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New dapsone -based Schiff base ligands and their Nickel (II) complexes as biological active molecules: Chemical synthesis, structural elucidation and biological studies

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Abstract:

In this investigation, the preparation and characterization of five diphenylsulphone derived Schiff base ligands, (L_1- L_5) using these ligands, Ni (II) complexes were synthesized. The structures of synthesized ligand and the resultant complexes were inspected using UV-Vis spectroscopy, Fourier transform infrared spectroscopy and ^{1}H NMR. The results from the above analytical techniques shown that the complexes are in an octahedral geometry. The Schiff base ligands, and nickel complexes have been determined as potential antimicrobial. The antimicrobial activity of the synthesized Schiff base ligands and their nickel complexes under study was carried out by using the agar well diffusion method.

Keywords: Schiff base; Nickel (II) complex; Antimicrobial activity.

1. Introduction

Schiff base ligand plays a essential role in coordination chemistry, as it is one of the most important chemical compounds in medicinal inorganic chemistry with several pharmacological activities [1]. The ease of synthesis, donor capacity, and its stability make it a more prominent organic ligand [2]. 4, 4'-diaminodiphenylsulphone (Dapsone), a sulphone analog, have been proved to be a powerful antimicrobial agent [3]. 4, 4'-diaminodiphenylsulphone (Dapsone) is used for the synthesis of various aromatic Schiff bases with biological properties. Salicylaldehyde and its derivatives are useful carbonyl precursors for the synthesis of a large variety of Schiff bases. Additional coordinating groups attached to salicylaldehyde increase the denticity of the Schiff bases.

Nickel complexes are extensively studied in coordination chemistry because of their stability and wide applications. These complexes can also act as good catalysts [4-5].Nickel(II) complexes with tetradentate N_2O_2 Schiff base ligands derived from salicylaldehyde can act as hydrogenation catalysts both homogeneously and heterogeneously in the cages of zeolitesX andY [6-8]. Ni (II) ion forms complexes with Schiff bases, in different geometries such as octahedral, tetrahedral, square planar, etc. Particularly, the octahedral and square planar geometries are most usual; however, tetrahedral, trigonal bipyramidal and square-based pyramidal geometries are not usual. Several reports in the previous literature depict that the transition metal complexs are effective anticancer agents [9-11]. These complexes can also act as potential catalysts. Previous literature reports suggested that heterocyclic compounds, particularly the N-substituted heterocycles upon reaction with metal salts yield their respective coordination complexes, which possess significant pharmacological activities [12-13]. The present study deals with the general experimental technique adopted to synthesize the Schiff bases, analytical procedures followed to characterize them and the biological activity that is antimicrobial activities were performed to know the biological potency of the prepared complexes

2. Experimental

2.1. Materials and methods

The Schiff base ligands were synthesized by reported literature method. All these chemicals/reagents were used without further purification. 4, 4’-diaminodiphenylsulphone, 2-hydroxy-benzaldehyde, 2-hydroxy-1-naphathaldehyde, 2-hydroxy-3-methoxy benzaldehyde, 5-bromo-2-hydroxybenzaldehyde, 5-chloro-2-hydroxybenzaldehyde were of analytical grade. . In the frequency ranges between 4000-100 cm^{-1} by means of Perkin Elmer FT-IR spectrophotometer, Fourier transform infrared spectral measurements were done. The ^1H- NMR spectra have been registered using TMS as an internal standard and DMSO as a solvent for ligands on Bruker spectrometer. The electronic absorption spectra of ligands and its resultant complexes have been recorded in range 200-1000 nm.

2.2. Chemical synthesis

2.2.1. Synthesis of ligands (L_1-L_5)

The preparation of a series of Schiff bases is schematically represented in Scheme 1. 4,4'-diaminodiphenyl Sulfone (Dapsone) is made to react with 2-hydroxy-benzaldehyde, 2-hydroxy-1-naphathaldehyde, 2-hydroxy-3-methoxy benzaldehyde, 5-bromo-2-hydroxybenzaldehyde, 5-chloro-2-hydroxybenzaldehyde in ethanol and the reaction mixture is refluxed for 3-4 h The precipitate produced were filtered, washout with ethanol and recrystallized to yield Schiff bases L_1, L_2, L_3, L_4, and L_5, respectively. The characterization data of the above Schiff base ligands are discussed below:

2,2'-(4,4'-sulfonylbis(4,1-phenylene)bis(azan-1-yl-1-ylidene))bis(methan-1-yl-1-ylidene)-diphenol (L_1):

