Indian Journal of Chemistry
Vol. 59A, November 2020, pp. 1666-1675

Investigation of molecular docking, biological and DFT studies of Schiff base transition metal complexes

A Sudha & S J Askar Ali*

PG and Research Department of Chemistry, The New College (Autonomous), Affiliated to University of Madras, Chennai-600014, India

*E-mail: sjaaresearchgroup@gmail.com

Received 10 February 2020; revised and accepted 29 July 2020

The Schiff base ligand obtained from the reaction of 2-amino-3-hydroxypyridine, 2,4,6-trihydroxy benzaldehyde is described. Cu(II), Ni(II), Co(II), and Zn(II)complexes have been analyzed by various spectroscopic techniques like FT-IR, UV-visible, mass spectrometry and NMR. Based on spectral data octahedral geometry has been assigned to the complexes. In the present study the prepared Schiff base ligand and all the metal complexes have been synthesized and studied for their in vitro anti diabetic, antioxidant and antibacterial activities. Geometry optimization and the chemical stability and reactivity of complexes clearly understood with help of frontier molecular orbital's (HOMO-LUMO) using B3LYP/LACVP++ basis sets based on density functional theory. Furthermore, Molecular docking study of the Schiff base ligand and their metal (II) complexes showed good binding score with human pancreatic α-amylase (PDB: 1HNY).

Keywords: Antibacterial, Antidiabetic, Antioxidant, Computational, Docking

Schiff bases are an important class of ligands in coordination chemistry and find extensive applications in different fields. Thus the main aim of this study was to design new Schiff base containing 2,4,6-trihydroxy benzaldehyde, 2-amino-3-hydroxypyridine the Cu(II), Ni(II), Co(II) and Zn(II) complexes were prepared and characterized. Recent years a great deal of interest in the synthesis and characterization of Schiff bases involving a pyridine ring. Pyridine ligands, which have been used in the coordination chemistry of a variety of metals [1-4] occupy a unique position in the synthesis of biologically active compounds.[5-6] In this study, we have described synthesis, characterization, with some new tridentate Schiff base ligands, which have been characterized by infrared (IR), UV-visible absorption, ^{1}H NMR, ^{13}C NMR and mass spectrometry. We have also investigated antibacterial activity of the complexes against *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis.*

The objective of the present study was to investigate the antioxidant activity of Schiff base ligand and their metal complexes, compared with that of the classical antioxidants, Vitamin C by in vitro total antioxidant activities (phosphomolybdenum methods) radical scavenging method. Therefore, in addition to natural antioxidants such as Vitamin E, Vitamin C, flavonoids and carotenoids with free radical scavenging potential may be relevant in the therapeutic and preventions of diseases[7]. The development of anti-diabetic metal complexes replacing insulin injection to regulate sugar levels appears to be interesting. Inhibition of α-amylase is an important enzyme which is secreted primarily by the salivary glands and the pancreas and to control post-prandial hyperglycemia. Diabetes mellitus (DM) is a metabolic disorder was resulting from a defect in insulin secretion, insulin action, or both leading to chronic hyperglycemia it is often accompanied with disturbances of carbohydrate, fat and protein metabolism and severe diabetic complications. The increased oxidative stress in different tissues of diabetic patients is caused by chronic hyperglycemia and plays a central role in the development of various associated complications including retinopathy, neuropathy, nephropathy, cardiovascular complications and ulceration[8–13]. Here we studied about anti diabetic activity in alpha-amylase method with various concentrations, the molecular docking study, geometry optimization and DFT calculations are also done for the prepared Schiff base ligand and its metal(II) complexes.

Materials and Methods

The chemical compound 2-amino-3-hydroxy pyridine obtained from Avra synthesis, 2,4,6-trihydroxy benzaldehyde obtain from sigma Aldrich,

metal(II) chloride salts are obtained from Sisco Research Laboratories (SRL) and used without any further purification. The solvents used for synthesis, purification process and other spectroscopic techniques were prior to using standard distillation process.[14] Infrared spectra were examined on a Perkin-Elmer FT-IR type 1650 spectrophotometer and UV-visible spectra in Perkin-Elmer Lambda-25 in the wavelength range 200–600 nm. The ESI-mass spectral techniques were performed in ESI-mass spectrophotometer using methanol as a solvent. The ^{1}H NMR and ^{13}C NMR spectra of the ligand were recorded with a Bruker 400 MHz NMR spectrophotometer. Theoretical and molecular docking studies carried using Schrodinger suite-2015 program.

Preparation of Schiff base ligand (HL)

To a methanolic solution of 2,4,6-trihydroxy benzaldehyde (2 mmol) refluxed with stirring by equimolar quantities of 2-amino-3-hydroxy pyridine (2 mmol) at 80 °C for 4 h. The resulting yellow solution was filtered and recrystallized with methanol. The obtained product was followed by TLC, after that the ligand was dried in vacuum desiccators. The obtained ligand is stable in air. Yield: 71%; Color: Dark brown; M.P. >250 °C; ^{1}H NMR (DMSO-d_6, δ, PPM): 5.75 (s,1H,C-OH), 6.39–8.25 (m,1H,Ar-H), 9.23 (s,1H, N=CH);^{13}C NMR (DMSO-d_6,δ, PPM): 112.86–139.91(Ar-C), 150.71(C=N);. IR (ν, cm^{-1}): 1557 (ν CH=N); 3324 (ν C=OH); λ_{max}(nm) in MeOH: 429, 312, 224; Positive-ion ESI–MS (MeOH) *m/z* (%): 245.

