Article

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Synthesis, Characterization and study of molecular docking of a new Azo-Schiff base ligand with its metal complexes

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Abstract:

The new heterocyclic ligand [8-((1E)-(2-(((4-fluorobenzylidene)amino)methyl)phenyl)diazenyl)-1,3-dimethyl-3,9-dihydro-1H-purine-2,6-dione] (**4F-DBAPD**) was prepared from the diazotization of Ortho-aminobenzylamine with (1,3-dimethyl-3,9-dihydro-1H-purine-2,6-dione), followed by the condensation of the resulting compound with 4- Floro Benzaldehyde. Different analytical and characterization techniques including (mass,^{1}HNMR, FT-IR and UV-Vis. spectroscopy and C.H.N elemental analysis) in the investigation of newly prepared ligand. A series of novel solid metal complexes of this ligand with Co (II), Ni (II), Cu (II) and Zn (II) were prepared and all complexes were characterization by techniques above, excluding the mass and the 1H-NMR spectroscopy of some prepared solid metal complexes and the use of flame atomic absorption spectroscopy to determine the percentages of metal ions in the prepared complexes also studied the magnetic susceptibility and molar conductivity of the metal complexes dissolved in DMSO at 1×10^{-3} M concentration laboratory temperature. The results of this studies showed that the coordination sites for the new Azo-Schiff base ligand with Co (II), Ni (II), Cu (II)and Zn (II) were to be through nitrogen of the theophylline ring, ,the nitrogen of azo group and the nitrogen of azomethine group . The Electronic spectral and magnetic measurement data predict octahedral structure of the complexes .All complexes showed that electrolytes properties. In the final stage of the study, Molecular docking technology was used to study the biological effect of the new ligand and its complexes as anti-lung cancer agents and to compare the most effective of them on this type of cancer to propose it as a treatment.

Keywords: Molecular docking , azo-Schiff complexes, lung cancer.

Introduction

Molecular docking is a computational technique used in drug discovery and molecular biology to predict the preferred orientation and binding affinity of a small molecule ligand to a target protein, typically a receptor or enzyme. This technique plays a crucial role in various aspects of drug design and development, as well as in understanding the molecular mechanisms of biological processes.[1,2]. The importance of molecular docking is include its importance as Drug Discovery and Development it is a vital tool in the process of drug discovery, where scientists aim to identify and design potential drug candidates that can interact with specific target proteins implicated in diseases. By simulating the interaction between small molecules (ligands) and target proteins, molecular docking helps in predicting the binding affinity and mode of action of potential drug candidates. This aids in the selection and optimization of lead compounds for further experimental validation, ultimately accelerating the drug development process.[3]. By docking thousands or even millions of compounds against a target protein, researchers can prioritize the most promising candidates for experimental testing, significantly reducing the time and resources required compared to traditional high-throughput screening methods.[4]

In order to Understanding the binding mode of a ligand to its target protein is essential for rational drug design. Molecular docking provides insights into the specific interactions between the ligand and protein, such as hydrogen bonding, hydrophobic interactions, and electrostatic interactions. This information helps in optimizing the chemical structure of ligands to improve their binding affinity and selectivity.[5] Molecular docking enables the prediction of potential off-target interactions between drug candidates and unintended proteins in the body. This is crucial for assessing the safety profile of drugs and minimizing the risk of adverse side effects. Moreover, molecular docking facilitates the exploration of polypharmacology, where a single drug can interact with multiple targets, leading to synergistic therapeutic effects or reduced drug resistance.[6,7]

Recently the Molecular docking in the modern researches is not limited to drug discovery; it is also valuable for elucidating the molecular mechanisms underlying biological processes.[8]. By simulating the binding of ligands to target proteins, researchers can gain insights into protein-ligand interactions, protein conformational changes, and signal transduction pathways, contributing to our understanding of disease pathogenesis and the development of novel therapeutic strategies.[9,10]

Azo-Schiff base compounds, known for their diverse biological activities, have garnered attention in cancer research due to their potential anticancer properties. While specific studies on their efficacy against lung cancer may be limited, several azo-Schiff base

compounds have shown promising anticancer activity in various cancer types, including lung cancer. [11,12]

Aromatic amines are versatile building blocks in organic chemistry, and their azo-Schiff base derivatives have shown potential anticancer activity. Researchers have synthesized azo-Schiff base derivatives of aromatic amines and evaluated their cytotoxic effects against lung cancer cells. These compounds have demonstrated promising anticancer activity by inhibiting cell growth and inducing apoptosis.[13] .Also the Azo-Schiff Base Derivatives of Phenothiazine have been investigated for their anticancer properties, and their azo-Schiff base derivatives have shown potential anticancer activity against various cancer types. Studies have reported the cytotoxic effects of azo-Schiff base derivatives of phenothiazine against lung cancer cells, suggesting their potential as novel anticancer agents.[14]. While these examples highlight the potential of azo-Schiff base compounds as anticancer agents against lung cancer, further research, including in vivo studies and clinical trials, is needed to evaluate their efficacy and safety for clinical applications. Additionally, structure-activity relationship studies and optimization of compound properties are crucial for the development of potent and selective azo-Schiff base derivatives as anticancer drugs. In summary, molecular docking is a powerful computational technique with diverse applications in drug discovery, virtual screening, structure-based drug design, mechanistic studies, and polypharmacology. Its importance lies in its ability to predict and analyze the interactions between small molecules and target proteins, thereby facilitating the development of new drugs and advancing our understanding of molecular biology.

Materials and Methods

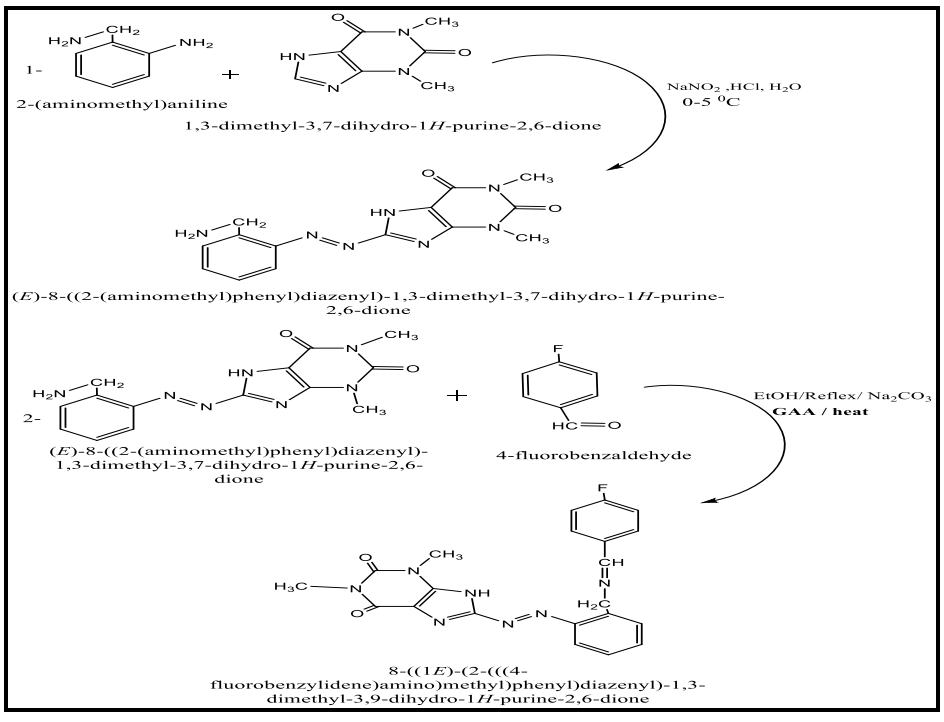
All chemicals were obtained from Merck, BDH and Sigma - Aldrich and used without further purification. Melting point were determined using model 9300 of ligand and its complexes. ^{1}HNMR spectra were recorded as solution in DMSO d6 as solvent using (varian 500MHZ Spectrophotometer) and Mass Spectra were recorded on Shimadzu Agilent Technologies 5975C. The UV-Visible spectra were recorded on Shimadzu spectrophotometer double band model 1700. Magnetic susceptibility measurements were carried out on a balance magnetic MSB-MKI using faraday method. The diamagnetic corrections were made by Pascal's constants. IR spectra were recorded on Shimadzu FTIR 8400 spectrometer using KBr pellet in the wavelength range 4000-400 cm-1. C.H.N Elemental analyses were performed by means of EURO 2012EA 300 C.H.N Elemental analysis.

