II) complexes (**1a-d**) were carried out based on density functional theory using function B3LYP and basis set LACVP++ [38]. The LACVP++ was effective core basis set because it is a combination of 6-31G basis set with the LANL2DZ. The optimized molecular structure of metal(II) complexes are illustrated in Figs. 6 and 7 and the selected bond angles, and bond lengths are given in Tables 7 and 8.
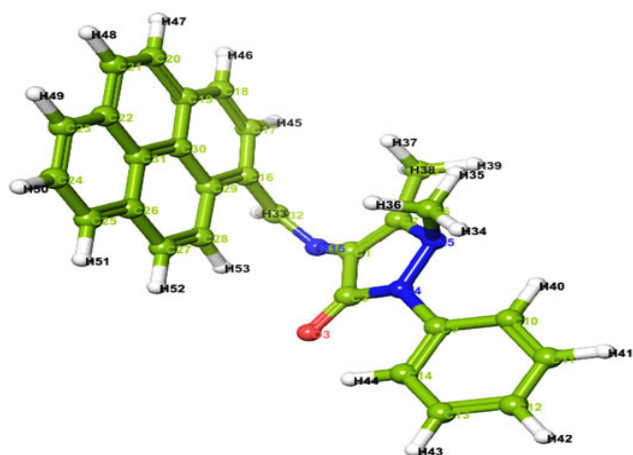
Fig. 6. Optimized molecular structure of Schiff base ligand (HL) using B3LYP/LACVP++ basis set

Conclusion

By interpretating the spectral data of the synthesized metal (II) complexes, the geometry of three metal(II) complexes (**1a-c**) were assigned as octahedral geometry where as Zn(II) complex (**1d**) exhibited square planar geometry. Moreover, biological activities of Schiff base ligand and its metal(II) complexes had shown a promising activity compared to their respective reference standard. Furthermore, the docking score value of complex **1c** has proven to be better binding interactions compared with other complexes. The frontier molecular orbital analysis revealed that the complex **1b** had shown more stable and higher reactivity due to the presence of a smaller energy band gap values than that of other metal complexes. Therefore, it is suggested that the synthesized Schiff base, (*Z*)-1,5-dimethyl-2-phenyl-4-((pyren-1-ylmethylene)amino)-1*H*-pyrazol-3(2*H*)-one and its metal(II) complexes were much useful for further biological investigations.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.
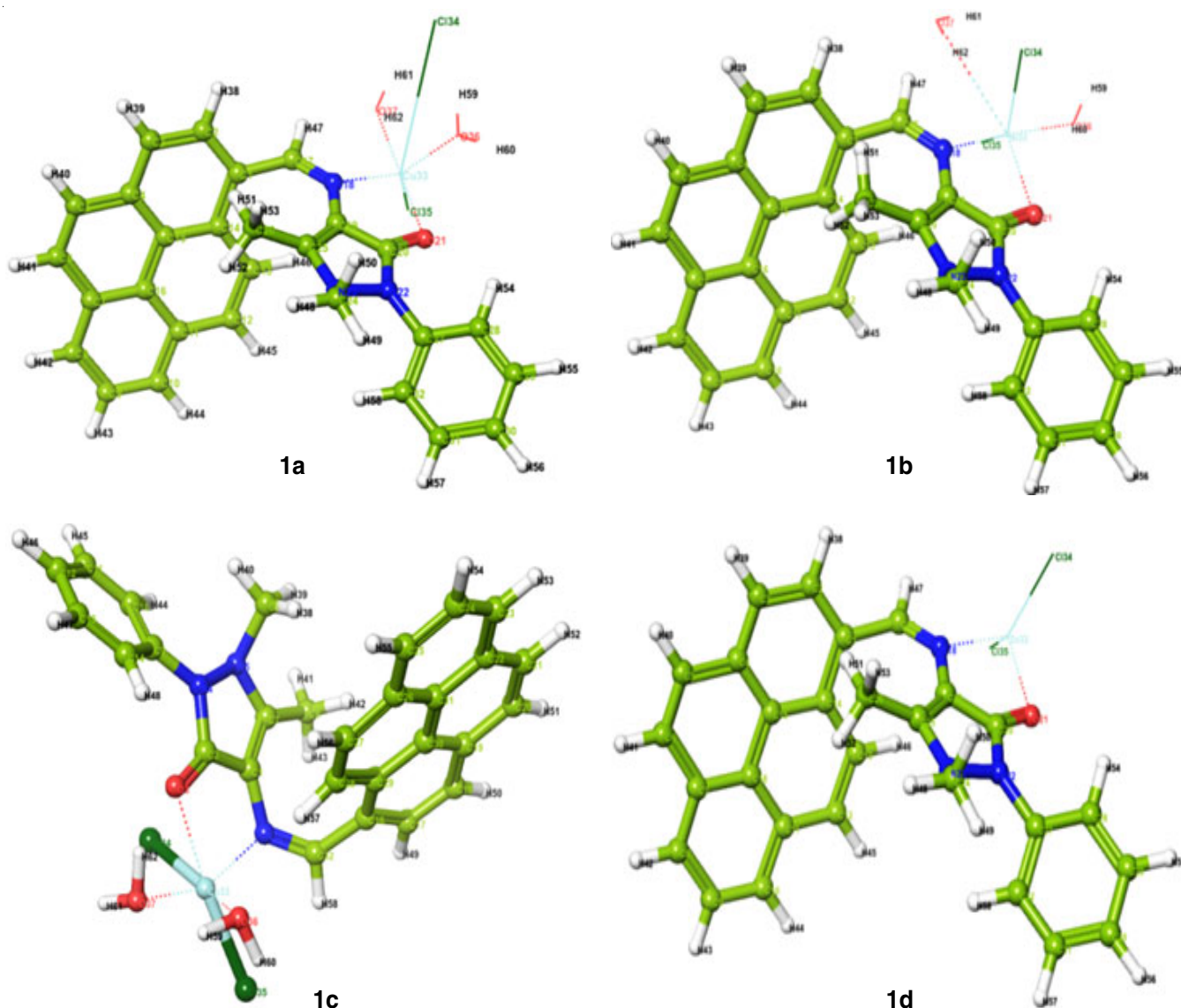
Fig. 7. Optimized molecular structure of Cu(II) (**1a**), Ni(II) (**1b**), Co(II) (**1c**) and Zn(II) (**1d**) complexes using B3LYP/LACVP++ basis set

