

Metal based antimicrobial agents: Synthesis, characterization, magnetic, conductivity properties and mechanistic insights through docking studies

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ABSTRACT

The efforts of microbes can significantly impact our physical well-being. The modern world is predominantly influenced by microbial species, and their actions will significantly affect what lies ahead as well. It is essential to regulate populations of microbes to avert the spread of diseases and infections, necessitating the use of antibiotics. Regrettably, their treatment resistance is increasingly a significant contributor to morbidity and mortality among patients currently. Consequently, we must concentrate on the conceptualization and creation of innovative antimicrobial substances to manage infectious diseases and disorders. A novel set of nickel(II), chromium(II), copper(II), cobalt(II), and manganese(II) chelates, produced via Mannich process comprising xanthene, salicylaldehyde, and hydrazine hydrate, described using spectrometric methodologies, magnetic studies, and molar conductivity analysis. All complexes are characterized by spectroscopic and magnetic data readings indicative of octahedral shape. The aforementioned substances were evaluated for antimicrobial effectiveness towards disease causing pathogenic microbes using the agar well diffusion method. All substances demonstrated enhanced efficacy with respect to the examined microbes and fungal organisms.

Keywords: Antimicrobial activity, Mannich base, Metal complexes, Xanthene.

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INTRODUCTION

Microbes are accountable for the disintegration and deterioration of substances that are organic. It is essential to regulate microbial diversity in order to avert the spread of diseases and infections¹. Antiquated medications are diminishing in effectiveness owing to escalating germ resistance, resulting in several fatalities. Currently, therapeutic failure attributed to multidrug-resistant microorganisms is an important health issue. Antimicrobial susceptibility significantly impairs human potential to combat illnesses generated by various microbes, in addition to affecting the efficacy of surgical procedures and chemotherapy for cancer. Prolonged exposure of these bacteria to antimicrobial substances often results in genetic alterations inside their cells. This renders drugs useless towards certain infections. The overuse of current medications is the primary source of this issue. Multidrug-resistant microbes have emerged as significant threats to public health. Annually, millions of individuals globally are impacted by these infections. There is an urgent necessity for the advancement of potent antibiotic substances to protect individuals from these bacterial species. Currently, numerous investigators are

diligently working to create novel antimicrobial drugs from various sources to address resistant microbial species^{2,3}. Conversely, metal ions perform various essential roles in human beings⁴. Deficiencies in certain metal ions can lead to various illnesses, such as delayed development resulting from inadequate zinc, cardiovascular disease stemming from copper insufficiency, and anemia due to iron shortage. Metal ions are crucial in biological studies for their functions as medicines and diagnostic instruments. Metals possess distinct characteristics, including diverse coordination pathways, compatibility with substrates composed of organic matter, and redox function. Due to its reactivity, metals are strictly monitored under standard settings. The characteristics of metallic components contribute to the development of metal-derived pharmaceuticals with promising therapeutic applications. Consequently, coordination complexes, utilized as medications or pharmaceuticals, have emerged as highly appealing probes in pharmacology⁵. Transition metal elements like iron, manganese, and copper play structural parts and are frequently associated with active areas of enzymes and proteins. Studies has demonstrated significant progress in employing transition metal complexes as therapeutic

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agents for various human disorders⁶. The advantages of coordination chemistry provide enhanced opportunities to utilize metal complexes as healing substances. These complexes offer a diverse range of functions, comprising anti-diabetic, anti-infective, and anti-inflammatory properties. Significant initiatives are dedicated to the utilization of metal chelates as pharmaceuticals. Despite several limits and adverse effects, metal chelates remain the most widely utilized cancer drugs and significantly contribute to medical therapies. The fabrication of metal-comprised pharmaceuticals is a topic of increasing relevance in inorganic, pharmaceutical, and medicinal chemistry, garnering significant interest as a strategy for developing novel pharmaceuticals⁷.

Mannich compounds, containing 'C-CH₂-N' chains, are fashioned through a condensation progression of active carbon hydrogen, either primary or secondary amines, and a carbonyl moiety. They serve as specialty compounds and pharmaceutical intermediates. Furthermore, they have garnered considerable research owing to their exceptional ligation properties and facile coordination with metallic ions⁸⁻¹⁰. Metal complexes of Mannich derivatives improve the effectiveness of its ligands in medicinal usage, comprising anti-inflammatory, antitumor, anti-HIV, antiviral, anticonvulsant, anticancer, antioxidants, antimalarial, and antimicrobial properties, along with in manufacturing applications such as detergents, polymer making, surfactants, and resins¹¹⁻²².

The chemistry of Mannich compounds is a rapidly evolving scientific domain in chemistry, specifically focusing on the extensive uses of Mannich substances and its associated complexes. The therapeutic properties of Mannich analogues are intriguing, as they present an intriguing class comprising functional pharmaceutical substances. The antimicrobial properties of these substances have heightened their significance owing to its remarkable medicinal and therapeutic usefulness^{23,24}. The synthetic simplicity and affinity for metal chelate development of Mannich derivatives facilitated the production of numerous metal complexes of various structural types²⁵⁻²⁷. These complexes, exhibiting diverse

structural behaviours, bonding relations, intriguing process, and multifaceted therapeutics, have proven pivotal in the advancement of coordination complexes. A comprehensive examination of the corrosion prevention efficacy of Mannich analogues is now being conducted using weight loss, potentiodynamic, and electrochemical impedance spectroscopy approaches^{28,29}. Consequently, the aforementioned research demonstrated that the ligand and the corresponding metal chelates are applicable across ecological domains. Antimicrobial effects of these metal complexes are extensively documented³⁰. The chelate effect, resulting from the overlap of electronic orbitals between ligands and metals, elucidates the specific antibacterial properties of these complexes³¹. Consequently, we want to evaluate the effectiveness of our complexes in antimicrobial capabilities using in-vitro experiments. This work is expected to create a substantial addition to the coordination chemistry of the aforementioned molecules.

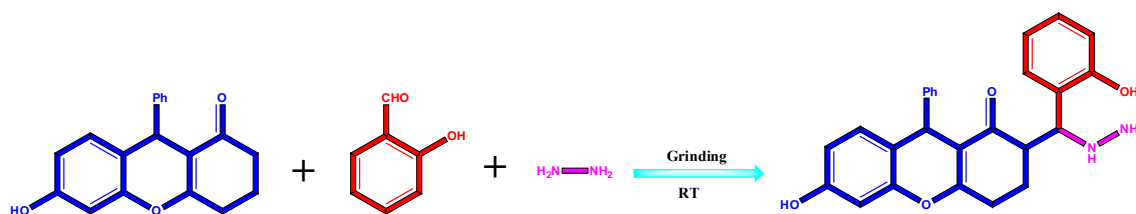
EXPERIMENTAL

Chemistry

All solvents and substances employed were of exceptional purity and procured from local chemical vendors. The complexes were identified through obtaining FT-IR spectra in the region of 500-4000 cm⁻¹. This was accomplished using Spectrum Two FT-IR spectrophotometer. The absorbance spectra of the ligand (**L1**) alongside corresponding chelates (**1-5**) were obtained via Thermo Fisher Scientific Evolution 60S within 200-800 nm to ascertain probable electronic shifts.

Preparation of Ligand (**L1**)

A reactants xanthene (0.02 mol, 5.85 g), hydrazine hydrate (0.02 mol, 1.0 mL) and salicylaldehyde (0.02 mol, 2.4 mL), was ground together in a mortar for 10 minutes. The reaction's development was observed using TLC. Upon completion of the chemical procedure identified as TLC, the resultant solution was deposited in crushed ice. The unprocessed product was subjected to filtration and dehydration. The ligand was purified by boiling in alcohol through recrystallization process. The preparation of ligand (**L1**) is demonstrated in Scheme 1.



Scheme 1. Preparation of ligand (**L1**)

Spectroscopic description of ligand (**L1**)

Brown residue; mf: C₂₆H₂₄N₂O₄; mp:158°C; mw: 428.47; HR-MS: m/z 430.90 (M⁺,30%); FT-IR (KBr, cm⁻¹): 3320 (-OH), 3160 (-NH), 1615 (-C=O), 1254 (-C-O-C); ¹H NMR (300 MHz, CDCl₃) δ 9.26 (OH, s, 2H), 8.34 (NH, s, 1H), 7.23-6.80 (Ar-H, m, 9H), 6.87-6.17 (Ph-OH, m, 3H), 5.80 (NH₂, s, 2H), 4.62 (-CH-Ph, s, 1H), 4.23 (CH-Ph, d, J

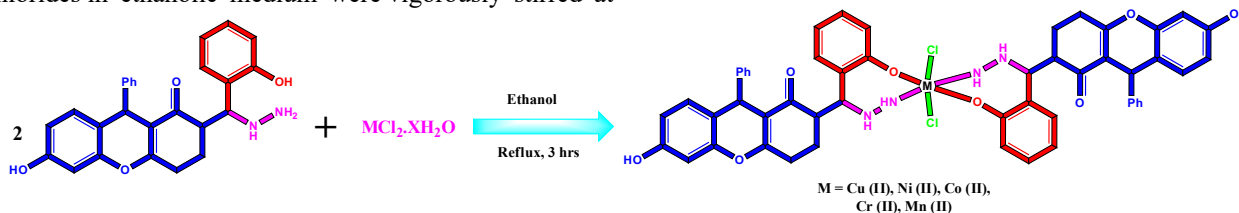
= 1.8 Hz, 1H), 2.80-1.23 (CHD, m, 5H); ¹³C NMR (300 MHz, CDCl₃) δ 196.2 (C=O, 1C), 162.4 (-C=C, 1C), 160.2, 152.3, 132.1, 110.5, 100.5 (Ar ring, 6C), 145.3, 130.3, 125.4, 120.3 (Ph ring, 12C), 108.2 (-C=C, 1C), 56.0 (-C-C-Ph, 1C), 52.3 (-C-NH, 1C), 40.2 (-CH-Ar, 1C), 25.6 (CH₂, 1C), 13.8 (CH₂, 1C); Elemental properties: Anal.