Synthesis of the new Azo- Schiff base ligand(4F-DBAPD):

The first step included preparing the azo dye. (0.01 mol, 1.222g) of ortho-aminobenzylamine was dissolved in (30mL) of distilled water, while keeping the

temperature of the reaction medium low between (0-5℃). After that, (5mL) was added. of concentrated HCl acid with continuous shaking of the solution. Likewise, (0.01 mol, 0.700g) of $NaNO_2$ was dissolved in (5mL) of distilled water and the solution was cooled to below zero degrees Celsius, after which the second cooled solution was added to the aromatic amine solution with shaking and stirring and the solution was left for (30 minutes) for the purpose Completion of the azotization process**,** This was followed by adding the diazonium salt solution drop by drop, with continuous stirring, to the compound solution, which consists of (0.01 mol, 1.80 g) Theophylline and (20mL) of sodium carbonate solution (40% Na_2CO_3) with the addition of (50mL) of ethanol, at a temperature (0℃) with continuous stirring and at (pH ≈7) by monitoring with PH paper, the resulting solution was left for two hours to complete the precipitation process, then the formed azo was filtered, washed with distilled water several times, dried, and recrystallized using hot absolute ethanol[15].

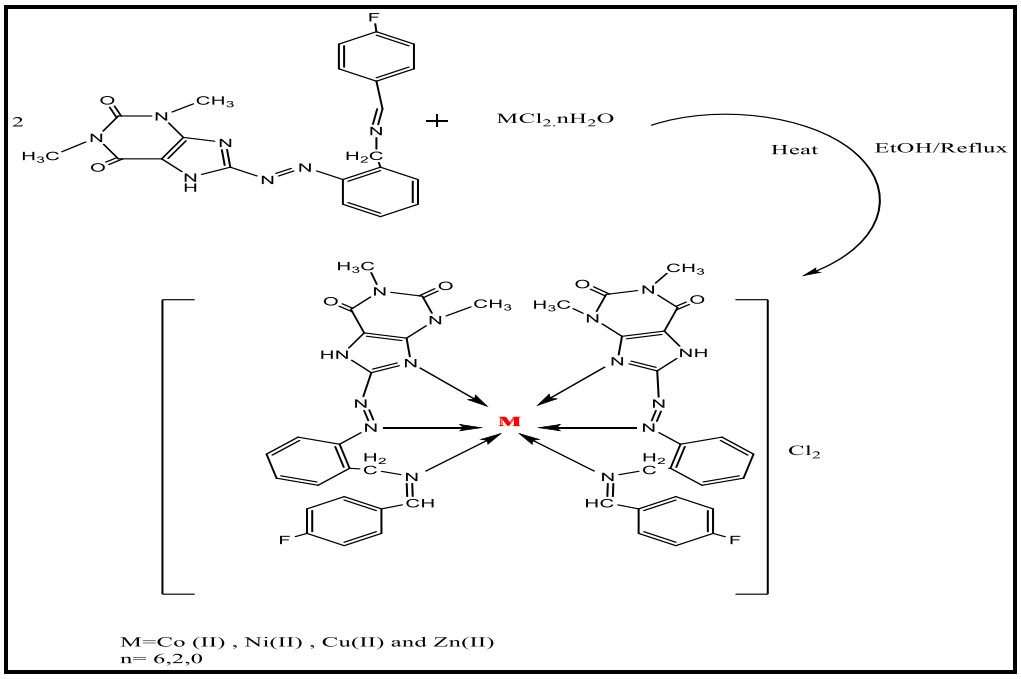
The second step included preparing the new azo ligand - Schiff base (4F-DBAPD), by dissolving (0.01 mol, 1.241 g) of 4-fluorobenzydehyde in (10 mL) of absolute ethanol, and stirring for (2 minutes), then adding (2-3) drops of glacial acetic acid, then left for (5 minutes) at laboratory temperature. After that, a solution prepared from dissolving (0.01 mol, 3.133g) of azo dye in (20 mL) of absolute ethanol is added, and it is heated. The solution lasted for (16 hrs) at a temperature of (78℃), and the new azo ligand - Schiff base (4F-2DIBP) was obtained. The course of the reaction was followed by the TLC method using (0.5mL methanol:4.5mL benzene) and then cooled. The product was dried, collected, and then recrystallized using hot absolute ethanol[16]. Its physical properties were listed in Table (1). **Scheme-1** shows the steps for preparing the azo ligand - the new Schiff base (4 F-DBAPD).



Scheme-1: Synthesis of new azo-Schiff base ligand(4F-DBAPD)

Synthesis of metal complexes:

The metal complexes were synthesized by mixing of (0.0002mol) in 10ml absolute ethanol solution of each of ($CoCl_2.6H_2O$, $NiCl_2.6H_2O$, $CuCl_2.2H_2O$ and $ZnCl_2$) with 10ml absolute ethanol solution of (0.156g, 0.0004mol) of new azo-Schiff base ligand in (1:2) (metal: ligand) ratio. The resulting mixture was refluxed for 1h.The products of complexes were isolated after reduced of volume by evaporation .They were filtered off and dried under vacuum [17].The physical properties of the complexes under study are listed in Table 1.Scheme 2 illustrates the steps of preparing the metal complexes with the ligand (4F-DBAPD).



Scheme- 2: Synthesis of the metal complexes

Table (1) Shows the physical properties of the new Azo Schiff base ligand and its complexes.