Synthesis of the complexes [M (HL)] (1a-1d)

To a methanolic solution Schiff base ligand (**HL**) (1mmol) mixing with methanolic solution of metal(II) chloride salts like Cu, Ni, Co and Zn (2 mmol) with constant stirring and reflux at 80 °C for 8 h. The resulting mixture was allowed to cool at room temperature and the resultant product was filtered, washed with cold methanol and dried. The obtained product was recrystallized from hot methanol and dried over in vacuum desiccator.

Synthesis of [Cu(HL)] (1a)

Yield: 67; Color: Brown; M.P. >300 °C (dec.); IR (ν, cm^{-1}) : 1548(ν C=N); 3610 (ν C=OH); 464(ν Cu-N), 587(ν Cu-O); λ_{max} (nm)) in MeOH: 462 (d-d), 393, 336, 259; Positive-ion ESI–MS (MeOH) *m/z* (%): 551.

Synthesis of [Ni(HL)] (1b)

Yield: 66%; Color: Light Brown; M.P.>300 °C (dec.); IR (ν, cm^{-1}) :1571(ν C=N); 3547 (ν C=OH); 464(ν Cu-N), 587(ν Cu-O); λ_{max} (nm) in MeOH: 433 (d-d), 309, 271, 220; Positive-ion ESI–MS (MeOH) *m/z* (%): 545.

Synthesis of [Co(HL)] (1c)

Yield: 63%; Color: Dark Brown; M.P. >300 °C (dec.); IR (ν, cm^{-1}) : 1567(ν C=N); 3648 (ν C=OH); 467(ν Cu-N), 586(ν Cu-O); λ_{max} (nm)) in MeOH: 429 (d-d), 312, 244, 224; Positive-ion ESI–MS (MeOH) *m/z* (%): 546.

Synthesis of [Zn(HL)] (1d)

Yield: 64%; Color: Coffee brown; M.P. >300 °C (dec.); IR (ν, cm^{-1}) : 1571(ν C=N); 3547 (ν C=OH); 463(ν Cu-N), 567(ν Cu-O); λ_{max} (nm)) in MeOH: 423 (d-d), 313, 213, 226; Positive-ion ESI–MS (MeOH) *m/z* (%): 551.

Antibacterial activity

In-vitro antibacterial activity against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis* were screened and assayed by disc diffusion method Ciprofloxacin were used as the standard.

Antioxidant activity

The total antioxidant potential were evaluated by using the phosphomolybdenum method. The total antioxidant capacity was based on the reduction of Mo(VI) to Mo(V) by accepting an electron from an antioxidant at acidic pH.

Antidiabetic activity

The antidiabetic activity was performed by using α-amylase inhibition method. 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, the 1% starch solution (1mL) was added and the reaction mixture was incubated for 30 min at 25 °C.

Molecular docking

The rigid molecular docking studies were performed by using maestro-v10.2 software integrated into the Schrodinger 2015-2 molecular modelling package installed on Intel Pentium 32 bit; x64 processor-based hp workstation with a Windows-10 operating system. The 3D structures of the complexes were sketched by using builder panel in maestro and fully optimized using the *Ligprep* module which executes addition of the hydrogen, regulates the rational bond angles and lengths, and adjusts the geometry and ring conformations.

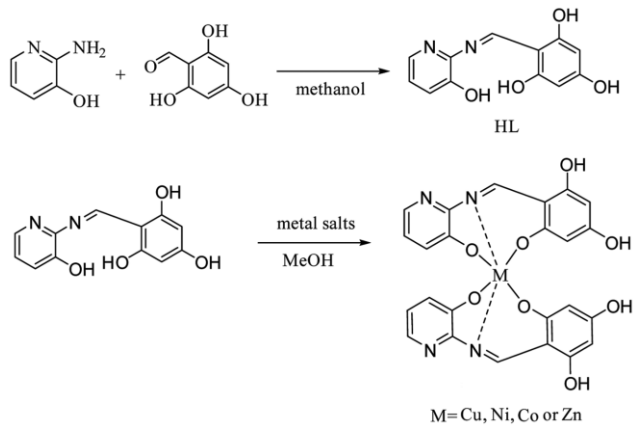
The crystallographic data of human pancreatic α-amylase (PDB:1HNY) were retrieved from Protein Data Bank (http://www.rcsb.org). Consequently, the receptor was fully optimized in the protein preparation wizard. In this stage it involves aligning bond order, adding polar hydrogen, delete water beyond 5Å from hetero atoms, adding missing side chain and finally incorporation of hydrogen bond corresponding to PH 7.0. The outputs were visualized by PyMol console for virtual examination of various binding modes.

Computational analysis

All the computational works were performed using jaguar v8.8 program as incorporated in Schrödinger suite 2015-2. The geometry optimization and the quantum chemical calculation of metal complexes and Schiff base ligand were optimized based on the density functional theory (DFT) using the B3LYP functional and 3-21G*++ basis set was used in all cases.

Results and Discussion

The Schiff base ligand (**HL**) was characterized by FT-IR, UV-visible and ^{1}H NMR techniques. The metal (II) complexes (**1a–1d)** were prepared by treating metal chlorides with the Schiff base ligand using methanol as solvent. The complexes have been isolated as a pure and stable compound. Based on coordination towards metal ions, the complexes were formulated as [Cu(HL)]**1a**, [Ni(HL)]**1b**, [Co(HL)]**1c** and [Zn(HL)]**1d**. All the complexes were quite soluble in common organic solvents such as methanol, ethanol, DMF and DMSO, less soluble in water and insoluble in hydrocarbon solvents (Scheme 1).