Found (Calcd): C, 72.86 (72.88); H, 5.63 (5.65); N, 6.55 (6.54) %.

Synthesis of metal complexes (1-5)

The synthesis was carried out in reflux condition with (0.02 mol) of ligand **L1** and (0.01 mol) of metallic chlorides in ethanolic medium were vigorously stirred at

600 rpm for about 6 hrs. After that, the resultant solution was kept in an atmosphere to evaporate. The produced substances were subjected to column chromatography with a mixture of eluant containing DCM:CH₃CN:CH₃OH (2:3:5 v/v) over silica gel. Metal chelates (**1-5**) remained produced according to the steps shown in Scheme 2.



Scheme 2. Production of metal chelates (**1-5**)

Solubility assessments

The dissolution of the metal chelates (**1-5**) as well as ligand (**L1**) in both aprotic and protic solvents has been assessed. The solvents utilized included chloroform, dimethyl sulfoxide, acetone, alcohol, and water. Following the solubility assessments, further experiments were conducted.

Magnetic behaviour

The incorporation of absorbance spectrum and magnetic behaviour can be utilized to ascertain the arrangement of the complex. Magnetic properties employed to determine the stereo chemical composition of a metallic complex having d⁵, d⁶, d⁷, d⁸, or d⁹ electronic arrangements, thereby notably determining if the complex assumes a square planar, octahedral, or tetrahedral geometry. Furthermore, those factors may signify whether the substance is spin-free or restricted. The magnetic characteristics of the metallic elements were studied through a Gouy apparatus to determine the optimal magnetic moment value for every atom. Hg[Co(SCN)₄] was utilized to calibrate the Gouy tube. The diamagnetic alterations for various atomic and structural parts were ascertained via Pascal's ratios. The effective magnetic moments (μ_{eff}) were calculated using Curie's method $\mu_{\text{eff}} = 2.84 [\text{M}_{\text{corr}} T]^{1/2}$ B.M., where M_{corr} signifies molar magnetic susceptibility and T denotes the absolute temperature whereby the inspections were conducted.

Antimicrobial assessment

The antifungal and antibacterial properties of ligand (**L1**) and metal chelates (**1-5**) were assessed utilizing the methodology outlined in our previous studies³².

Molecular docking

The interaction and entrapping process between the ligand (**L1**), chelates (**1-5**), and targets 1KZN and 1FI4 remained inspected utilizing docking simulations via Autodock Vina 1.1.2³³. The crystalline frameworks of target proteins (PDB ID: 1FI4 & 1KZN) were attained from the PDB site to evaluate their antimicrobial activity. The 3D structures of inhibitors **L1** and chelates (**1-5**) were acquired utilizing the ChemDraw Ultra 12.0 and Chem3DPro softwares. The requisite files for the docking operations were produced using the AutoDock Tools 1.5.6 computing programme suite. The grid setting for the 1KZN protein were established with a size (x, y, z = 22, 20, 20) and central point (x,y,z = 18.839, 26.702, 37.939). The grid setting for the 1FI4 protein were established with a size (x, y, z = 24, 22, 24) and central point (x,y,z = 21.935, 57.745, 20.018). The separation among each point on the grid is 1.0 Å. The exhaustiveness measure had an integer of 8. The other variables were adjusted to its real settings. The inhibitor exhibiting the least docking score is regarded as the prospective candidate. The docking outcomes were assessed using the Pymol and Biovia Discovery Studio visualizer.

RESULTS AND DISCUSSION

Solubility and physicochemical properties

The solubility metrics and physicochemical properties of the ligand (**L1**) and its chelates (**1-5**) were displayed in Table 1. Dissolution assessment reveals that both the ligand (**L1**) and related chelates (**1-5**) display complete dissolution in DMSO than other solvents.

Table 1: Solubility and physicochemical properties of the ligand (**L1**) and chelates (**1-5**)

Compound	Colour	Melting point (°C)	Solubility			
			Water	Chloroform	Ethanol	DMSO
(L1)	Brown	158	Insoluble	Sparingly soluble	Soluble	Soluble
[Cu(L1) ₂]Cl ₂	Pale blue	178	Insoluble	Insoluble	Insoluble	Soluble
[Ni(L1) ₂]Cl ₂	Bright green	202	Insoluble	Insoluble	Partially soluble	Soluble

[Co(L1) ₂]Cl ₂	Pink	215	Insoluble	Insoluble	Insoluble	Soluble
[Cr(L1) ₂]Cl ₂	Pale brown	176	Insoluble	Partially soluble	Insoluble	Soluble
[Mn(L1) ₂]Cl ₂	Black	248	Insoluble	Insoluble	Insoluble	Soluble

Conductivity and magnetic behaviour

The experiment was conducted using Systonic (Model: S-942). The non-electrolytic behaviour of the chelates was validated through assessing the conductance property of 10⁻³ M solutions of each complex in DMSO. The metal chelates (1-5) demonstrated a molar conductance value from 17 to 26 Ω⁻¹mol⁻¹cm². The conductance

investigations specified that chloride atoms form complexes with metal centers, demonstrating its part as ligands rather than free atoms. The shape of the produced chelates might be exaggerated through the metal:ligand proportions (1:2) and the classes of electrolytes exploited in the experiment. Table 2 delineates the conductance and magnetic characteristics of metal chelates (1-5).

Table 2: Conductivity and magnetic behaviour of metal chelates (1-5) with ligand (L1)

S. No	Complexes	Conductance (Ω ⁻¹ mol ⁻¹ cm ²)	Magnetic Susceptibility (μ _{eff.} B.M)
1.	[Cu(L1) ₂]Cl ₂	17	2.35
2.	[Ni(L1) ₂]Cl ₂	24	3.47
3.	[Co(L1) ₂]Cl ₂	21	5.16
4.	[Cr(L1) ₂]Cl ₂	22	4.53
5.	[Mn(L1) ₂]Cl ₂	26	5.07

NMR assessment of ligand (L1)

Fig. 1 shows the ¹H NMR spectrum of the Mannich analogue (L1) that was studied. The -CH₂ protons linked to salicylaldehyde and hydrazine are noticed as a singlet at 4.62 ppm, whereas the -OH moiety are found at 9.26 ppm. The benzene ring protons display a multiplet between 7.23 - 6.80 ppm. Another piece of confirmation supporting the ligand's synthesis is the absence of a signal matching the

proton of -NH₂ group, that was removed throughout the Mannich reaction. In the ¹³C NMR spectra, the peaks at 196.2 and 162.4 ppm correspond to the carbonyl and alkene moieties of the xanthene residue, accordingly. The aromatic carbons displayed signal at 160.2-120.3 ppm (Fig. 3). The presence of a signal at 40.2 ppm signifies that the -CH₂ group is linked to hydrazine hydrate and salicylaldehyde.

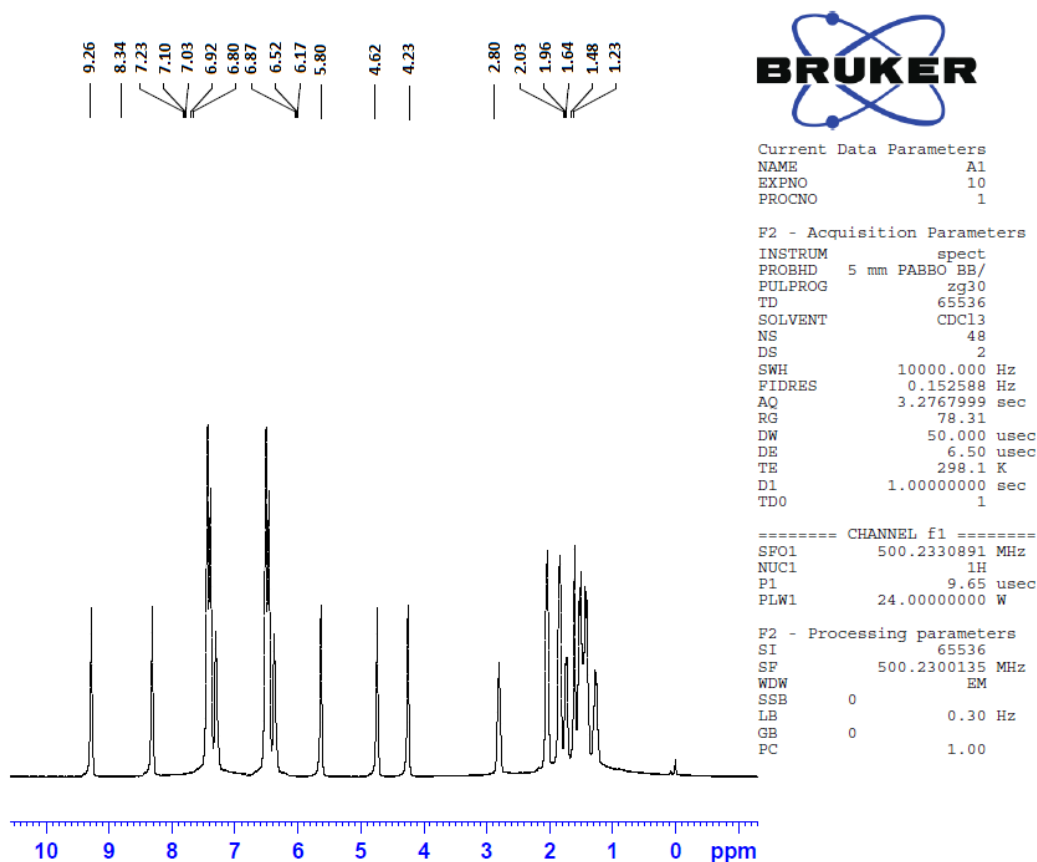


Fig. 1: ¹H-NMR spectra of ligand (L1)