No	Chemical formula	Color	M.Wt g/Mole	M.P°C	Yield%	R_f
1	$L=C_{21}H_{18}N_7FO_2$	yellow	419.15	169-171	95	0.59
2	$[Co(L)_2]Cl_2$	Olive	968.67	237-239	81	0.61
3	$[Ni(L)_2]Cl_2$	Brown	966.43	244-246	78	0.77
4	$[Cu(L)_2]Cl_2$	Reddish Brown	973.29	280-282	86	0.65
5	$[Zn(L)_2]Cl_2$	Light Brown	975.12	200-202	91	0.54

Molecular docking study

A molecular docking study was conducted using the MOE 2015 docking software. The AZD9291 complex, which included wild type EGFR, was obtained from the Protein Data Bank (PDB ID: 4ZAU). The co-crystallized structure was removed, followed by the deletion of water molecules and addition of polar hydrogen atoms. Kollman charges were assigned to each atom, and non-polar hydrogen atoms were merged with the protein structure. The criteria for hydrogen bond formation included a distance of 1.9 Å between donor and acceptor atoms, with a tolerance of 0.5 Å, and an acceptor-hydrogen-donor angle of at least 120°. The structures were then saved in .pdbqt file format for further analysis using MOE. The ligands' 3D structures were generated by drawing their 2D structures using ACD/ChemSketch and converting them to 3D using the same software. All structures were saved as .pdb files for input into MOE. The ligand structures were subsequently saved in .pdbqt format to perform the docking in MOE. The center of the docking box was set to the ligand center, and grid energy calculations were performed. Default parameters were used for the MOE 2015 docking calculations, generating 10 docked conformations for each compound. Genetic algorithms were employed for the energy calculations[18,19].

Results and discussion:

All complexes are Freely soluble in DMF, DMSO ,Methanol and Ethanol .Also They are stable in air .The ligand and its metal complexes were characterized by elemental analysis Table (2) ,molar conductivities, magnetic susceptibility, IR,UV-Vis,(Mass and ^{1}H,MNR spectrum for the ligand) .The analytical data of the complexes are in agreement with the experimental data .The value reveal that the metal to ligand ratio was(1:2) (M:L) and were presented in table.2.The magnetic susceptibility of the chelate complexes at room temperature were consistent with octahedral geometry, So as the around the central metal ions. All of chelate complexes prepared in this work showed higher conductivity values. This proves that complexes have an electrolytic nature[20].

Table (2) shows the element Analysis the new azo Schiff base ligand

(4F-DBAPD) and its complexes.

No	Formula	(Found) Calc. %			
		C%	H%	N%	M%
1	L= 4F-DBAPD	60.14 (60.17)	4.33 (4.21)	23.38 (23.152)	----------
2	$[Co(L)_2]$ Cl_2	52.08 (52.42)	3.75 (3.81)	20.24 (20.29)	6.08 (6.11)
3	$[Ni(L)_2]$ Cl_2	52.09 (52.12)	3.75 (3.91)	20.25 (20.36)	6.06 (6.18)
4	$[Cu(L)_2]$ Cl_2	51.83 (51.90)	3.73 (3.98)	20.15 (20.41)	6.53 (6.90)
5	$[Zn(L)_2]$ Cl_2	51.73 (51.79)	3.72 (3.76)	20.11 (20.23)	6.70 (6.81)

Mass spectrum of the new ligand:

The mass spectra of the new azo Schiff base ligand(4F-DBAPD) was recorded at room temperature .The obtained peaks confirm the proposed formulae for the compound .The mass spectrum of Ligand show the molecular ion peak at m/z+ 419.15 compound ($\mathbf{C_{21}H_{18}N_7FO_2}$) confirm the proposed formulae for compound . Due to the large molecular weight, high bombardment energy, and the large number of heterogeneous atoms in its chemical structure, which confirm the validity of the proposed formula for the compound. Figure 1 showed the mass spectrum of ligand [21].

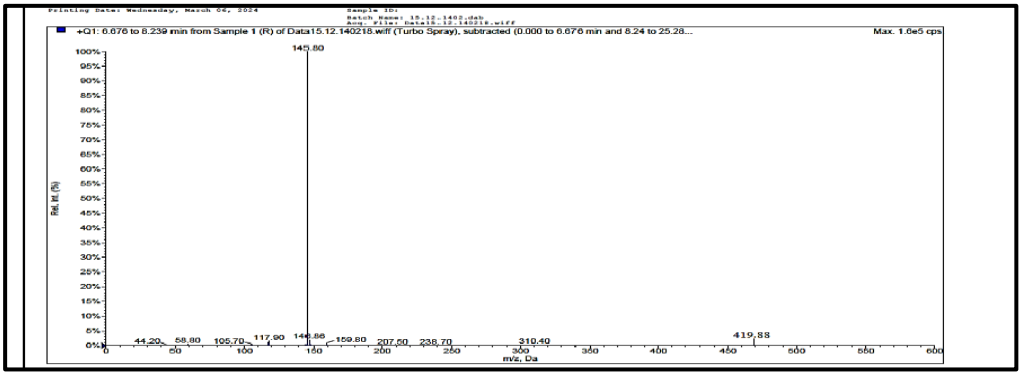
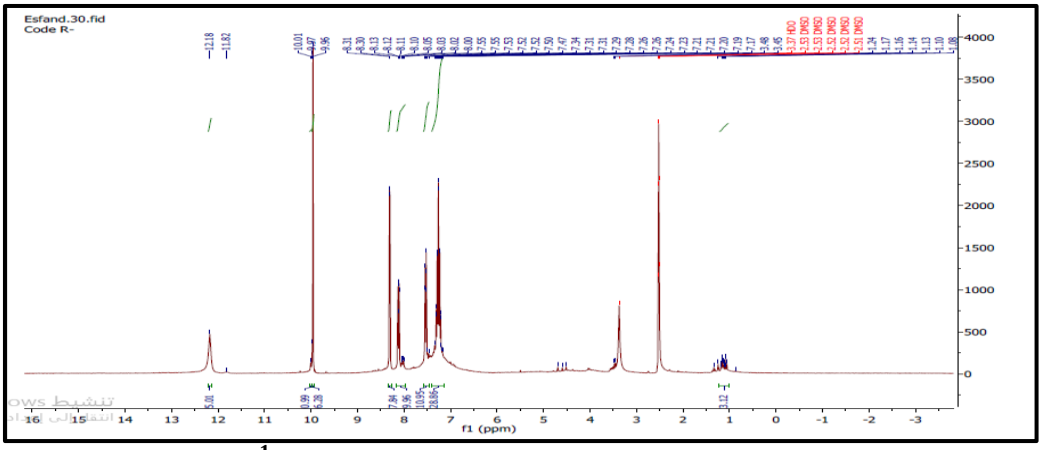


Fig1: Mass spectrum of the new azo Schiff base ligand .

^{1}H-NMR Spectra

The spectrum of newly synthesized ligand(4F-DBAPD) gave a satisfactory data and the molecular structure was assigned on the basic of ^{1}H - NMR chemical shift by using DMSO-d^6 as a solvent with TMS as an internal reference. The 1H-NMR spectrum of the ligand showed clear signals involved singlet at δ (2.5) (ppm) belong to the protons of solvent (DMSO-d^6) and singlet signal at δ (3.37) ppm which was assigned to HDO , multiples signals at δ (7.17-8.31) ppm which were assigned to phenyl and heterocyclic protons of rings .Singlet at δ (3.48) ppm belong to the proton of methyl(CH_2), Singlet at δ (1.24) ppm belong to the proton of methyl(CH_3). Singlet at δ (9.96) ppm belong to the proton of (–CH=N), Singlet at δ (12.18) ppm belong to the proton of –C-NH theophylline ring [22] , as shown in Fig.(2).