Scheme 1 — Synthesis of Schiff base ligand and its metal(II) complexes

Spectral characterization

The ^{1}H and ^{13}C NMR spectra of the samples were recorded on Bruker 300 MHz and 75 MHz spectrometer. The chemical shifts are reported in ppm (δ) with TMS as internal standard. The ^{1}H NMR study is to help in the structural elucidation of the ligands as well as in locating precisely the donor site or sites of a ligand. The ^{1}H NMR spectra of the ligand shows the signals at 6.39–8.25 (m) δ for aromatic protons and 9.23 (s)δ for azomethine proton. The peak at 5.75 (s)δ attributed to –OH group they shown in Supplementary Data, Fig. S1.^{13}C NMR spectra of Schiff base ligand showed the azomethine carbon signal at 150.71 ppm. The aromatic carbon signals are seen at 112.86–139.91 ppm range depending on their electronic environment in Supplementary Data, Fig. S2.

ESI-mass spectra (TOF-MS) of the Schiff base ligands and their complexes were recorded on micromax Q-TOF model with ES+ mode in methanol. The mass spectrum of the Schiff base ligand (HL) showed the molecular ion peak at m/z 245 corresponding to $[C_{12}H_{10}N_2O_5]$ ion. Also the spectrum exhibited peaks for the fragments at m/z 123 and 120 corresponding to $[C_5H_{10}O_3]^+$ and $[C_6H_5N_2O]^+$, respectively. The spectra of Cu(II), Ni(II), Co(II) and Zn(II) complexes showed molecular ion peaks at m/z 551, 545, 546 and 551, respectively that are equivalent to their molecular weight they shown in Supplementary Data, Figs S3 and S4. The fragment ion peak is observed at m/z 246 which corresponds to the original molecular weight of the Schiff base under investigation.

Selected infrared vibrational stretching frequencies of the free Schiff base ligand and the metal complexes, which are useful for determining the mode of coordination of the ligand. The FT-IR spectra of Schiff base ligand and metal(II) complexes (**1a-1d**). The spectrum of the ligand **HL** shows a broad band in the region 3324 cm^{-1} assignable to intramolecular hydrogen bonded OH groups. The absence of these bands, noted in the spectra of the complexes, indicates the deprotonation of the intramolecular hydrogen bonded OH groups on in the region of 3438–3648 cm^{-1}. The spectra of the ligand show the characteristic –C=N bands in the region 1557–1564 cm^{-1}, which are shifted to lower frequencies in the spectra of the complexes (1548–1571 cm^{-1}) indicating the involvement of the azomethine nitrogen in chelation with the metal ion. The IR spectra of the metal complexes also show some new bands in the region 450–467 cm^{-1} and 500–587 cm^{-1} which are

probably due to the formation of M-O and M-N bonds[15-16], respectively (Supplementary Data, Fig. S5).

The molecular electronic absorption spectra of the free Schiff base ligand and the metal complexes are often very important in the evaluation of results furnished by other methods of structural check. The electronic spectral measurements were used for assigning the stereo chemistries of metal ions in the complexes depending on the sites and number of *d–d* transition peaks. The electronic absorption spectra of ligands and their complexes were registered at the wavelength range 200–600 nm and at 298 K. The ligand exhibits absorption bands in UV–visible region around 355 nm which is assigned to n→π* transition originating from the imine function of the Schiff base ligand. The absorption bands of complexes at λ_{max}= 390–407 nm is assigned to charge transfer with in Schiff base ligands. Furthermore a long and broad band lying in the region 423–462 nm could be mainly attributed to the d → d transition in the structure of the prepared complexes shown in Supplementary Data, Fig. S6.

Antibacterial activity

In vitro antibacterial activity of The Schiff base ligand **(HL)** and its metal (II) complexes **(1a-1d)** have been screened and assayed by disc diffusion method against various pathogenic bacterias such as *Pseudomonas aeruginosa, Escherichia coli, Bacillus subtilis, Staphylococcus aureus,* ciprofloxacin were used as the standard for bacterial studies. Furthermore, the zone of inhibition study revealed that the synthesized compounds possessed antibacterial activity against the tested microbes as described in Table 1 and Supplementary Data, Fig. S7. It has been observed that the metal complexes have a higher activity than that of the free ligand.[17-22]

Antioxidant activity

Total antioxidant capacity (Phosphomolybdenum assay)

The total antioxidant potential of the Schiff base ligand and their metal complexes were evaluated by using the phosphomolybdenum method[23] which is based on the reduction of Mo(VI) to Mo(V) by accepting of an electron from antioxidant at acidic pH. Total antioxidant activities of ligand and complex were observed. About 3 mL of antioxidant reagent (0.6 M H_2SO_4, 28 mM Na_3PO_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 phosphomolybdenum 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 using a spectrophotometer. The total antioxidant activities were calculated using the given formula.

$$TOA = \lfloor (A_t - A_c)/A_t \rfloor \times 100 \quad \ldots(1)$$

Where A_t is absorbance of test and A_c is absorbance of control. The results of total antioxidant capacity of Schiff base ligand (**HL)** and their metal Cu(II)**1a**, Ni(II)**1b**, Co(II)**1c**, and Zn(II)**1d** complexes were summarized as respectively in Table 2 and in Supplementary Data, Fig. S8. Among the tested compounds Cu(II)**1a** complex shows the maximum total antioxidant activity.