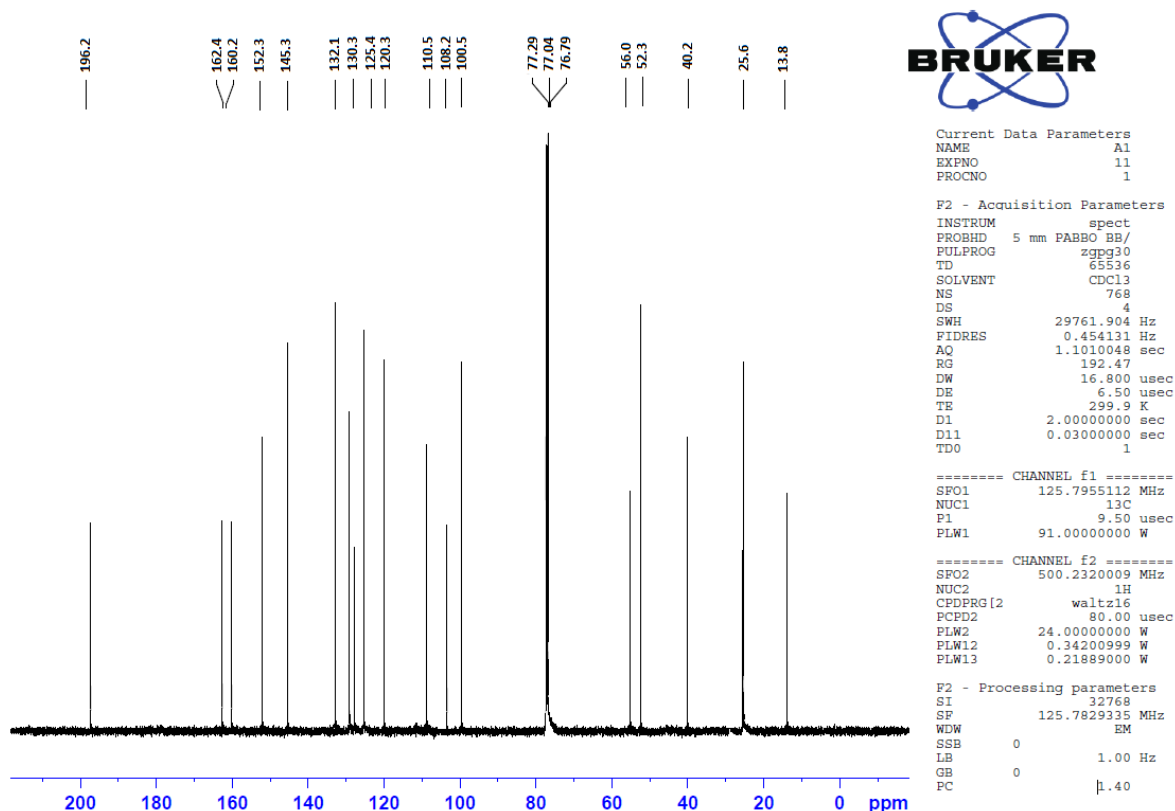


Fig. 2: ¹³C-NMR spectra of ligand (L1)

HR-MS studies

Fig. 3 illustrates the HR-MS spectra of the ligand (**L1**) under consideration. The mass of ligand (**L1**) was ascertained to be 428.47 via empirical observation, subsequently corroborated via HR-MS analysis, which indicated a m/z value of 430.90. The molecular ion peak

was observed at a m/z of 182.93. The further fragmentation patterns perceived at m/z values of 355.53, 281.29, 260.56, 230.87, 186.60, 154.87, 136.68, 76.75, and 43.68, respectively.

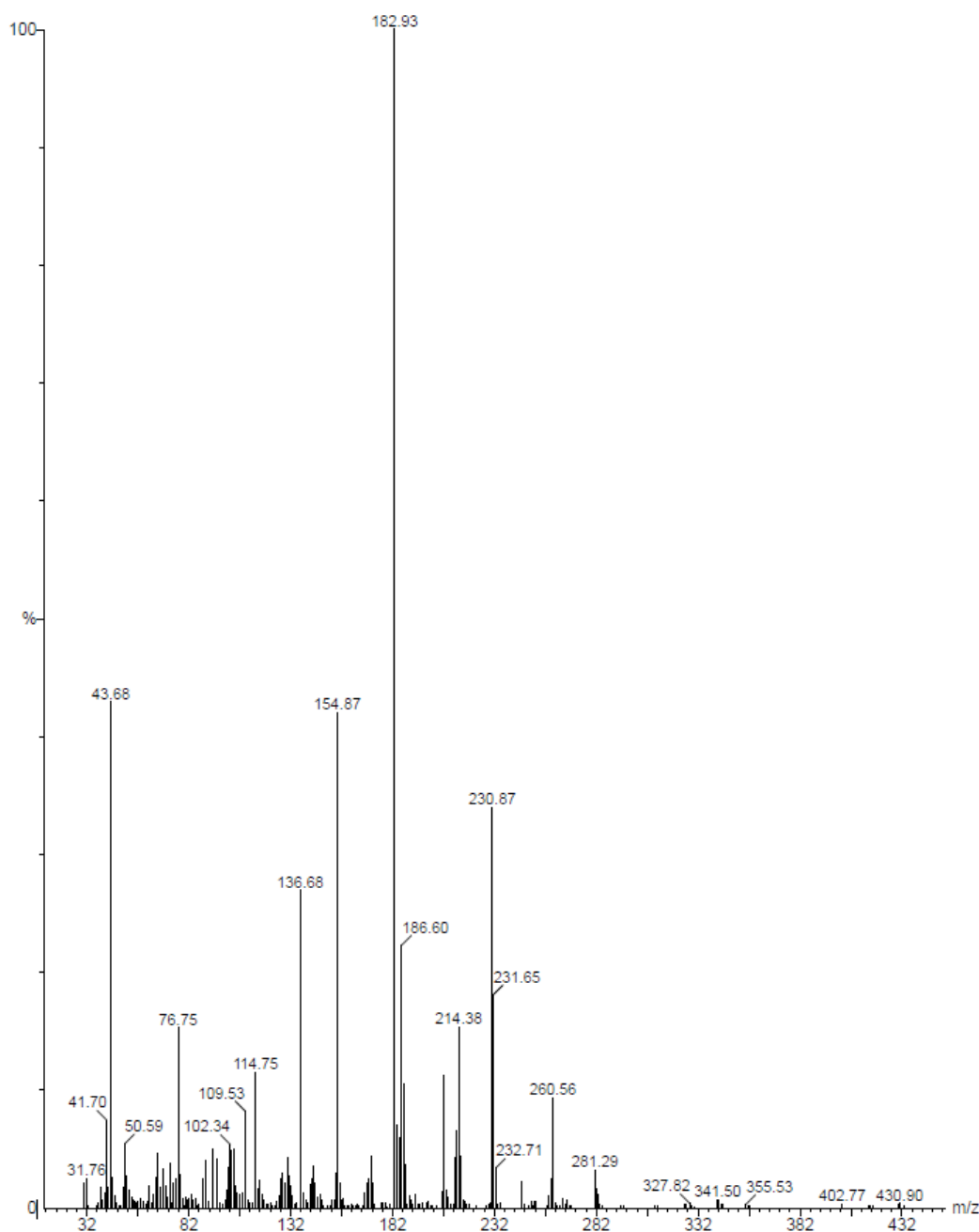


Fig. 3: HR-MS spectra of ligand (L1)

FT-IR analysis

The significant finding in the ligand FT-IR spectrum (Fig. 4) revealed a distinct peak at 3320 and 3160 cm^{-1} , attributable to the hydroxyl and amine groups. The amine and hydroxyl peaks displayed a wavenumber variation in each complexes (Fig. 5-9), indicating that the amine nitrogen and hydroxyl oxygen were coordinated through

metal centers. The development of metal chelates (**1-5**) is shown via the advent of a specific band at 756-726 cm^{-1} , indicative of the M-O linkage. The M-Cl linkage is indicated through appearance of a prominent band at 554-510 cm^{-1} . Table 3 displays the infrared spectrum data for ligand **L1** and metal chelates (**1-5**).

Table 3: FT-IR analysis of chelates (1-5) and the ligand (L1)

Compound	Functional moieties / Wavenumber (cm^{-1})				
	-NH	-C=O	-OH	M-Cl	M-O
(L1)	3160	1615	3320	-	-
[Cu(L1) ₂]Cl ₂ (1)	3246	1615	3368	548	751
[Ni(L1) ₂]Cl ₂ (2)	3056	1618	3344	530	726

[Co(L1) ₂]Cl ₂ (3)	3196	1616	3368	510	756
[Cr(L1) ₂]Cl ₂ (4)	3013	1615	3240	523	726
[Mn(L1) ₂]Cl ₂ (5)	3056	1617	3252	554	744