Fig(2): ^{1}H-NMR spectrum of the ligand (4F-DBAPD)

Infrared Spectra studies

The IR spectra of the complexes are compared with that of the free ligand to determine the changes that might have taken place during the Complexation [23,24] all data are listed in table (3).

Table (3) FTIR spectra frequencies for the new azo Schiff base ligand and its metal complexes in cm^{-1}

Compounds	C—H Alph.	N—H	C—H Ar.	C=O	C=N Endo cyclic	C=N Schiff	N=N	M—N	M—N
L	2931 2978	3203	3047	1635	1579	1517	1390	.....	.....
$[CoL_2]Cl_2$	2981	3439	3049	1635	1581	1517	1388	472	536
$[NiL_2]Cl_2$	2933	3385	3053	1635	1583	1519	1388	464	597
$[CuL_2]Cl_2$	2980 2933	3169	3049	1637	1581	1521	1388	466	532
$[ZnL_2]Cl_2$	2933	3523	3051	1629	.....	1521	1386	590	426

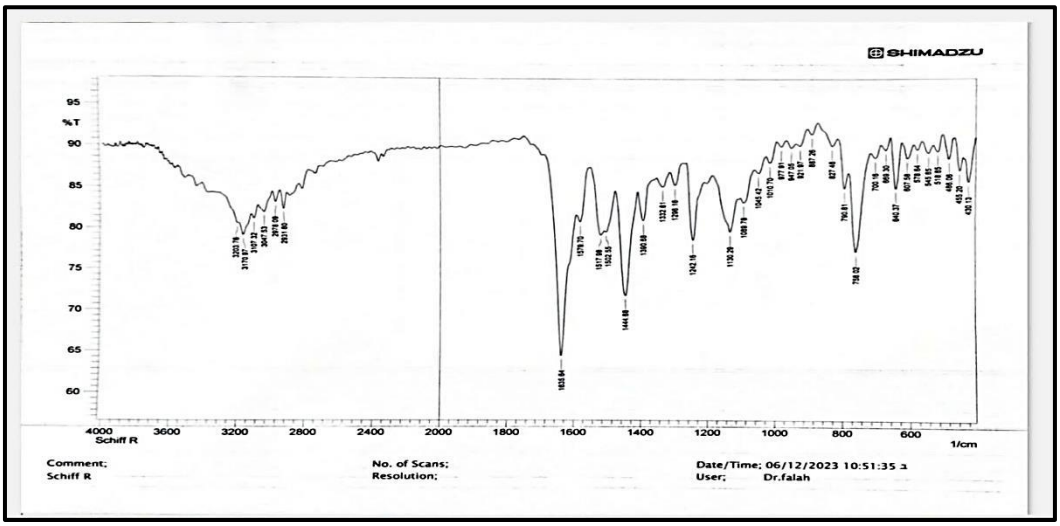


Fig (3): IR-spectra of the ligand

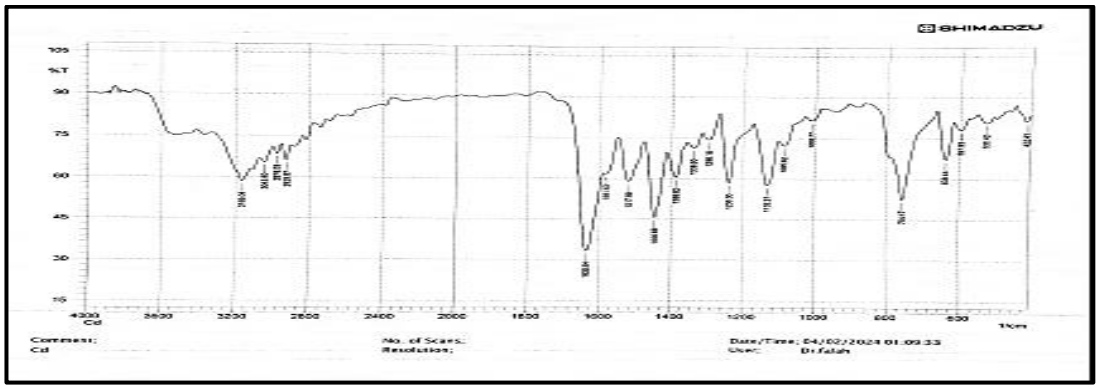


Fig (4): IR-spectra of Co (II) complex

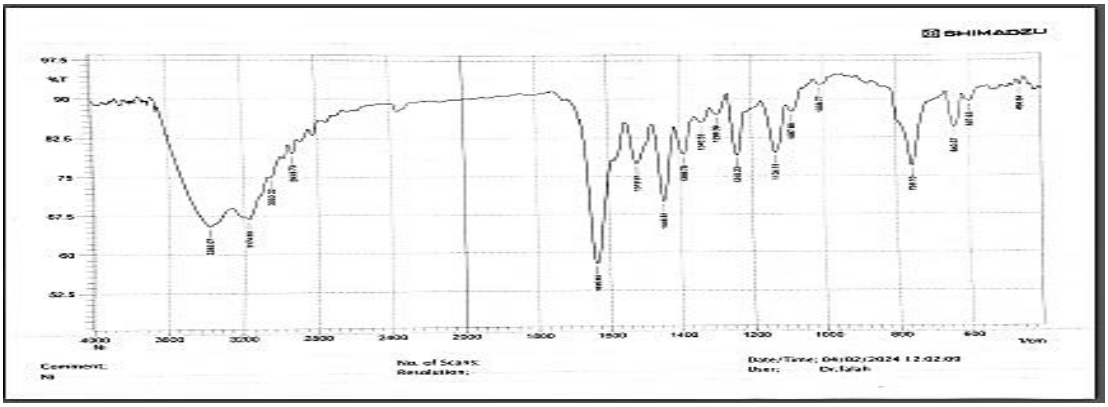


Fig (5): IR-spectra of Ni(II) complex

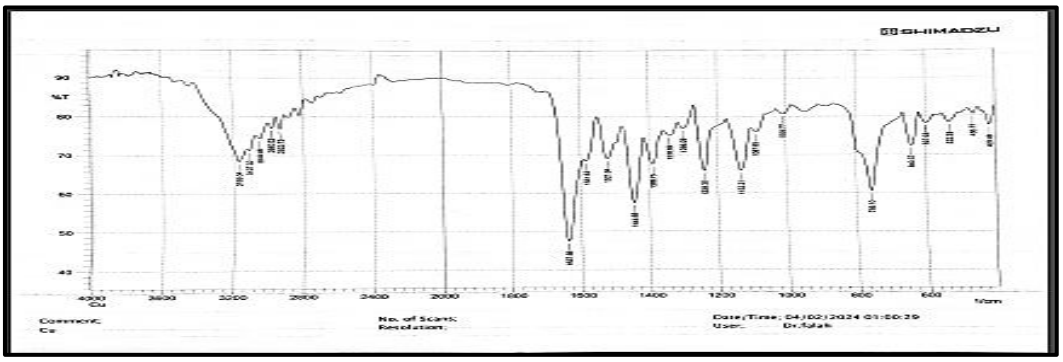


Fig (6): IR-spectra of Cu(II) complex

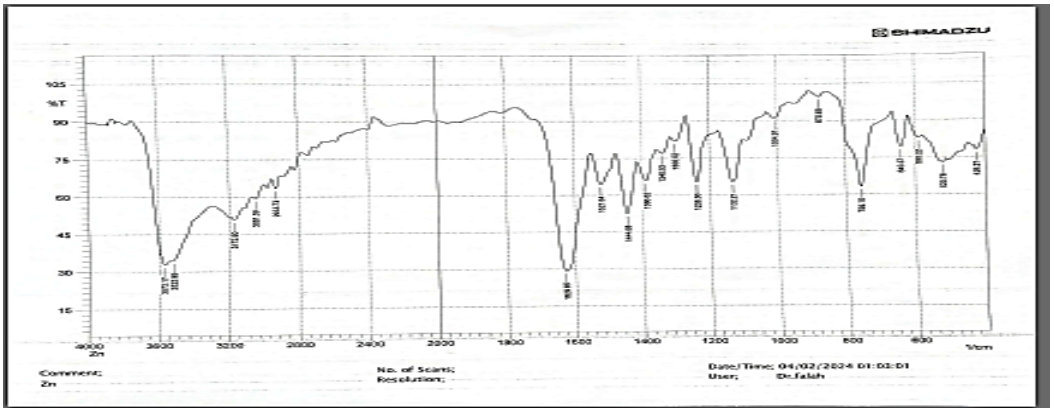


Fig (7): IR-spectra of Zn(II) complex

Magnetic susceptibility:

The results of the magnetic susceptibility measurements are listed in the table (4) where the magnetic moment value of the magnetic moment of Co(II) ,Ni (II) and Cu(II) Complexes reach (4.98, 2.97 ,1.76) B.M respectively , which indicates the presence of the paramagnetic characteristic [24]. As for the complexes of Zn(II), it has shown Di magnetic properties due to Electron cover saturation (nd) in the electrons [25]

Measurement of molar conductivity:

From the results obtained, it is clear that the molar electrical conductivity measurements for solutions of Chelate complexes of ions under study with the new ligand and with concentration of (1×10^{-3}) molar per complex at the laboratory temperature and using ETOH as solvent , were ranged from (88.12-75.89)S. $cm^2.mol^{-1}$and listed in table (4), We find the ionic properties of all these complexes. These results are identical to what was stated in the literature for metallic complexes with ionic properties [24].

Table (4) Molar conductivity and Magnetic susceptibility values for the Complexes

compounds	μ_{eff} (B.M)	Λ_M(S.cm^2 . mol^{-1})
$[CoL_2]Cl_2$	4.98	81.22