Antidiabetic activity

α-Amylase inhibition technique

The α-Amylase inhibitory activity of this Schiff base ligand and metal complexes was performed by using α-Amylase inhibition method with various concentrations (10, 50, 100, 250 and 500 µg/mL) according to our former publication.[24] Briefly, 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, the 1% starch solution (1mL) was added and the reaction mixture was incubated for 30 min at 25 °C. In order to

Table 1 — Antibacterial activity of Schiff base ligand (HL) and metal(II) complexes (1a-1d) of against Pathogenic bacteria by disc diffusion method

Compounds	Inhibition Zone (mm)			
	P. aeruginosa	*E. coli*	*S. aureus*	*B. subtilis*
HL	9	11	14	13
1a	11	13	11	14
1b	9	11	16	20
1c	12	14	11	15
1d	13	12	13	17
Ciprofloxacin	12	13	17	24

Table 2 — Antioxidant activity of Schiff base ligand (HL) and metal(II) complexes (1a-1d) with various concentrations

Compounds	Concentration (μg/mL)				
	10	50	100	250	500
HL	10.12	15.44	33.45	48.71	56.92
1a	11.11	16.38	34.58	47.25	58.82
1b	10.78	16.02	34.26	47.11	58.56
1c	11.09	16.13	34.47	47.21	58.69
1d	10.24	15.51	33.67	46.77	57.35
Vitamin C	22.43	32.11	69.78	82.23	94.55

Table 3 — Antidiabetic activity of Schiff base ligand (HL) and metal(II) complexes (1a-1d) with various concentrations

Compounds	Concentration (μg/mL)				
	10	50	100	250	500
HL	6.72	10.33	29.82	39.47	51.57
1a	5.89	11.72	31.33	41.22	54.59
1b	5.68	11.42	31.27	41.51	54.18
1c	5.95	11.96	31.94	41.76	54.90
1d	5.77	11.36	31.28	40.64	54.02
Acarbose	18.22	26.33	44.69	63.29	81.52

stop the enzymatic reaction, DNSA reagent (1mL) was added as the 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 using a spectrophotometer instrument. The measured absorbance was compared with that of the control experiment. The percentage inhibition was calculated from the given formula

$$\%\ of\ Inhibition = 100 \times \lfloor A_t - (A_t/A_c) \rfloor \quad \ldots(2)$$

Where, A_t is absorbance of test and A_c is absorbance of control. The measured absorbance was compared with that of the control experiment and the obtained results were considered as criteria for the percentage of α -Amylase inhibition.[25,26] As shown, Schiff base ligand (**HL**) and metal complexes (Cu(II)**1a**, Ni(II)**1b**, Co(II)**1c**, and Zn(II)**1d**) revealed an inhibitory action similar to the widely used commercial drug (Acarbose) against pancreatic α – Amylase. The compounds were summarized as respectively in Table 3 and in Supplementary Data, Fig. S9. Among the tested compounds Co(II)**1c** complex shows the maximum antidiabetic activity.

Molecular docking studies

The molecular docking calculation based on the most probable interaction between the drug molecules[27] and a target protein. In this docking study, the molecular interaction of Schiff base ligand and its metal complexes was chosen to predict the binding site inside the target protein, To study the molecular interaction of compounds, crystallographic data of human pancreatic α-amylase (PDB:1HNY) was retrieved from Protein Data Bank. In the protein preparation wizard, first manually removing bound ligands and water (beyond 3Å) molecules followed by addition of hydrogen to the protein.

Thereafter, minimization was carried out using force field OPLS-2005 until it reached a cut-off 0.01Å RMSD. The complex structures were constructed by using CHEM SKETCH and converted into PDB format suitable for docking program using OPENBABEL. The output results were visualized with help of PyMOL. The docking score value and various modes of binding interaction with the target protein predicted in Figs 1 & 2 and the data were summarized in Table 4. The figure give a clear idea about that the active sites of docked protein well stabilized by H-bond, π-π stacking interactions, and hydrophobic contacts. The docking score values of ligand and metal(II) complexes were found to be −5.511, −4.436, −5.372, −3.577 and −5.193 kcal mol^{-1}. When the docking scores value is more negative, the binding nature of a complex with the receptor is greater.

Computational analysis

Theoretical investigation of Schiff base ligand (**HL**) and its metal(II) complexes were performed using jaguar v8.8 program as incorporated in Schrödinger suite 2015-2. The geometries of metal(II) complexes (**1a-1d)** were optimized based on the density functional theory (DFT) using the B3LYP/LACVP++ basis set was used in all cases.

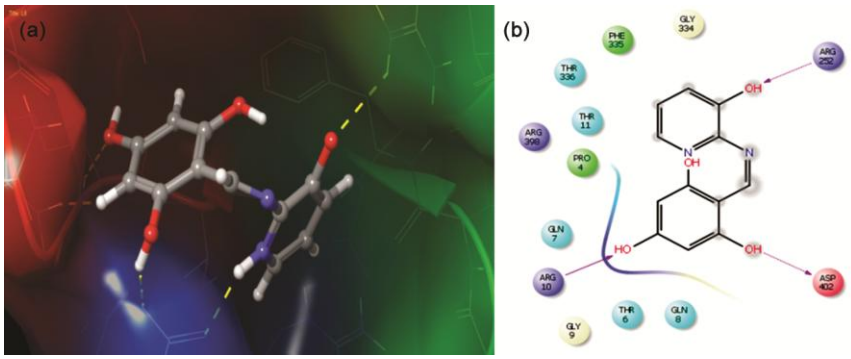


Fig. 1 —3D (a) and 2D (b) interaction of Schiff base ligand (HL)