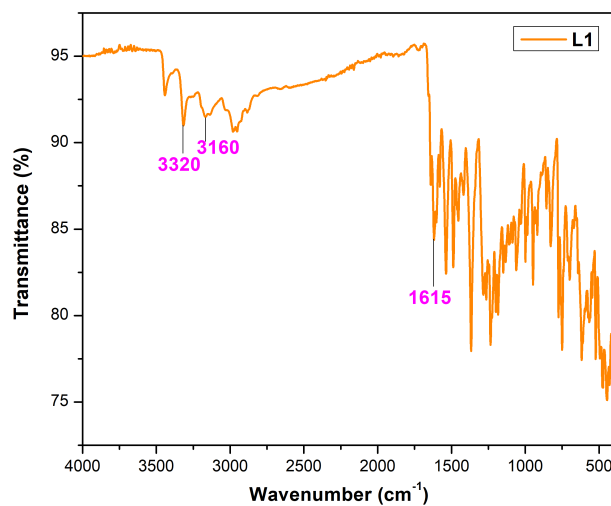


Fig. 4: FT-IR spectra of Ligand L1

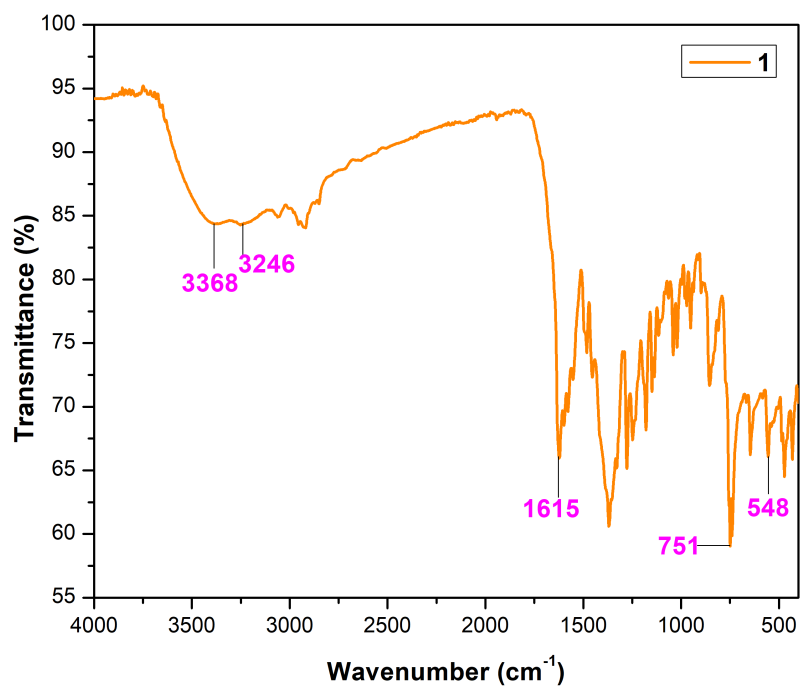


Fig. 5: FT-IR spectra of complex 1

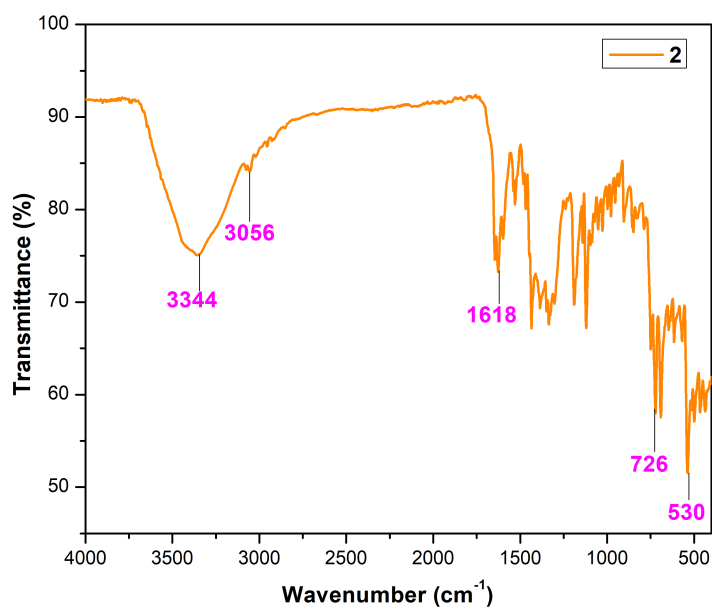


Fig. 6: FT-IR spectra of complex 2

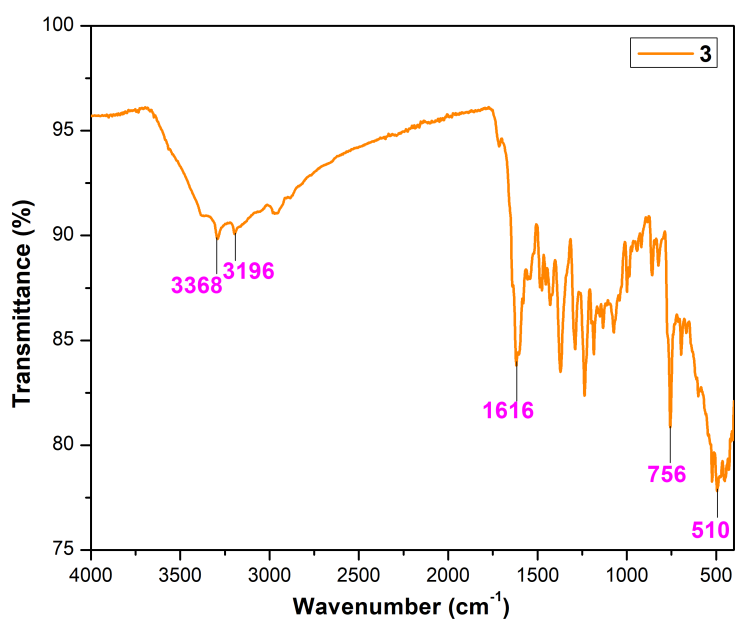


Fig. 7: FT-IR spectra of complex 3

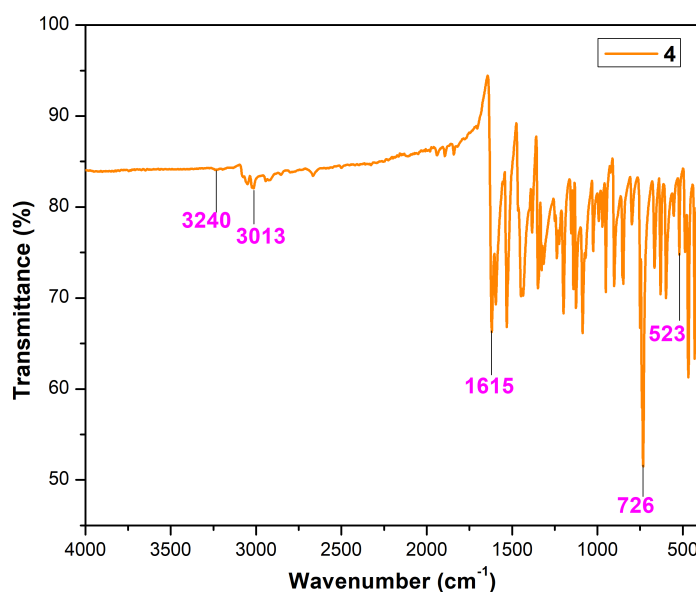


Fig. 8: FT-IR spectra of complex 4

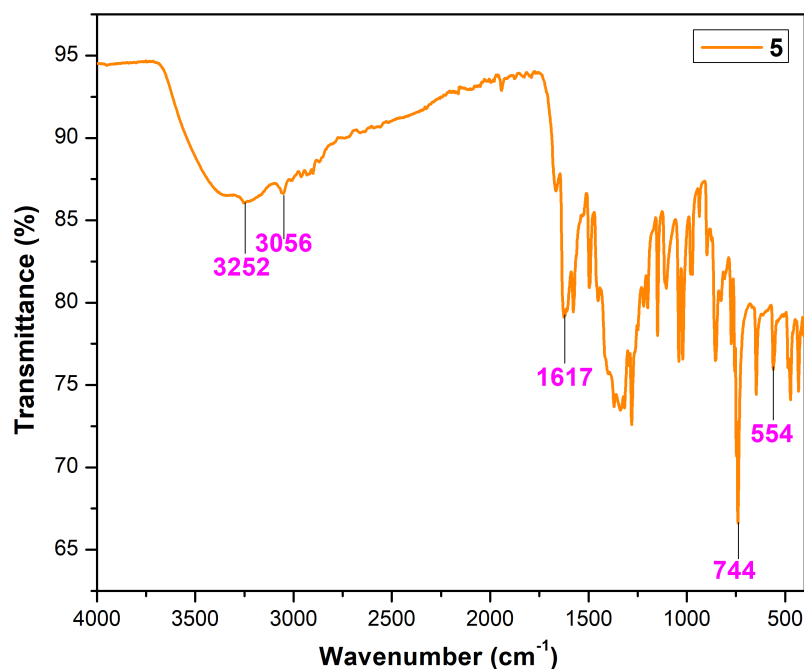


Fig. 9: FT-IR spectra of complex 5

UV-Vis analysis

The absorbance spectra of ligand (L1) revealed two λ_{max} at 297 and 396 nm, consistent to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ changes, individually (Fig. 10). The metal chelates displayed three different peaks in their electronic spectra. Intra-ligand

changes were discerned using two separate peaks detected at 255-260 and 294-316 nm. The compound was indicated by the peak detected in the 371-410 nm array, ascribed to LMCT shifts (Fig. 11-15).

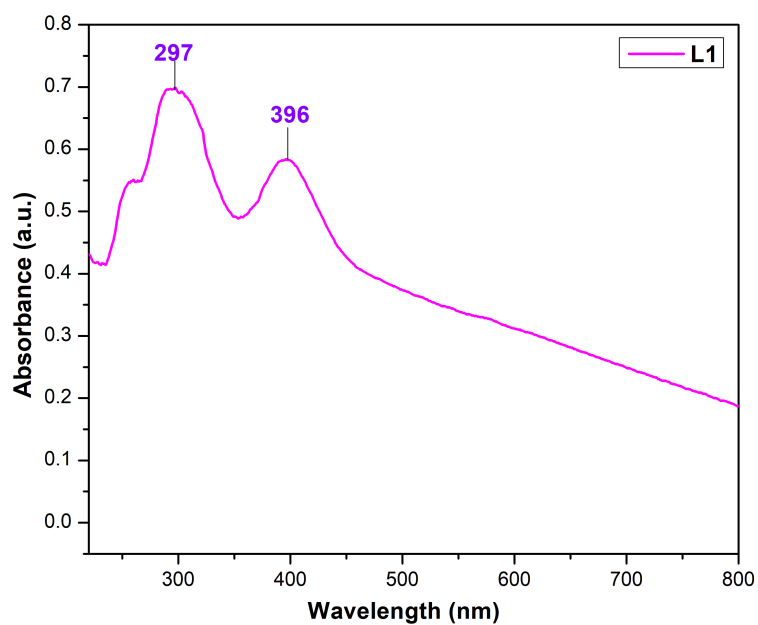


Fig. 10: UV-Vis spectra of ligand L1.