$[NiL_2]Cl_2$	2.97	79.05
$[CuL_2]Cl_2$	1.76	75.89
$[ZnL_2]Cl_2$	Dia	88.12

Electronic spectra:

The electronic absorption spectra are very useful in the estimation of effects equipped thru out her approaches of structural exploration.

The spectrum of the new ligand (4F-DBAPD) in solvent (ETOH) showed three absorption peaks, two at (214 nm and 242 nm) respectively due to the electron transition of the type ($\pi \rightarrow \pi^*$) while the second peak was attributed at (295 nm) to the electron transition ($n \rightarrow \pi^*$) due to the ligand having double bonds with atoms having unshared electron pairs .

The spectrum of the ligand was compared with that of the cobalt (II) complex, which showed an absorption peak at (262 nm) due to intra-ligand charge transfer (IL. CT) and an absorption peak at (610 nm) has been attributed to the electron transition ν3 = $^4T_1g \rightarrow {}^4T_1g$ (P) This fact is consistent with the literature on the appearance of this band in octahedral cobalt(II) complexes (39).

The UV-visible spectrum of nickel (II) complex solution recorded an absorption peak at (295 nm, 33898.30 cm^{-1}) was detected at (340 nm). to the electron transition ν3=$^3A_2g(F)\rightarrow {}^3T_1g$ (P) and this is consistent with what was mentioned in the literature regarding octahedral nickel(II) complexes.

While the UV-visible spectrum of copper (II) complex solution showed an absorption peak at (319 nm) that was attributed to the internal charge transfer in the ligand (IL.CT) and a broad absorption peak at (771 nm) due to the to the electron transition (($^2Eg \rightarrow {}^2T_2g$), and this is consistent with what was mentioned in the literature (40).

As for electronic spectra of the zinc(II) complex with new ligand, they does not possess type (d-d) electronic transmissions because of the fullness of the five (d) orbitals. As new peaks appeared in the metal ion complexes that were not visible in the ligand spectrum, this indicates the consistency of the metal ion with the new ligand due to the charge transfer (C.T)(41). the spectrum of the free ligand is red-shifted in complexes due to ligand to metal charge transfer (LMCT) transition , suggesting an octahedral geometry around metal(II) in the complexes as showed in Fig.(6) ,(7)and (8) .