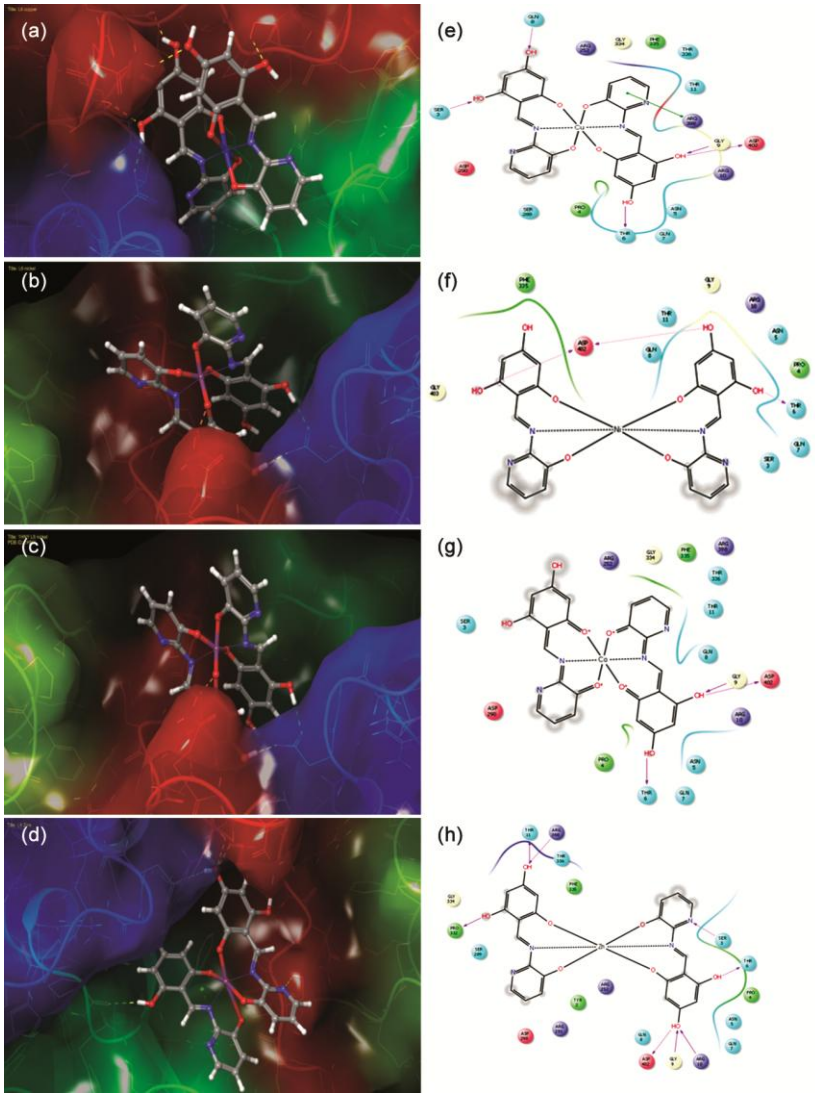


Fig. 2 — 3D (a-d) and 2D (e-h) interaction of Cu(II) 1a, Ni(II) 1b, Co(II) 1c and Zn(II) 1d complexes

Frontier molecular orbital

The frontier molecular orbitals Schiff base ligand (HL) and its metal(II) complexes (**1a-1d**) were represented in Fig. 3. The chemical stability or reactivity of compounds associated with a function of frontier molecular orbital's (FMO's).[28] It involves an interaction of energy levels between HOMO and LUMO of the reacting molecules. The highest

Table 4 — Docking parameters of the Schiff base ligand **HL** and metal(II) complexes **1a-1d**

Compounds	Docking score kcal.mol^{-1}	Active sites with a mode of interaction		
		H-bond	π-π stacking	Hydrophobic contacts
HL	-5.511	ARG 10, ASP 402, ARG 252	NIL	PRO 4, PHE 335
1a	-4.436	ASP 402, GLY 9, THR 6, GLN8, SER 3	ARG 398	PRO 4, PHE 335
1b	-5.372	ASP 402, THR 6	NIL	PRO 4, PHE 335
1c	-3.577	ASP 402, THR 6, GLY 9	NIL	PRO 4, PHE 335
1d	-5.193	SER 3, ARG 398, THR11, ARG 10, PRO 332, ASP 402, GLY 9, THR 6	NIL	PRO 4, PHE 335, PRO 332, TYR 2

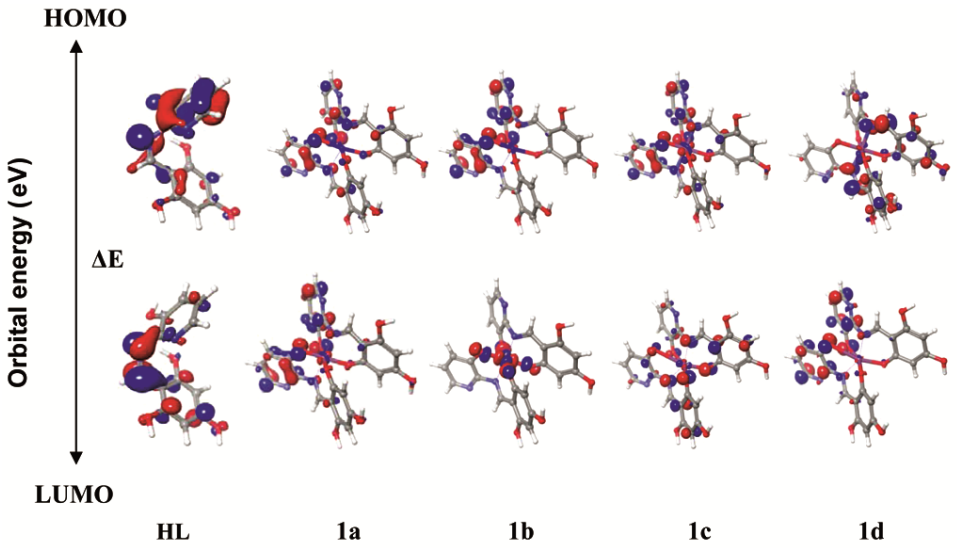


Fig. 3 — FMO of investigated of Schiff base ligand (HL), Cu(II)1a, Ni(II)1b, Co(II)1c and Zn(II)1d

occupied molecular orbital's (HOMO) capable of donating electrons to the empty orbital's of acceptor molecules while lowest unoccupied molecular orbitals (LUMO) have tendency to accept electrons from acceptor[29].