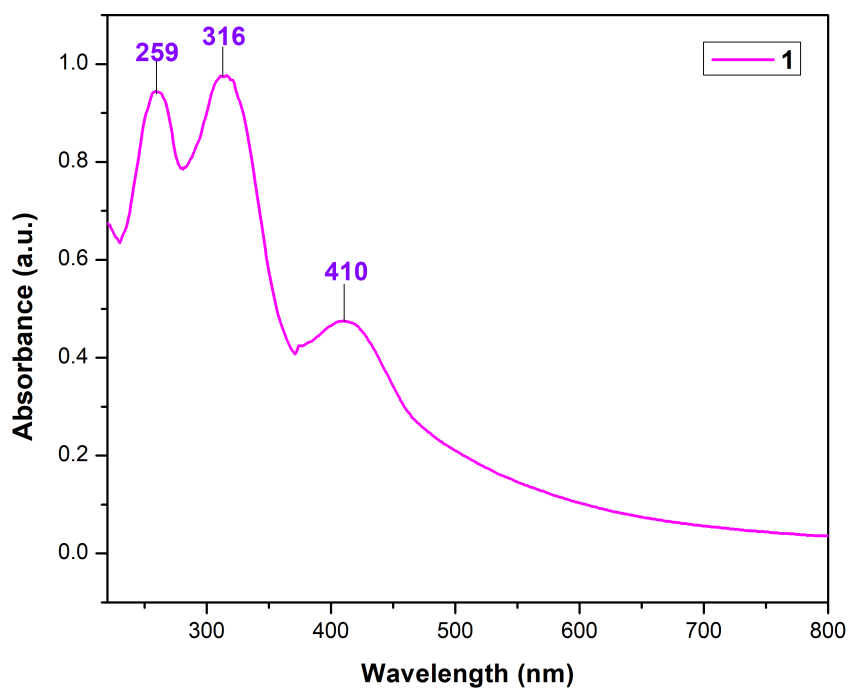


Fig. 11: UV-Vis spectra of complex 1

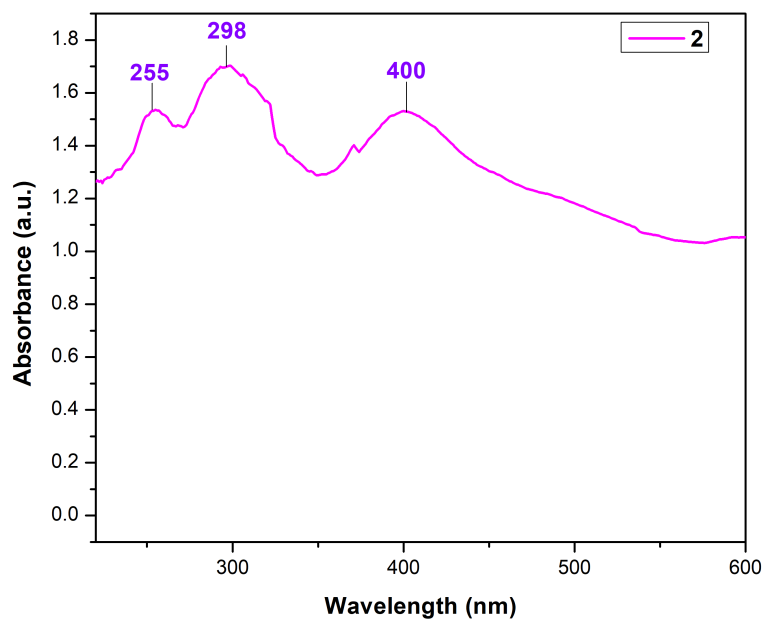


Fig. 12: UV-Vis spectra of complex 2

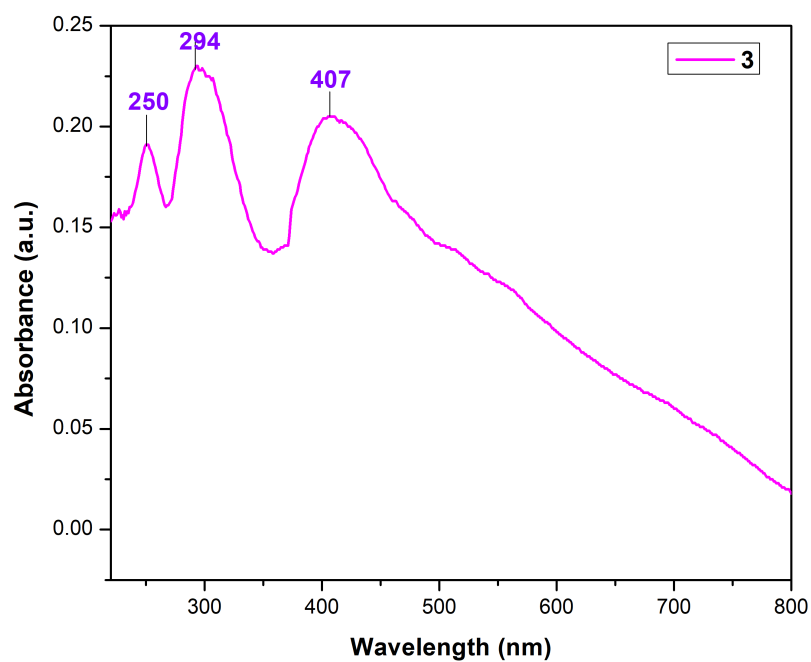


Fig. 13: UV-Vis spectra of complex 3

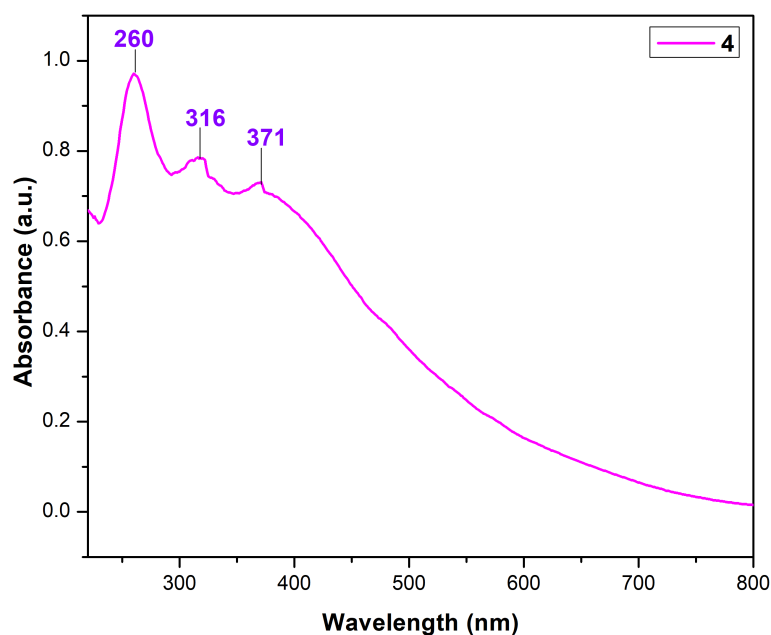


Fig. 14: UV-Vis spectra of complex 4

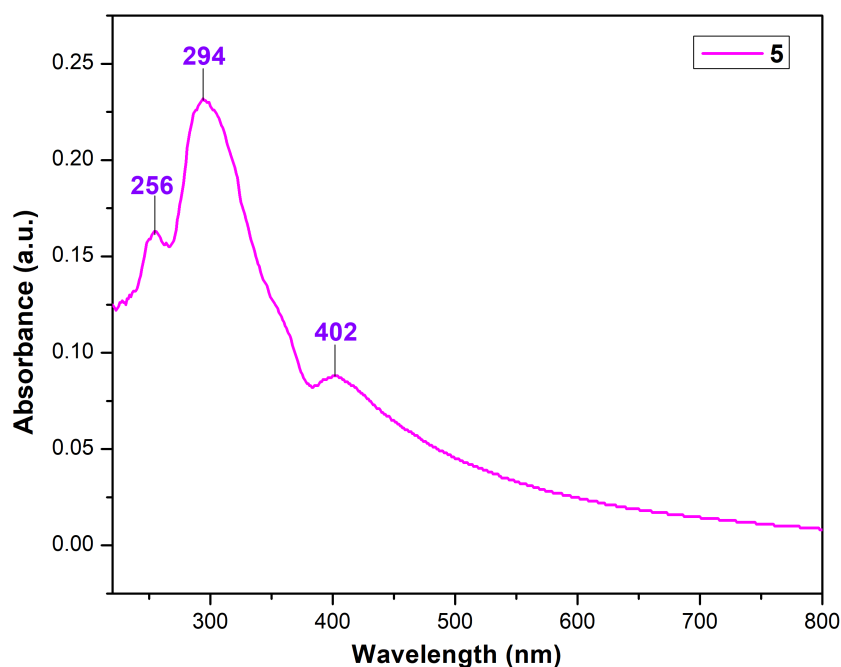


Fig. 15: UV-Vis spectra of complex 5

EPR spectra

Fig. 16 displays the EPR spectra of $[\text{Cu}(\text{L1})_2\text{Cl}_2]$ (**1**). Analysis based on EPR spectra may elucidate the allocation of both paired and unpaired electrons and the development of ligand-metal bonds. Copper (II) complexes have unique properties in chemistry of coordination, exhibiting numerous shapes for example octahedral, square pyramidal, tetrahedral, and square

planar, that may be distinguished through EPR spectrum. The EPR constraints $g^\perp$, g_{avg} , $g^\parallel$, and G are utilized to ascertain if a substance has tetrahedral or octahedral configuration. The existence of an electron that is unpaired in the $d_{x^2-y^2}$ orbital is validated through the condition that the $g^\parallel > g^\perp > 2.0023$. The $g^\parallel$ and $g^\perp$ measurements for the $[\text{Cu}(\text{L1})_2\text{Cl}_2]$ (**1**) was recorded at 2.1288 and 2.0415, individually. Covalent nature is indicated by a $g^\parallel < 2.3$,

whereas an ionic behaviour is indicated by a $g^{\parallel} > 2.3$. The $g^{\parallel}$ value (2.1288) is smaller than 2.3, demonstrating that the substance is covalent. Hathaway asserts that G values < 4 designate substantial connection with metal centers, but

G values > 4 signify little charge transference. In this instance, the $G = 3.1036$, signifying significant contact with the metal center. The $[\text{Cu}(\text{L1})_2\text{Cl}_2]$ (**1**) has a octahedral shape, as shown through its EPR features.