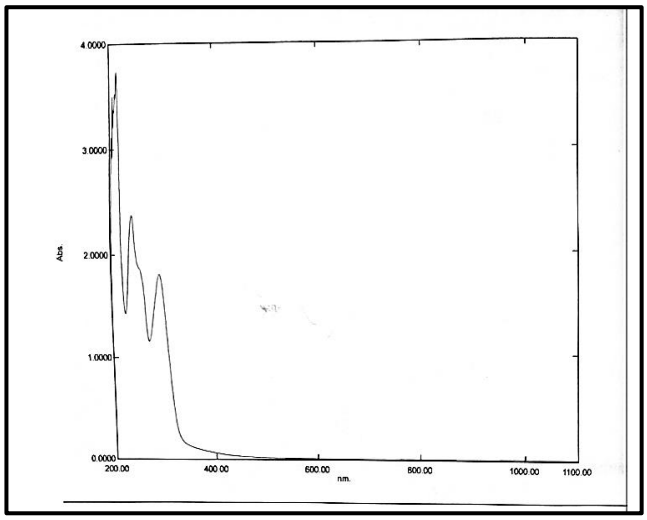


Fig (8): UV-Vis spectra of new Ligand

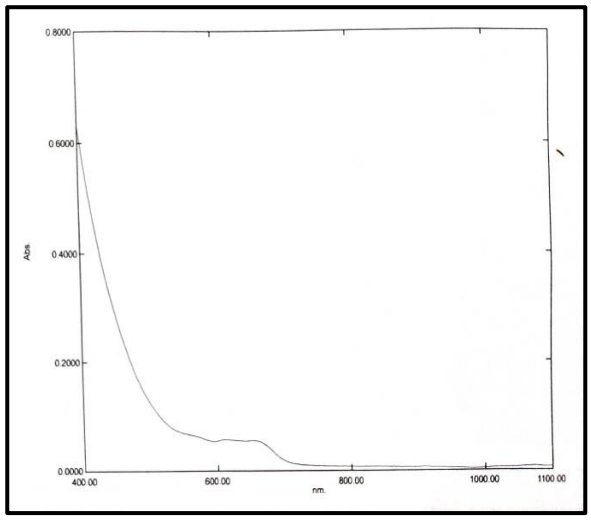


Fig (9): UV-Vis spectra of Co (II) complex

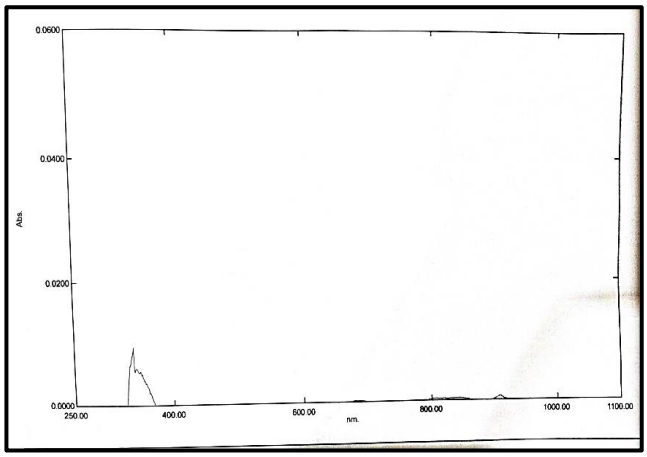


Fig (10): UV-Vis spectra of Ni(II) complex

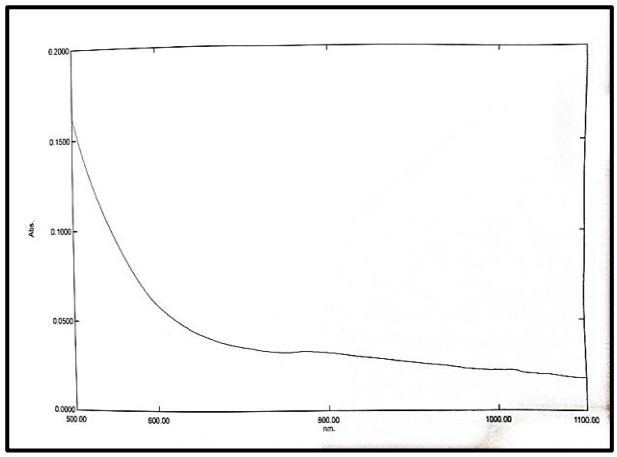


Fig (11): UV-Vis spectra of Cu (II) complex

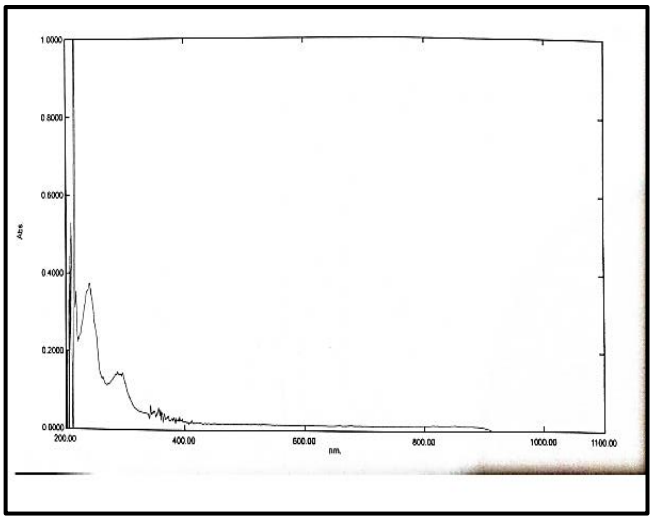


Fig (12): UV-Vis spectra of Zn (II) complex

Proposed Structural:

From the results reached it is possible to proposed an octahedral structure of all metal complexes with new Azo Schiff base ligand(4F-DBAPD). The results of these studies showed that the coordination sites for the new Azo-Schiff base ligand with Co (II), Ni (II), Cu (II) and Zn (II) were to be through nitrogen of the theophylline ring, ,the nitrogen of azo group and the nitrogen of azo-azomethine group . The Electronic spectral and magnetic measurement data predict octahedral structure of the complexes .All complexes showed that electrolytes properties The Proposed Structural of metallic complexes can be illustrated in the Fig (13) .

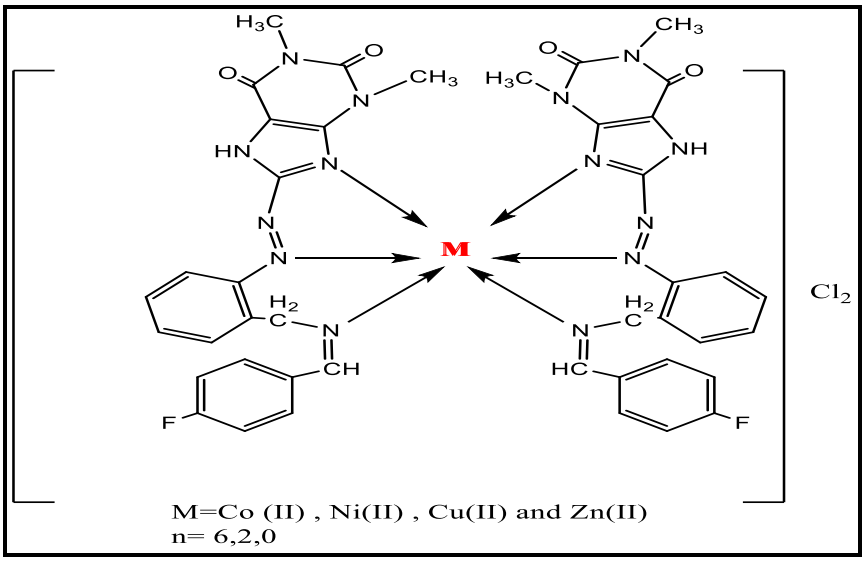


Fig.(13): Proposed Structural of the metal complexes

Molecular Docking Study

The Molecular docking studies of selected compounds (ligand and its metal complexes) were performed using the MOE 2015. A well characterized AZD9291 complex with wild type EGFR (PDB code: 4ZAU) was used as the template. The binding energies of docked compounds towards the target receptor are shown in Figures (14- 18)

respectively. The active pocket ligand consisted of 4 amino acid residues including TYR 764, ASN 700, GLN 701, and SER 768. All the docked molecules showed good to moderate binding energy towards the target receptor EGFR, at (-5.6333) kcal/mol.

The Co(II)-Complex of this compound formed strong interactions with LEU 703, LEU 1017 and LEU 1017 residues whereas the binding energy value of (-6.5482) kcal/mol.

In contrast, the Ni(II), Cu(II) and Zn(II) metal complexes were observed to be stabilized in the active site and exhibited low binding energy values of (-6.0270, -6.9742 and -6.0160) kcal/mol, respectively. Among these, **Cu(II)-Complex** showed maximum binding energy[26].