The important quantum parameters like HOMO–LUMO energy gap (ΔE), chemical potentials (Pi), absolute electronegativities (χ), absolute softness (σ), absolute hardness (η), global electrophilicity (ω), global softness (S), and additional electronic charge (ΔN_{max}) can be calculated according to following relations.[30]

$$\Delta E = E_{LUMO} - E_{HOMO} \quad \ldots(3)$$

$$\eta = \frac{E_{LUMO} - E_{HOMO}}{2} \quad \ldots(4)$$

$$\chi = -\frac{(E_{HOMO} - E_{LUMO})}{2} \quad \ldots(5)$$

$$\sigma = \frac{1}{\eta} \quad \ldots(6)$$

$$Pi = -\chi \quad \ldots.(7)$$

$$S = \frac{1}{2\eta} \quad \ldots.(8)$$

$$\omega = \frac{Pi^2}{2\eta} \quad \ldots(9)$$

$$\Delta N_{max} = \frac{-Pi}{\eta} \quad \ldots(10)$$

The energy difference between (ΔE) E_{LUMO} and E_{HOMO} more abundantly determine the activity of compounds. The observed energy band gap values for Schiff base ligand **(HL)** and its metal complex, Cu(II)**1a**, Ni(II)**1b**, Co(II)**1c** and Zn(II)**1d** is found to be 4.77 eV, 1.07 eV, 2.46 eV, 3.41 eV and 1.17 eV, respectively. It was found that the Cu(II) **1a** complex showed lowest band gap and easier to transits electron from ground (HOMO) state to excited state (LUMO) at low frequency compared to other complexes. The calculated quantum parameters are listed in Table 5.

Geometry optimization

The geometry optimization for synthesized Schiff base ligand **(HL)** and metal(II) complexes (**1a-1d)** were carried out by maestro software inbuilt in

Table 5 — The calculated quantum parameters of the investigated Schiff base ligand (**HL**) and metal(II) complexes (**1a-1d**)

Compounds	HOMO eV	LUMO eV	ΔE eV	χ	η	σ	Pi	S	ω	ΔN max
HL	-5.70	-0.93	4.77	3.31	2.38	0.41	-3.31	0.20	2.30	1.38
1a	-5.16	-4.09	1.07	4.62	0.53	1.86	-4.62	0.93	19.94	8.61
1b	-5.31	-2.85	2.46	4.08	1.23	0.81	-4.08	0.40	6.77	3.31
1c	-5.22	-1.80	3.41	3.51	1.70	0.58	-3.51	0.29	3.62	2.05
1d	-4.98	-3.80	1.17	4.39	0.58	1.70	-4.39	0.85	16.44	7.48

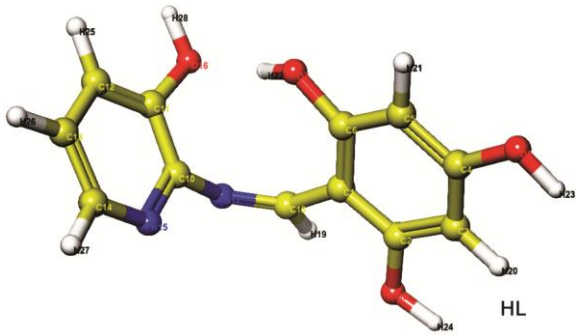


Fig. 4 — Optimized molecular structure of Schiff base ligand (HL) using B3LYP/LACVP++ basis set