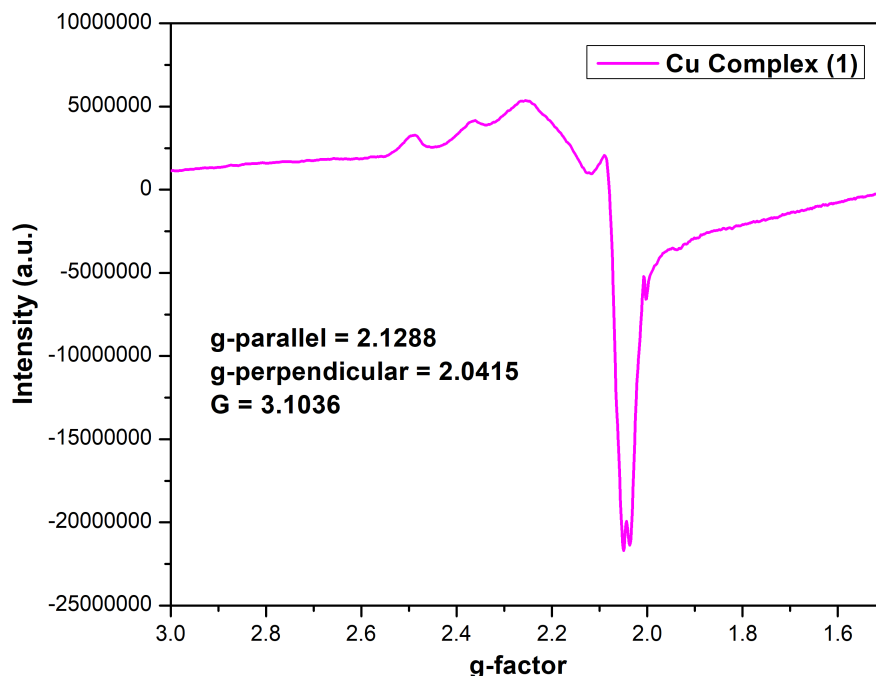


Fig. 16: EPR spectra $[\text{Cu}(\text{L1})_2\text{Cl}_2]$ (**1**)

Antibacterial assessment

The synthesized ligand (**L1**) and chelates (**1-5**) were assessed for antibacterial activity. The ligand (**L1**) shown reduced effect relative to the corresponding complexes (**1-5**). The assessment was administered in a controlled environment. $[\text{Cu}(\text{L1})_2\text{Cl}_2]$ (**1**) demonstrated notable efficacy (MIC = 3 $\mu\text{g/mL}$) against *S. aureus*. The $[\text{Co}(\text{L1})_2\text{Cl}_2]$ (**3**) shown more efficacy against *K.*

pneumoniae than the standard Ciprofloxacin, demonstrated through its inferior MIC value of 6 $\mu\text{g/mL}$, compared to Ciprofloxacin (MIC: 8 $\mu\text{g/mL}$). The $[\text{Co}(\text{L1})_2\text{Cl}_2]$ (**3**) exhibited equivalent action towards *S. aureus* (MIC: 4 $\mu\text{g/mL}$) related to Ciprofloxacin (MIC: 4 $\mu\text{g/mL}$). Chelates **1** (Cu II), **2** (Ni II), and **3** (Co II) having exceptional activity relative to complexes (**1-5**). The outcomes were revealed in Table 4.

Table 4: Antibacterial properties of ligand (**L1**) and chelates (**1-5**)

Compounds	MIC in $\mu\text{g/mL}$				
	<i>E. coli</i>	<i>S. aureus</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	
L1	18	26	24	18	
1	8	3	16	10	
2	4	6	12	6	
3	10	4	6	8	
4	8	10	10	5	
5	12	8	13	7	
Ciprofloxacin	6	4	8	2	

Antifungal studies

The research investigated the antifungal efficacy of the synthesized ligand (**L1**) and its chelates (**1-5**). In comparison to analogous chelates, the ligand (**L1**) shown decreased effect. $[\text{Cu}(\text{L1})_2\text{Cl}_2]$ (**1**) exhibited notable action against *C. albicans*, exhibiting a MIC of 5 $\mu\text{g/mL}$. $[\text{Ni}(\text{L1})_2\text{Cl}_2]$ (**2**) and $[\text{Cr}(\text{L1})_2\text{Cl}_2]$ (**4**) exhibited equivalent efficacy, having a MIC of 13 $\mu\text{g/mL}$ against *C. albicans*.

The $[\text{Ni}(\text{L1})_2\text{Cl}_2]$ (**2**) shown superior action against *C. neoformans* relative to standard clotrimazole. The MIC of the $[\text{Ni}(\text{L1})_2\text{Cl}_2]$ (**2**) was 3 $\mu\text{g/mL}$, while the MIC of clotrimazole was 4 $\mu\text{g/mL}$. $[\text{Cr}(\text{L1})_2\text{Cl}_2]$ (**4**) and $[\text{Mn}(\text{L1})_2\text{Cl}_2]$ (**5**) exhibited equivalent action, with a MIC of 12 $\mu\text{g/mL}$ towards *C. neoformans*. $[\text{Co}(\text{L1})_2\text{Cl}_2]$ (**3**) revealed a reduced MIC of 9 $\mu\text{g/mL}$ towards *A. niger*, in contrast to the standard clotrimazole, having MIC of 12

µg/mL. Chelates (**1**) and (**4**) exhibited equivalent action, with a MIC of 11 µg/mL against *M. audouinii*. Chelates **1** (Cu II), **2** (Ni II), and **3** (Co II) have considerable effect

relative to chelates (**1-5**). The results were encapsulated in Table 5.

Table 5: Antifungal studies of ligand (L1) and chelates (1-5)

Compounds	MIC in µg/mL			
	<i>C. albicans</i>	<i>M. audouinii</i>	<i>A. niger</i>	<i>C. neoformans</i>
L1	16	18	20	24
1	05	11	15	07
2	13	08	23	03
3	11	13	09	17
4	13	11	15	12
5	15	06	16	12
Clotrimazole	08	10	12	04

In-silico docking assessment

Docking examinations were accomplished to provide a comprehensive grasp of the probable pathways behind biological activities. The receptors PDB ID: 1FI4 and PDB ID: 1KZN were chosen as biological aims to evaluate antimicrobial efficacy against microorganisms^{34,35}. The inhibitors **L1**, complexes (**1-5**), ciprofloxacin and clotrimazole were examined for its docking contacts towards targets 1FI4 and 1KZN using the Autodock Vina tool. Chelates (**1-5**) demonstrate superior docking scores (-8.4, -8.7, -8.9, -7.2, -7.7 kcal/mol) relative to ligand **L1** (docking score: -6.1 kcal/mol) and ciprofloxacin (docking score: -6.0 kcal/mol) inside the 1KZN target. The formation of H-bonds substantially enhances the stability of ligand-protein interactions. The optimal bond length between H-donor and H-acceptor molecules is within 3.5 Å³⁶. The bond lengths of H-bonding across the examined substances were all under 3.5 Å in its corresponding proteins, which demonstrated very strong H- bonding. The inhibitor **L1** forms two H-bonds with the target 1KZN. Asp73 (bond length: 2.11 Å) and Thr165 (bond length: 2.30 Å) engaged in H- bonding relations. The amino acids containing Ala47, Ile78, and Pro79 facilitated hydrophobic interactions. Complex (**3**) forms four H-bonds with the target 1KZN. The amino acids Asp49 (bond length: 2.13 Å), Glu50 (bond length: 2.13 Å), Arg76 (bond length: 2.51 Å), and Ser121 (bond length: 2.14 Å) engaged in H-bonding interactions. Hydrophobic associations were promoted through the amino acids Ala53, Pro79, and Ile90. Ciprofloxacin did not form any hydrogen-bonded structures with the protein 1KZN. Hydrophobic relations

transpired among the amino acids Asp73, Ala47, Ile90, Ile78, Asn46, and Glu50. Figs. 17-23 depict the hydrophobic and H-bonding interactions amongst the substances **L1**, complexes (**1-5**), ciprofloxacin and the amino acids in 1KZN target. The chelates (**1-5**) establish superior docking scores (-9.5, -8.0, -10.3, -7.5, -7.1 kcal/mol) relative to ligand **L1** (docking score: -6.2 kcal/mol) and clotrimazole (docking score: -6.7 kcal/mol) at the 1FI4 protein, respectively. The inhibitor **L1** forms one H-bond alongside the receptor 1FI4. Asp302 was involved in aforementioned interactions, with a bond length of 2.58 Å. The amino acids containing Ala119 and Ala122 promoted hydrophobic interactions. Complex **3** forms one H-bond alongside target 1FI4. The amino acid Ser155 (bond length: 2.90 Å) was entangled in H-bonding connections. Hydrophobic relationships were accompanied via the amino acids Asn306, Lys18, Ala122, Asp302, Ala119, Ala303, Phe260, and Ala15. The clotrimazole establishes single H-bond connection alongside target 1FI4. The amino acid Arg158 (bond length: 5.83 Å), engaged in a H-bonding contact. Hydrophobic responses were promoted through the amino acids Ala303, Tyr19, Ala119, Lys18, Phe260, Trp20, Asp302, and Ala15. Figs. 24-30 illustrate the hydrophobic and hydrogen bonding interactions that occur among amino acids in the 1FI4 target and inhibitors **L1**, together with complexes (**1-5**) and clotrimazole. The findings demonstrate that complexes (**1-5**) possess significantly more inhibitory efficacy than ligand **L1** and the controls clotrimazole and ciprofloxacin regarding antimicrobial activities. The results have been elucidated and made available in Table 6 and Table 7.