S (Kcal/mol)	**RMSD (Å)**
-5.6333	**1.4937**

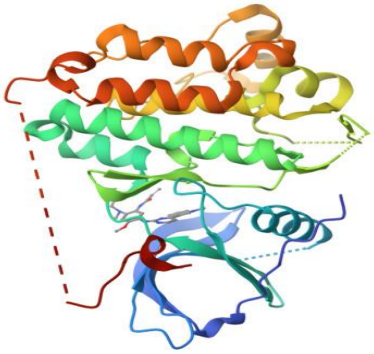
Ligand Interactions Report

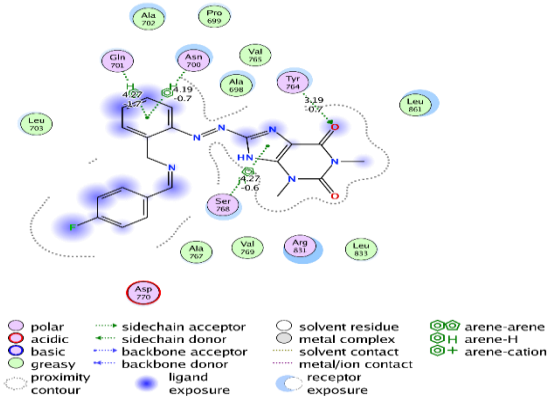
Wed Feb 21 01:47:38 2024 (MOE 2015.10)

4ZAU: TRANSFERASE/TRANSFERASE INHIBITOR / 4ZAU

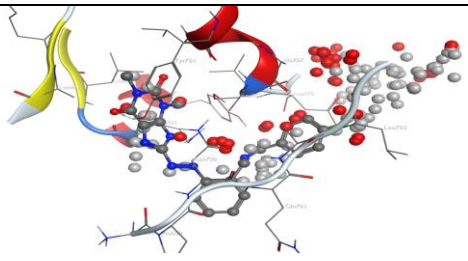
Ligand	Receptor				Interaction	Distance	E (kcal/mol)
O6 9	OH	TYR	764	(A)	H-acceptor	3.19	-0.7
6-ring	CA	ASN	700	(A)	pi-H	4.19	-0.7
6-ring	N	GLN	701	(A)	pi-H	4.27	-1.7
5-ring	CB	SER	768	(A)	pi-H	4.27	-0.6

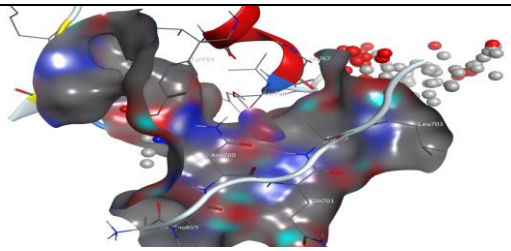
Ligand Interactions





Protein ID (4ZAU) | **2D**





3D | **Map**

Fig. 14. Detailed analysis of the interactions between protein and ligand in 2D, 3D, and map views, (S=the final score is the score of the last step, RMSD_refine=the mean square deviation between the laying before refinement and after refinement pose).

S (Kcal/mol)	RMSD (Å)
-6.5482	1.6436

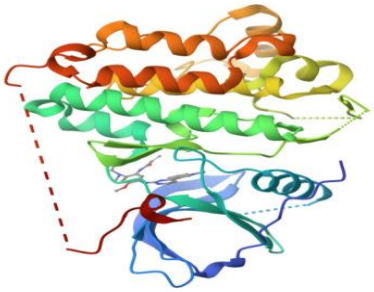
Ligand Interactions Report

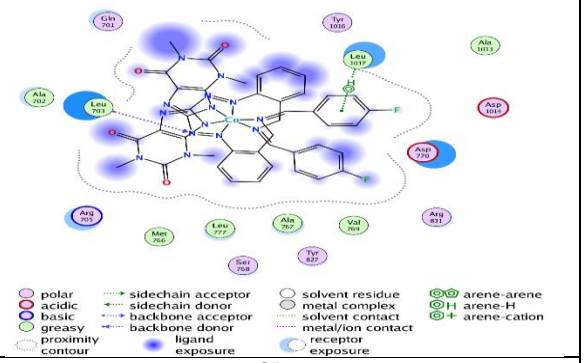
Wed Feb 21 07:22:30 2024 (MOE 2015.10)

4ZAU: TRANSFERASE/TRANSFERASE INHIBITOR / 4ZAU

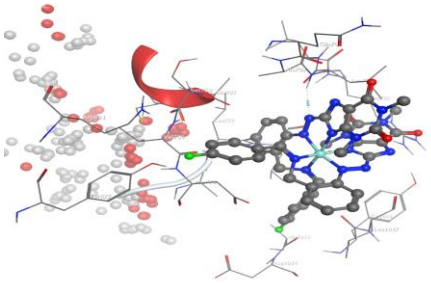
Ligand	Receptor				Interaction	Distance	E (kcal/mol)
N46 69	N	LEU	703	(A)	H-acceptor	3.38	-3.2
6-ring	CA	LEU	1017	(A)	pi-H	4.47	-0.7
6-ring	CG	LEU	1017	(A)	pi-H	3.87	-0.9

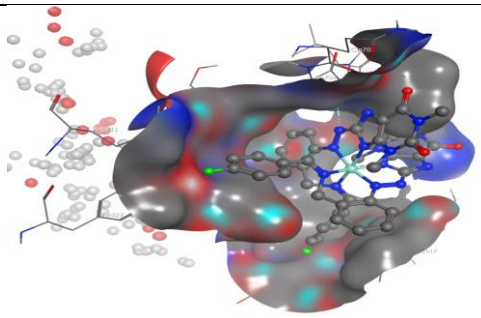
Ligand Interactions





Protein ID (4ZAU) | **2D**





3D | **Map**

Fig. 15. Detailed analysis of the interactions between protein and Co (II) complex in 2D, 3D, and map views, (S=the final score is the score of the last step, RMSD_refine=the mean square deviation between the laying before refinement and after refinement pose).

S (Kcal/mol)	RMSD (Å)
-6.0270	1.4519

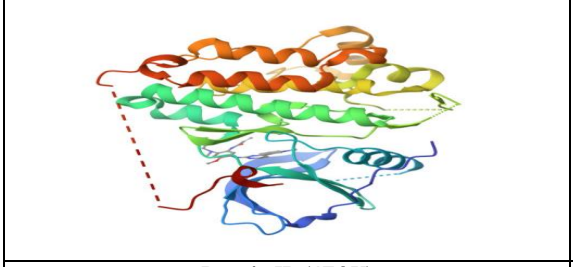
Ligand Interactions Report

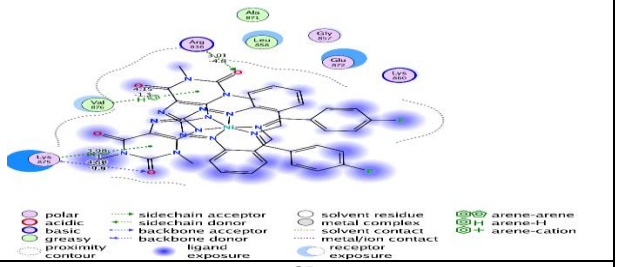
Wed Feb 21 02:41:19 2024 (MOE 2015.10)

4ZAU: TRANSFERASE/TRANSFERASE INHIBITOR / 4ZAU

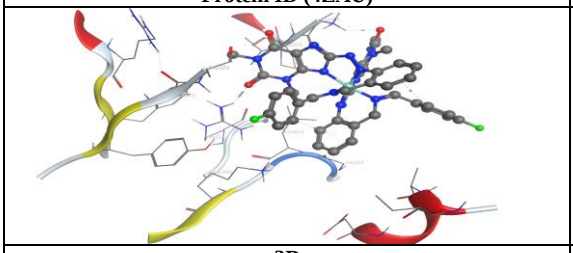
Ligand	Receptor				Interaction	Distance	E (kcal/mol)
O1 1	NH2	ARG	836	(A)	H-acceptor	3.01	-4.8
O45 68	N	LYS	875	(A)	H-acceptor	3.10	-1.3
6-ring	N	LYS	875	(A)	pi-cation	3.98	-1.0
6-ring	CB	LYS	875	(A)	pi-H	4.58	-0.6
6-ring	CB	VAL	876	(A)	pi-H	4.15	-1.3