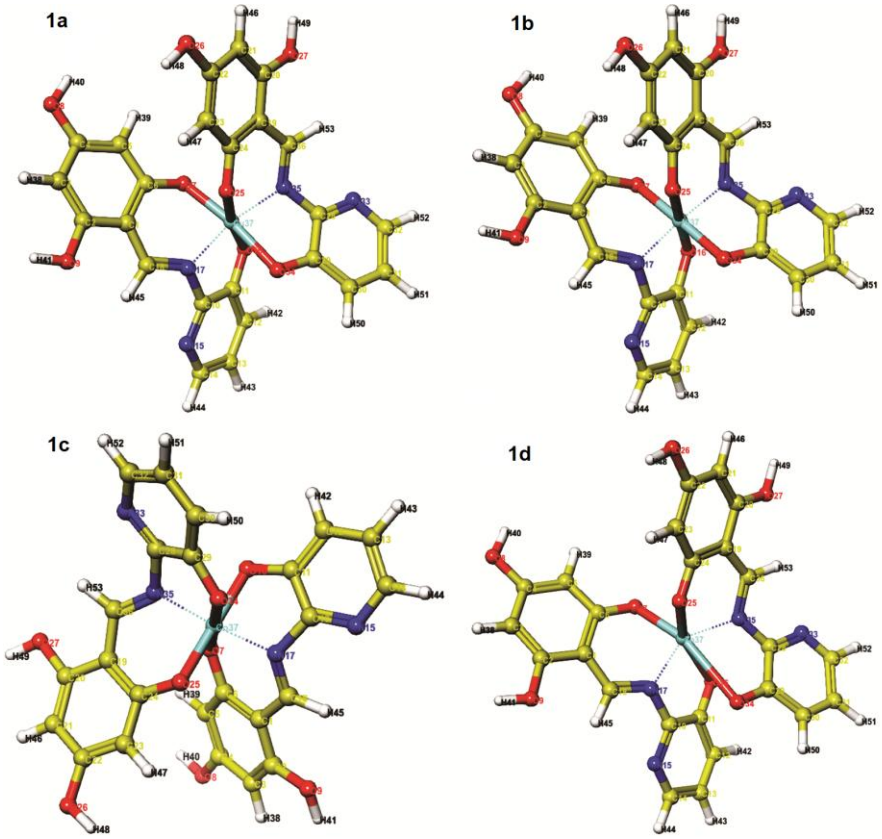


Fig. 5 — Optimized molecular structure of Cu(II)1a, Ni(II)1b, Co(II)1c and Zn(II)1d using B3LYP/LACVP++ basis set

Schroedinger-suite based density functional theory using function B3LYP and LACVP++ basis set.[31] The optimized molecular structures of the ligand and metal(II) complexes were illustrated in Figs 4 & 5 and the selected bond length and bond angle values of the Schiff base and its complexes were given in the Table 6 & 7.

Table 6 — Selected optimized geometry parameters of metal (II) complexes (1a-1d) by B3LYP method using LACVP++ basis set

Bond length (Å)							
[Cu(HL)] 1a		**[Ni(HL)] 1b**		**[Co(HL)] 1c**		**[Zn(HL)] 1d**	
Cu(37)-N(35)	1.925	Ni(37)-N(35)	1.860	Co(37)-N(35)	1.864	Zn(37)-N(35)	1.898
Cu(37)-N(17)	1.925	Ni(37)-N(17)	1.860	Co(37)-O(34)	1.863	Zn(37)-N(17)	1.897
Cu(37)-O(34)	2.054	Ni(37)-O(34)	1.863	Co(37)-O(25)	1.855	Zn(37)-O(34)	2.675
Cu(37)-O(25)	1.929	Ni(37)-O(25)	1.851	Co(37)-N(17)	1.863	Zn(37)-O(25)	1.946
Cu(37)-O(16)	2.052	Ni(37)-O(16)	1.863	Co(37)-O(16)	1.863	Zn(37)-O(16)	2.649
Cu(37)-O(7)	1.929	Ni(37)-O(7)	1.851	Co(37)-O(7)	1.855	Zn(37)-O(7)	1.944

Table 7 — Selected optimized geometry parameters of metal (II) complexes (1a-1d) by B3LYP method using LACVP++ basis set

Bond angle (deg)							
[Cu(HL)] 1a		**[Ni(HL)] 1b**		**[Co(HL)] 1c**		**[Zn(HL)] 1d**	
N(35)-Cu (37)-N(17)	165.214	N(35)-Ni(37)-O(34)	85.166	N(35)-Co(37)-O(34)	85.099	N(35)-Zn(37)-O(34)	72.152
N(35)-Cu (37)-O(34)	82.193	N(35)-Ni(37)-O(25)	88.855	N(35)-Co(37)-O(25)	89.504	N(35)-Zn(37)-O(25)	89.508
N(35)-Cu (37)-O(25)	86.052	N(35)-Ni(37)-N(17)	174.245	N(35)-Co(37)-N(17)	174.311	N(35)-Zn(37)-N(17)	139.924
N(35)-Cu (37)-O(16)	86.298	N(35)-Ni(37)-O(16)	90.509	N(35)-Co(37)-O(16)	90.651	N(35)-Zn(37)-O(16)	74.113
N(35)-Cu (37)-O(7)	105.065	N(35)-Ni(37)-O(7)	95.350	N(35)-Co(37)-O(7)	94.744	N(35)-Zn(37)-O(7)	120.783
N(17)-Cu (37)-O(34)	86.244	O(34)-Ni(37)-O(25)	94.620	O(34)-Co(37)-O(25)	95.749	O(34)-Zn(37)-O(25)	106.117
N(17)-Cu (37)-O(25)	104.951	O(34)-Ni(37)-N(17)	90.462	O(34)-Co(37)-N(17)	90.561	O(34)-Zn(37)-N(17)	73.518
N(17)-Cu (37)-O(16)	82.258	O(34)-Ni(37)-O(16)	82.992	O(34)-Co(37)-O(16)	82.964	O(34)-Zn(37)-O(16)	63.905
N(17)-Cu (37)-O(7)	86.069	O(34)-Ni(37)-O(7)	177.585	O(34)-Co(37)-O(7)	178.726	O(34)-Zn(37)-O(7)	162.331
O(34)-Cu (37)-O(25)	99.209	O(25)-Ni(37)-N(17)	95.236	O(25)-Co(37)-N(17)	94.597	O(25)-Zn(37)-N(17)	119.683
O(34)-Cu (37)-O(16)	77.781	O(25)-Ni(37)-O(16)	177.572	O(25)-Co(37)-O(16)	178.685	O(25)-Zn(37)-O(16)	162.662
O(34)-Cu (37)-O(7)	172.072	O(25)-Ni(37)-O(7)	87.752	O(25)-Co(37)-O(7)	85.513	O(25)-Zn(37)-O(7)	86.935
O(25)-Cu (37)-O(16)	172.100	N(17)-Ni(37)-O(16)	85.237	N(17)-Co(37)-O(16)	85.159	N(17)-Zn(37)-O(16)	72.627
O(25)-Cu (37)-O(7)	84.662	N(17)-Ni(37)-O(7)	88.866	N(17)-Co(37)-O(7)	89.513	N(17)-Zn(37)-O(7)	89.768
O(16)-Cu (37)-O(7)	99.244	O(16)-Ni(37)-O(7)	94.640	O(16)-Co(37)-O(7)	95.775	O(16)-Zn(37)-O(7)	106.153