TABLE-7
SELECTED OPTIMIZED GEOMETRY PARAMETERS OF METAL(II)
COMPLEXES (**1a-d**) BY B3LYP METHOD USING LACVP++ BASIS SET

Bond angle (°)							
[Cu(HL)] (**1a**)		[Ni(HL)] (**1b**)		[Co(HL)] (**1c**)		[Zn(HL)] (**1d**)	
O(21)-Cu(33)-N(18)	86.845	O(37)-Ni(33)-N(18)	77.801	N(15)-Co(33)-O(3)	77.909	O(21)-Zn(33)-N(18)	88.131
O(21)-Cu(33)-O(37)	174.524	O(37)-Ni(33)-O(21)	166.085	N(15)-Co(33)-O(37)	140.080	O(21)-Zn(33)-Cl(35)	115.060
O(21)-Cu(33)-O(36)	86.696	O(37)-Ni(33)-O(36)	105.535	N(15)-Co(33)-O(36)	88.541	O(21)-Zn(33)-Cl(34)	108.151
O(21)-Cu(33)-Cl(34)	130.114	O(37)-Ni(33)-Cl(35)	65.556	N(15)-Co(33)-Cl(35)	102.266	N(18)-Zn(33)-Cl(35)	102.486
O(21)-Cu(33)-Cl(35)	97.648	O(37)-Ni(33)-Cl(34)	67.061	N(15)-Co(33)-Cl(34)	97.030	N(18)-Zn(33)-Cl(34)	114.231
N(18)-Cu(33)-O(37)	90.086	N(18)-Ni(33)-O(21)	89.319	O(3)-Co(33)-O(37)	62.566	Cl(35)-Zn(33)-Cl(34)	123.217
N(18)-Cu(33)-O(36)	123.825	N(18)-Ni(33)-O(36)	176.512	O(3)-Co(33)-O(36)	77.124	N(18)- Zn(33)-C(19)	106.667
N(18)-Cu(33)-Cl(34)	105.346	N(18)-Ni(33)-Cl(35)	95.664	O(3)-Co(33)-Cl(35)	156.105	N(18)-Zn(33)-C(17)	122.318
N(18)-Cu(33)-Cl(35)	116.769	N(18)-Ni(33)-Cl(34)	95.087	O(3)-Co(33)-Cl(34)	84.066	N(22)-C(20)-O(21)	126.438
O(37)-Cu(33)-O(36)	91.257	O(21)-Ni(33)-O(36)	87.263	O(37)-Co(33)-O(36)	77.941	H(45)-C(17)-N(18)	114.460
O(37)-Cu(33)-Cl(34)	46.619	O(21)-Ni(33)-Cl(35)	111.203	O(37)-Co(33)-Cl(35)	111.481	O(21)-C(20)-C(19)	126.579
O(37)-Cu(33)-Cl(35)	87.783	O(21)-Ni(33)-Cl(34)	120.048	O(37)-Co(33)-Cl(34)	84.846	C(25)-C(19)-N(18)	139.129
O(36)-Cu(33)-Cl(34)	46.041	O(36)-Ni(33)-Cl(35)	84.932	O(36)-Co(33)-Cl(35)	78.992	C (20)-C(19)-N(18)	112.431
O(36)-Cu(33)-Cl(35)	119.400	O(36)-Ni(33)-Cl(34)	87.237	O(36)-Co(33)-Cl(34)	158.822	C(19)-N(18)-C(17)	130.315
Cl(34)-Cu(33)-Cl(35)	117.316	Cl(35)-Ni(33)-Cl(34)	127.610	Cl(35)-Co(33)-Cl(34)	119.292	H(45)-C(17)-N(18)	114.460

TABLE-8
SELECTED OPTIMIZED GEOMETRY PARAMETERS OF METAL(II)
COMPLEXES (**1a-d**) BY B3LYP METHOD USING LACVP++ BASIS SET

Bond length (Å)							
[Cu(HL)] (**1a**)		[Ni(HL)] (**1b**)		[Co(HL)] (**1c**)		[Zn(HL)] (**1d**)	
Cu(33)-N(18)	1.963	Ni(33)-N(18)	1.824	Co(33)-N(15)	1.862	Zn(37)-N(18)	1.976
Cu(33)-O(37)	1.946	Ni(33)-O(37)	3.400	Co(33)-O(37)	1.989	Zn(37)-O(21)	1.980
Cu(33)-O(36)	1.919	Ni(33)-O(36)	1.883	Co(33)-O(36)	2.056	Zn(37)-Cl(35)	2.203
Cu(33)-O(21)	2.006	Ni(33)-O(21)	2.041	Co(33)-O(3)	2.799	Zn(37)-Cl(34)	2.194
Cu(33)-Cl(35)	2.306	Ni(33)-Cl(35)	2.303	Co(33)-Cl(35)	2.440	–	–
Cu(33)-Cl(34)	3.907	Ni(37)-Cl(34)	2.229	Co(33)-Cl(34)	2.266	–	–

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