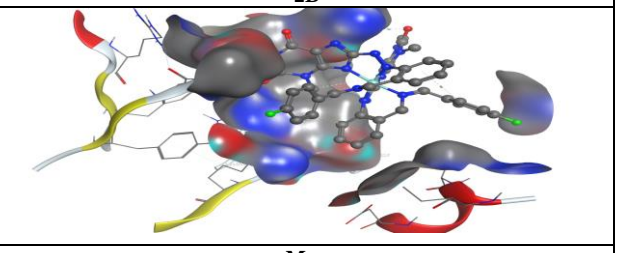
Ligand Interactions





Protein ID (4ZAU) | 2D





3D | Map

Fig. 16. Detailed analysis of the interactions between protein and Ni (II) complex in 2D, 3D, and map views, (S=the final score is the score of the last step, RMSD_refine=the mean square deviation between the laying before refinement and after refinement pose).

S (Kcal/mol)	RMSD (Å)
-6.9742	1.3531

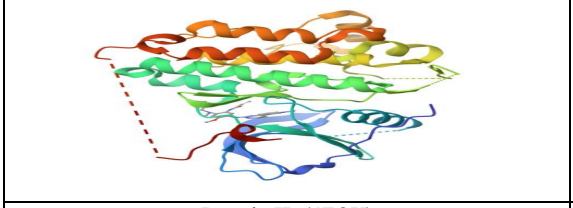
Ligand Interactions Report

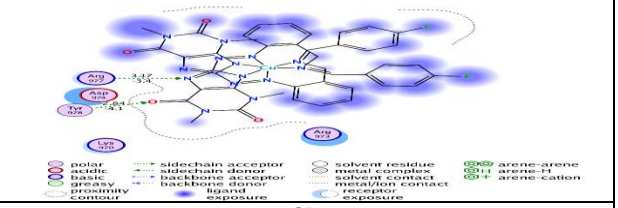
Wed Feb 21 02:12:58 2024 (MOE 2015.10)

4ZAU: TRANSFERASE/TRANSFERASE INHIBITOR / 4ZAU

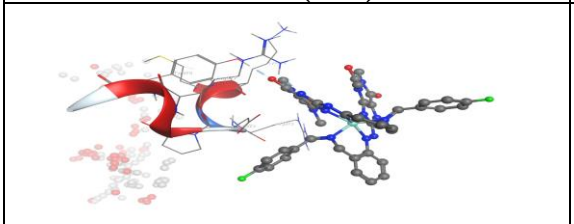
Ligand	Receptor				Interaction	Distance	E (kcal/mol)
N35 52	NH1	ARG	977	(A)	H-acceptor	3.17	-3.4
O40 60	OH	TYR	978	(A)	H-acceptor	2.84	-4.1

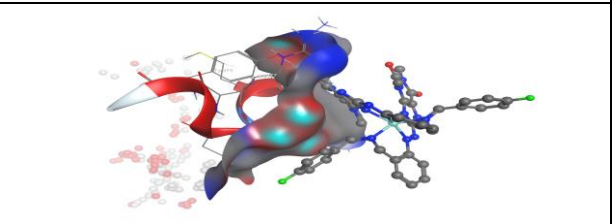
Ligand Interactions





Protein ID (4ZAU) | 2D





3D | Map

Fig. 17. Detailed analysis of the interactions between protein and Cu (II) complex in 2D, 3D, and map views, (S=the final score is the score of the last step, RMSD_refine=the mean square deviation between the laying before refinement and after refinement pose).

S (Kcal/mol)	RMSD (Å)
-6.016	0.9349

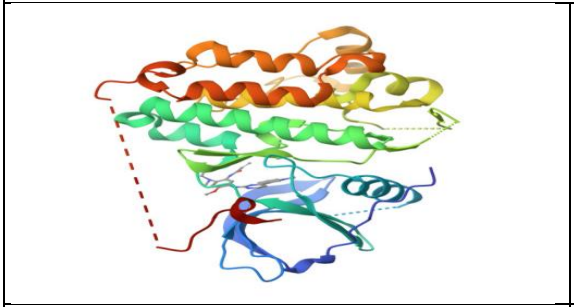
Ligand Interactions Report

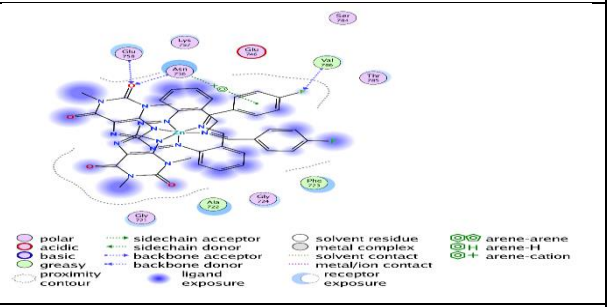
Wed Feb 21 20:31:01 2024 (MOE 2015.10)

4ZAU: TRANSFERASE/TRANSFERASE INHIBITOR / 4ZAU

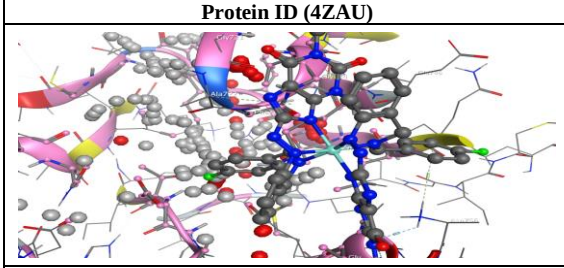
Ligand		Receptor				Interaction	Distance	E (kcal/mol)
O1	1	N	ASN	756	(A)	H-acceptor	2.90	-2.2
O1	1	N	GLU	758	(A)	H-acceptor	3.15	-3.8
F24	35	N	VAL	786	(A)	H-acceptor	3.14	-0.7
6-ring		N	ASN	756	(A)	pi-cation	4.29	-3.0

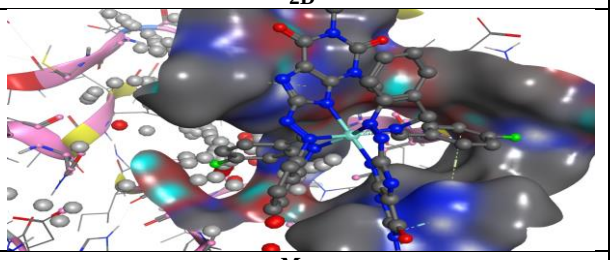
Ligand Interactions





Protein ID (4ZAU) | **2D**





3D | **Map**

Fig. 18. Detailed analysis of the interactions between protein and Zn (II) complex in 2D, 3D, and map views, (S=the final score is the score of the last step, RMSD_refine=the mean square deviation between the laying before refinement and after refinement pose).

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