Table 6: Docking findings of inhibitors (1-5) and L1 towards target 1KZN

Inhibitors	Docking score (kcal/mol)	No. of H-bonds	H-bonding residues (Bond length Å)
L1	-6.1	2	Asp73 (2.11), Thr165 (2.30)
1	-8.4	0	-
2	-8.7	0	-
3	-8.9	4	Asp49 (2.13), Glu50 (2.13), Arg76 (2.51), Ser121 (2.14)
4	-7.2	0	-
5	-7.7	0	-
Ciprofloxacin	-6.0	0	-

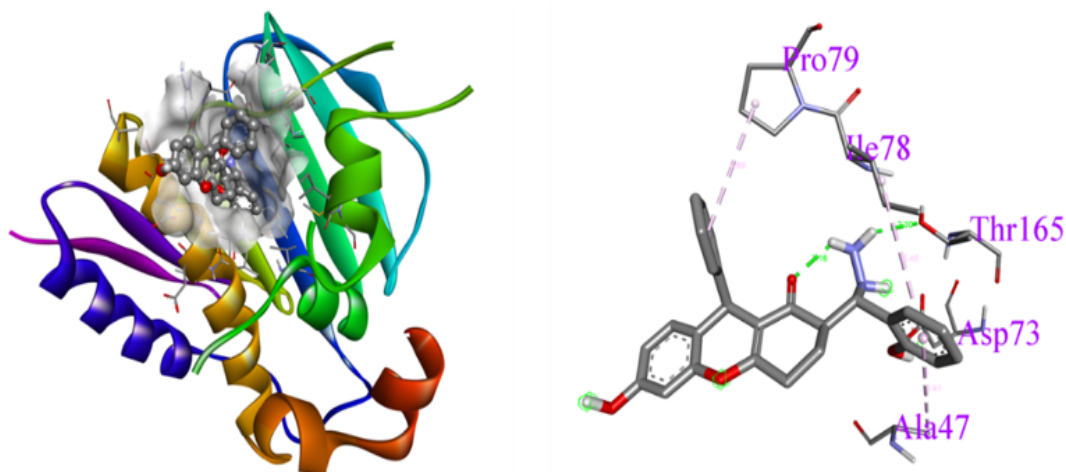


Fig. 17: Interactions of ligand L1 surrounded by aminoacids in 1KZN

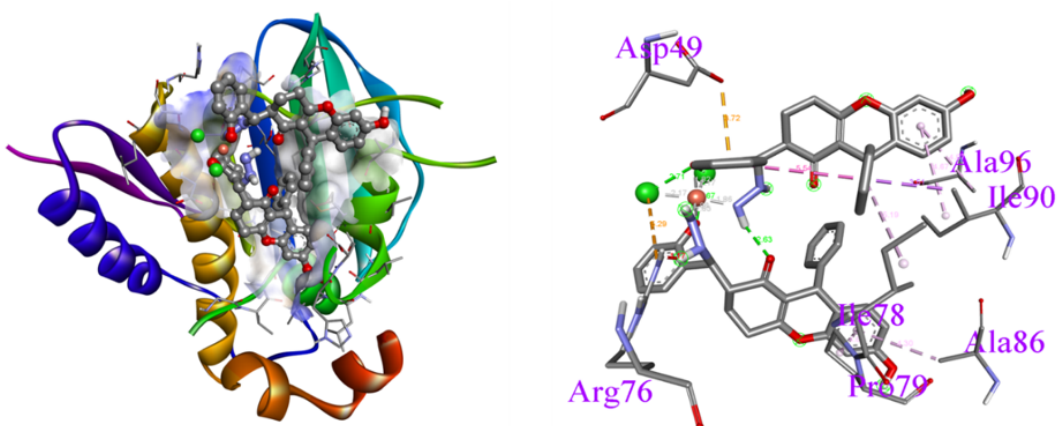


Fig. 18: Interactions of complex 1 surrounded by aminoacids in 1KZN

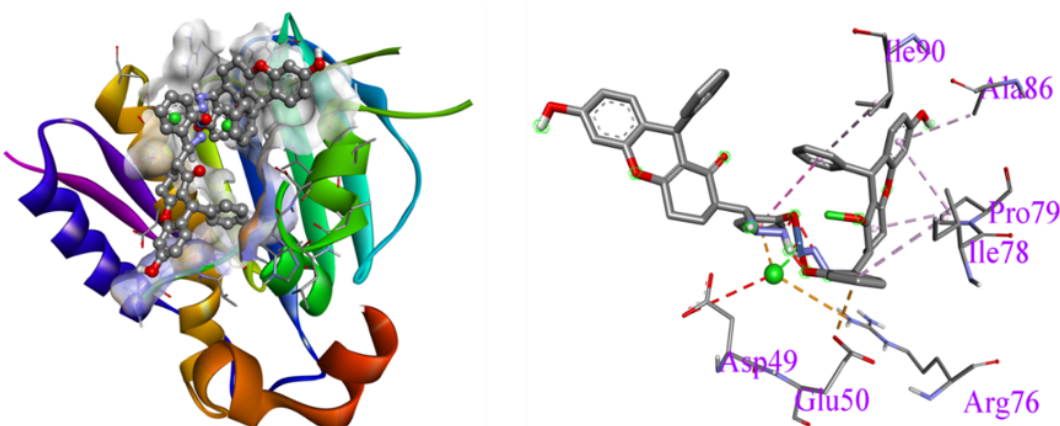


Fig. 19: Interactions of complex 2 surrounded by aminoacids in 1KZN

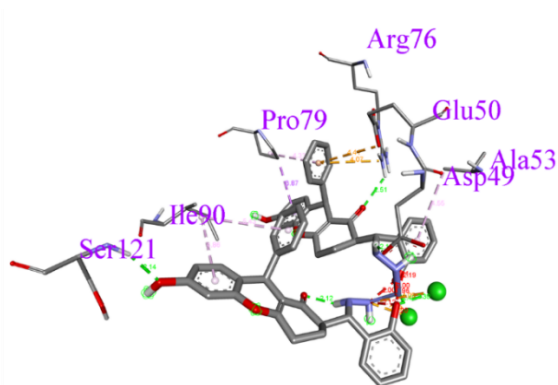
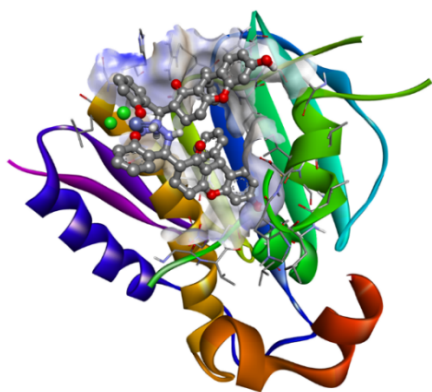


Fig. 20: Interactions of complex 3 surrounded by aminoacids in 1KZN

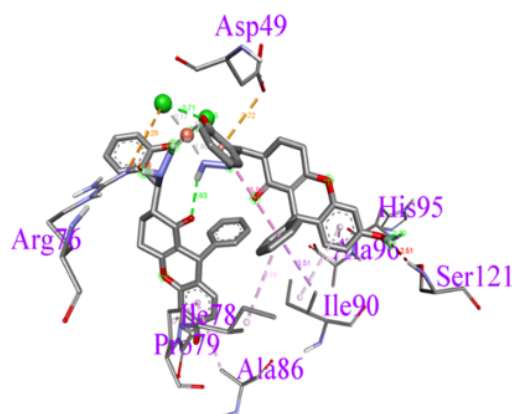
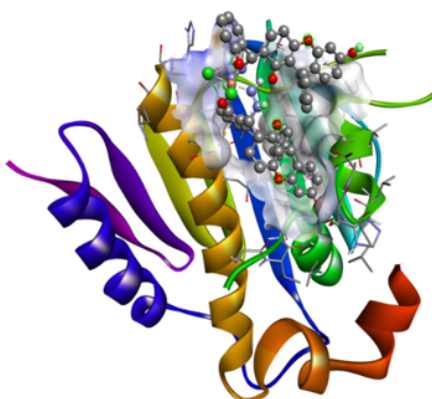


Fig. 21: Interactions of complex 4 surrounded by aminoacids in 1KZN

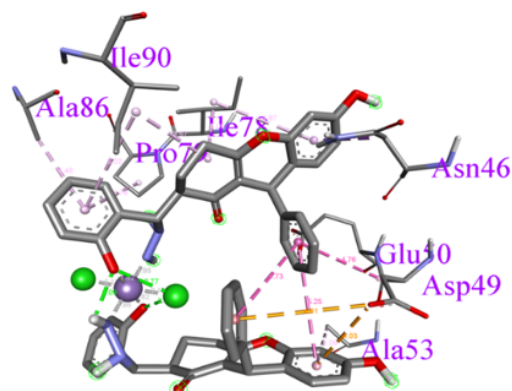
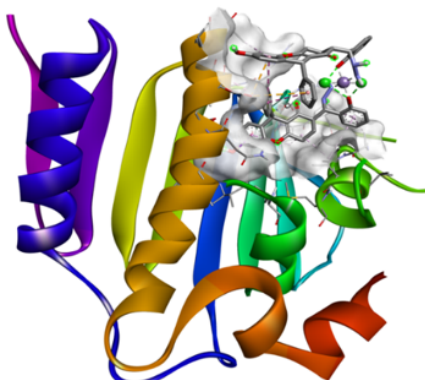