Conclusions

In summary of metal(II) complexes (**1a-1d**) derived from Schiff base ligand (**HL**) and these complexes showed three coordination through Schiff base ligand. Based on spectroscopic investigations and their correlations with the available data of known compounds proposed octahedral structures of metal complexes have been illustrated. They show very good antidiabetic, antioxidant and antimicrobial activity of the compounds.All the complexes were strongly interact with crystallographic data of human pancreatic α-amylase (PDB:1HNY)and the best docking score value observed for complex **1b** was consistent with experimental results obtained from an antidiabetic activity. Finally, the frontier molecular orbital's results showed higher activity and more stable because of small energy gap for Cu(II)**1a** and lower activity for Co(II)**1c** complex. Therefore, these investigated compounds may be considered as promising candidates for further biological purpose.

Acknowledgment

Allthe authors express their gratitude to The New College, VIT University Vellore and Indian Institute Technology Madras for providing help in spectral data.

Supplementary Data

Supplementary Data associated with this article are available in the electronic form at http://nopr.niscair.res.in/jinfo/ijca/IJCA_59A(11)1666-1675_SupplData.pdf.

Reference

1 Shavit M & Tshuva E Y, *Euro J Inorg Chem*, 9 (2008) 1467.
2 Dubois L, Pécaut J, Charlot M F, Baffert C, Collomb M N, Deronzier A & Latour J M, *Chem Euro J*, 14 (2008) 3013.
3 Zhao M, Helms B, Slonkina E, Friedle S, Lee D, DuBois J, Hedman B, Hodgson K O,Fréchet J M & Lippard SJ, *J Am Chem Soc*, 130 (2008) 4352.
4 Yang C I, Wernsdorfer W, Tsai Y J, Chung G, Kuo T S, Lee G H, Shieh M & Tsai H L, *Inorg Chem*, 47 (2008) 1925.
5 Vasconcellos-Dias M, Nunes C D, Vaz P D, Ferreira P & Calhorda M J, *Euro J Inorg Chem*, 18 (2007) 2917.
6 Son J K, Zhao L X, Basnet A, Thapa P, Karki R, Na Y, Jahng Y, Jeong T C, Jeong B S, Lee C S & Lee ES, *Euro J Med Chem*,43 (2008) 675.
7 Soare J R, Dinis T C, Cunha A P & Almeida L, *Free Radical Res*, 26 (1997) 469.
8 Bastaki A, *Inter J Diabetes Metab*, 13 (2005) 111.
9 Baynes J W & Thorpe S R, *Diabetes*, 48 (1999) 1.
10 Callaghan M, Ceradini D J & Gurtner G C, *Antioxid Redox Signal*, 7 (2005) 1476.
11 Kandra L, *J Mol Struc-Theochem*, 666 (2003) 487.
12 Whitcomb D C & Lowe M E, *Dig Dis Sci*, 52 (2007) 1.
13 Tangphatsornruang S, Naconsie M, Thammarongtham C & Narangajavana J, *Plant Physio Biochem*, 43 (2005) 821.
14 Nakamoto K & McCarthy PJ, *Spectroscopy and Structure of Metal Chelate Compounds*, (Wiley) 1968.
15 Narang K K & Aggarwal A, *Inorganica Chim Acta*, 9 (1974) 137.
16 Kusanur R A, Ghate M & Kulkarni M V, *J Chem Sci*, 116 (2004) 265.
17 Anjaneyulu Y & Rao R P, *Synth React Inorg Met-Org Chem*, 16 (1986) 257.
18 Horsfall J G, *Bot Rev*, 11 (1945) 357.
19 Belaid S, Landreau A, Djebbar S, Benali-Baitich O, Bouet G & Bouchara J P, *J Inorg Biochem*, 102 (2008) 63.
20 Dharmaraj N, Viswanathamurthi P & Natarajan K, *Transit Met Chem*, 26 (2001) 105.
21 Banuppriya G, Sribalan R & Padmini V, *Chemistry Select*, 2 (2017) 9168.
22 Abdel-Aty A M, Salama W H,Fahmy A S & Mohamed S A, *Sci Hortic*, 246 (2019) 155.
23 Banuppriya G, Sribalan R, Fathima S A & Padmini V, *Chem Biodivers*, 15 (2018) 1800105.
24 Valentina P, Ilango K, Chander S & Murugesan S, *Bioorg Chem*, 74 (2017) 158.
25 Naeem F, Nadeem H, Muhammad A, Zahid M A & Saeed A, *Open Chem J*, 5 (2018).
26 Ponnusamy S, Haldar S, Mulani F, Zinjarde S, Thulasiram H & RaviKumar A, *PloS ONE*, 10(2015).
27 Mohapatra S, Prasad A, Haque F, Ray S, De B & Ray S S, *J Appl Pharm Sci*, 5 (2015) 042.
28 Zhang D Q, Gao L X & Zhou G D, *Corros Sci*, 46 (2004) 3031.
29 El-Ghamaz N A, Ghoneim M M, El-Sonbati A Z, Diab M A, El-Bindary A A & El-Kader M A, *J Saudi Chem Soc*, 21 (2017) S339.
30 Abdel-Rahman L H, Abu-Dief A M, El-Khatib R M & Abdel-Fatah S M, *Bioorg Chem*, 69 (2016) 140.
31 Tyagi P, Chandra S, Saraswat B S & Sharma D, *Spectrochim Acta Part A*, 143 (2015) 1.