Fig. 22: Interactions of complex 5 surrounded by aminoacids in 1KZN

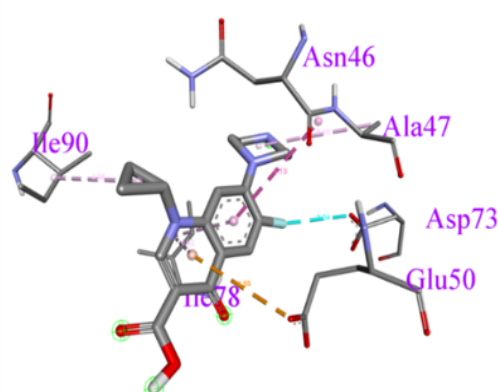
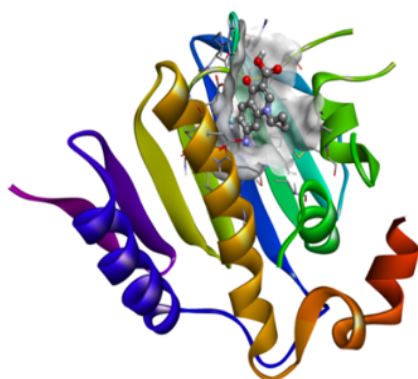


Fig. 23: Interactions of ciprofloxacin surrounded by aminoacids in 1KZN

Table 7: Molecular docking dealings of inhibitors (1-5) and L1 towards target 1FI4

Inhibitors	Docking score (kcal/mol)	No. of H-bonds	H-bonding residues (Bond length Å)
L1	-6.2	1	Asp302 (2.58)
1	-9.5	1	Ala119 (2.94)
2	-8.0	1	Arg158 (2.31)
3	-10.3	1	Ser155 (2.90)
4	-7.5	1	Ala119 (2.94)
5	-7.1	0	-
Clotrimazole	-6.7	1	Arg158 (2.62)

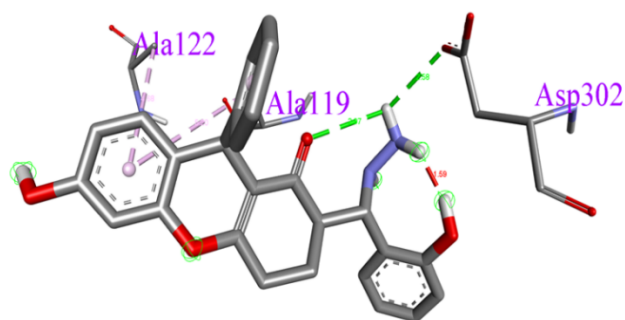


Fig. 24: Interactions of ligand L1 surrounded by aminoacids in 1FI4

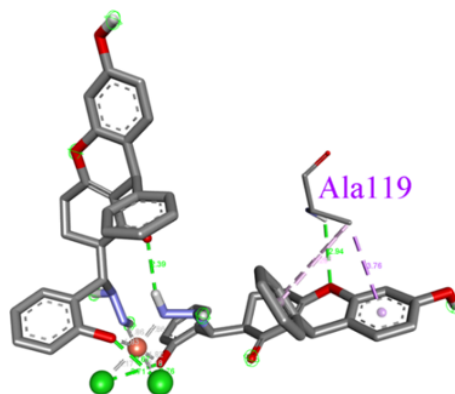


Fig. 25: Interactions of complex 1 surrounded by aminoacids in 1FI4

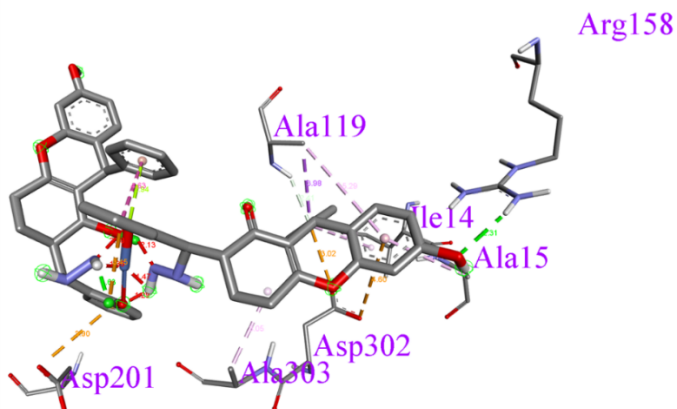


Fig. 26: Interactions of complex 2 surrounded by aminoacids in 1FI4

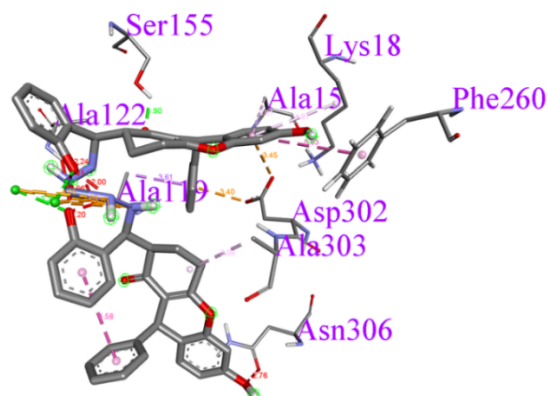
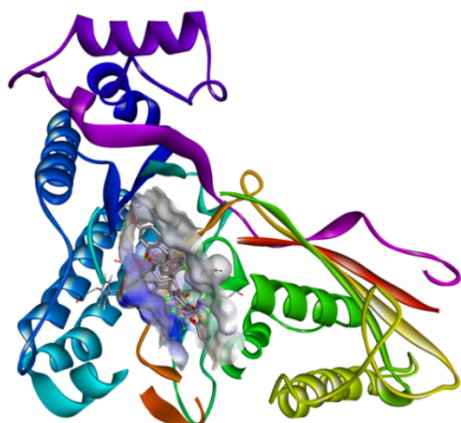


Fig. 27: Interactions of complex 3 surrounded by aminoacids in 1FI4

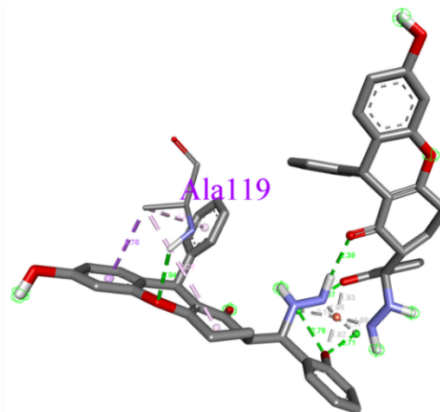


Fig. 28: Interactions of complex 4 surrounded by aminoacids in 1FI4

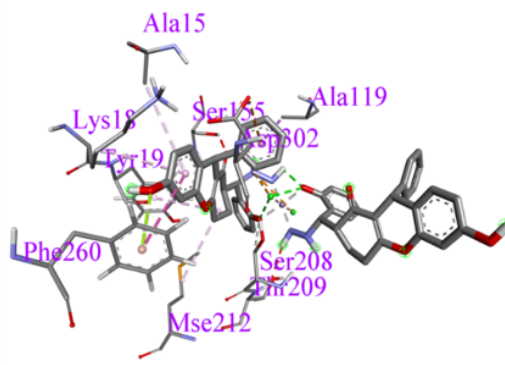


Fig. 29: Interactions of complex 5 surrounded by aminoacids in 1FI4

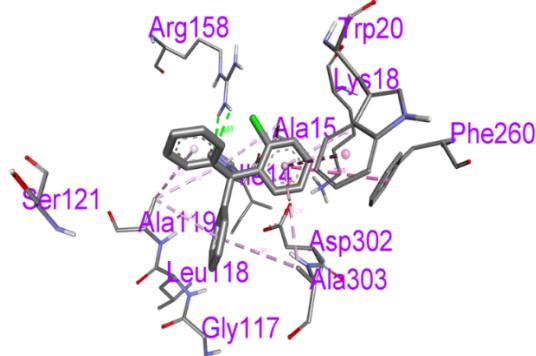


Fig. 30: Interactions of clotrimazole surrounded by aminoacids in 1FI4

CONCLUSION

This paper examines the coordination behaviour of a Mannich base analogue synthesized via the interaction of salicylaldehyde, hydrazine hydrate, and xanthene. The produced ligand (**L1**) was employed to synthesize metal chelates (**1-5**) of the $[M(L1)_2Cl_2]$ configuration. The complexes were further analysed via magnetic, spectroscopic, and analytical techniques. The ligand (**L1**) having bidentate nature and coordination with metal center via the oxygen atom of salicylaldehyde and the nitrogen atom of hydrazine hydrate. The conductance behaviour suggest that the Cl_2 molecules are coordinated to the metal centers as ligands, instead of independent ions. The synthesized chelates (**1-5**) have octahedral shape, determined via its magnetic and UV-Vis spectra. Additionally, the metal chelates and ligand were subjected to screening to assess its antimicrobial effectiveness against various pathogenic microbes. The metal complexes exhibited notable antimicrobial characteristics associated with the ligand (**L1**) and control, as confirmed through docking tests.

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Data Availability Statement

This research article contains all of the data that was obtained and examined.

Ethical Approval Statement

This study will not include any animal or human study.

Informed Consent Statement

This study will not include any animal or human study, informed consent was not required.

Author's Contributions

Manimegalai Ramasamy: Writing & Research work; Gurunathan Velayutham: Antimicrobial & Docking studies; Ramar Pitchaipillai: Manuscript preparation & Supervision.

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