Yield : 77%; mp: 231°C; FT-IR (KBr, ν/cm^{-1}): 3459 (OH), 3376 (Ar-C-H), 1615 (C=N), 1566 (C=C), 1274 (asymmetric -SO_2-stretch), 1185 (symmetric -SO_2- stretch); ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 12.56 (1H, s, Ar-OH), 8.80 (1H, s, Azomethine), 6.55-8.05 (8H, m, Ar-H)

1,1'-(4,4'-sulfonylbis(4,1-phenylene)bis(azan-1-yl-1-ylidene))bis(methan-1-yl-1-ylidene)-dinapthalen-2-ol (L_2)

Yield : 82%; mp: 239 °C; FT-IR (KBr, ν/cm^{-1}): 3434 (OH), 3222 (Ar-C-H), 1619 (C=N), 1544 (C=C), 1283 (asymmetric -SO_2-stretch), 1186 (symmetric -SO_2- stretch); ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 12.83 (1H, s, Ar-OH), 8.72 (1H, s, Azomethine), 6.49-8.01 (10H, m, Ar-H)

2,2'-(4,4'-sulfonylbis(4,1-phenylene)bis(azan-1-yl-1-ylidene))bis(methan-1-yl-1-ylidene)bis-(4-bromophenol) (L_3)

Yield : 68%; mp: 233 °C; FT-IR (KBr, ν/cm^{-1}): 3432 (OH), 3230 (Ar-C-H), 1621 (C=N), 1547 (C=C), 1275 (asymmetric -SO_2-stretch), 1182 (symmetric -SO_2- stretch) 547 (C-Br); ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 12.92 (1H, s, Ar-OH), 8.68 (1H, s, Azomethine), 6.67-8.23 (7H, m, Ar-H)

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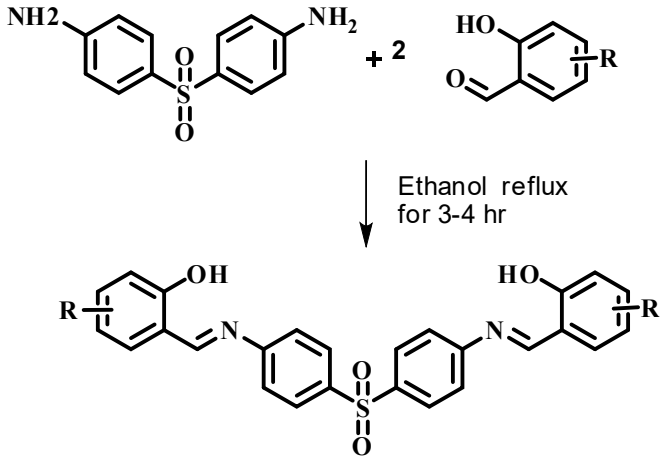
6,6'-(4,4'-sulfonylbis(4,1-phenylene)bis(azan-1-yl-1-ylidene))bis(methan-1-yl-1-ylidene)bis-(2-methoxyphenol) (L_4)

Yield : 80%; mp: 249 °C; FT-IR (KBr, ν/cm^{-1}): 3427 (OH), 3236 (Ar-C-H), 1612 (C=N), 1579 (C=C), 1273 (asymmetric -SO_2-stretch), 1187 (symmetric -SO_2- stretch); ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 12.89 (1H, s, Ar-OH), 8.70 (1H, s, Azomethine), 6.50-7.82 (7H, m, Ar-H), 3.81 (3H, s,-OCH3)

2,2'-(4,4'-sulfonylbis(4,1-phenylene)bis(azan-1-yl-1-ylidene))bis(methan-1-yl-1-ylidene) bis-(4-chlorophenol) (L_5):

Yield : 86%; mp: 260 °C; FT-IR (KBr, ν/cm^{-1}): 3457 (OH), 3241 (Ar-C-H), 1627 (C=N), 1563 (C=C), 1268 (asymmetric -SO_2-stretch), 1181 (symmetric -SO_2- stretch); ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 12.70 (1H, s, Ar-OH), 8.51 (1H, s, Azomethine), 6.67-7.97 (7H, m, Ar-H)



Scheme 1. General Synthetic route of Schiff base ligands (L_1-L_5).

2.2.2. Synthesis of Nickel (II) complexes (C_1- C_5).

A solution of 0.1 M (4.56 g) of the Schiff base ligand (L_1) was dissolved in hot ethanol in a round bottom flask. To this, a solution of 0.102 M (2.41 g) of nickel chloride in ethanol was then added with continuous stirring. The above reaction mixture was refluxed for 3-4 hours. The coloured precipitate obtained was then filtered, washed with ethanol and dried. Nickel (II)

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complexes with other Schiff bases (L_1-L_5) were synthesized using above procedure. The synthesized complexes are characterized using physico-chemical techniques. The tentative structures of the prepared complexes are showed in Figure 1.

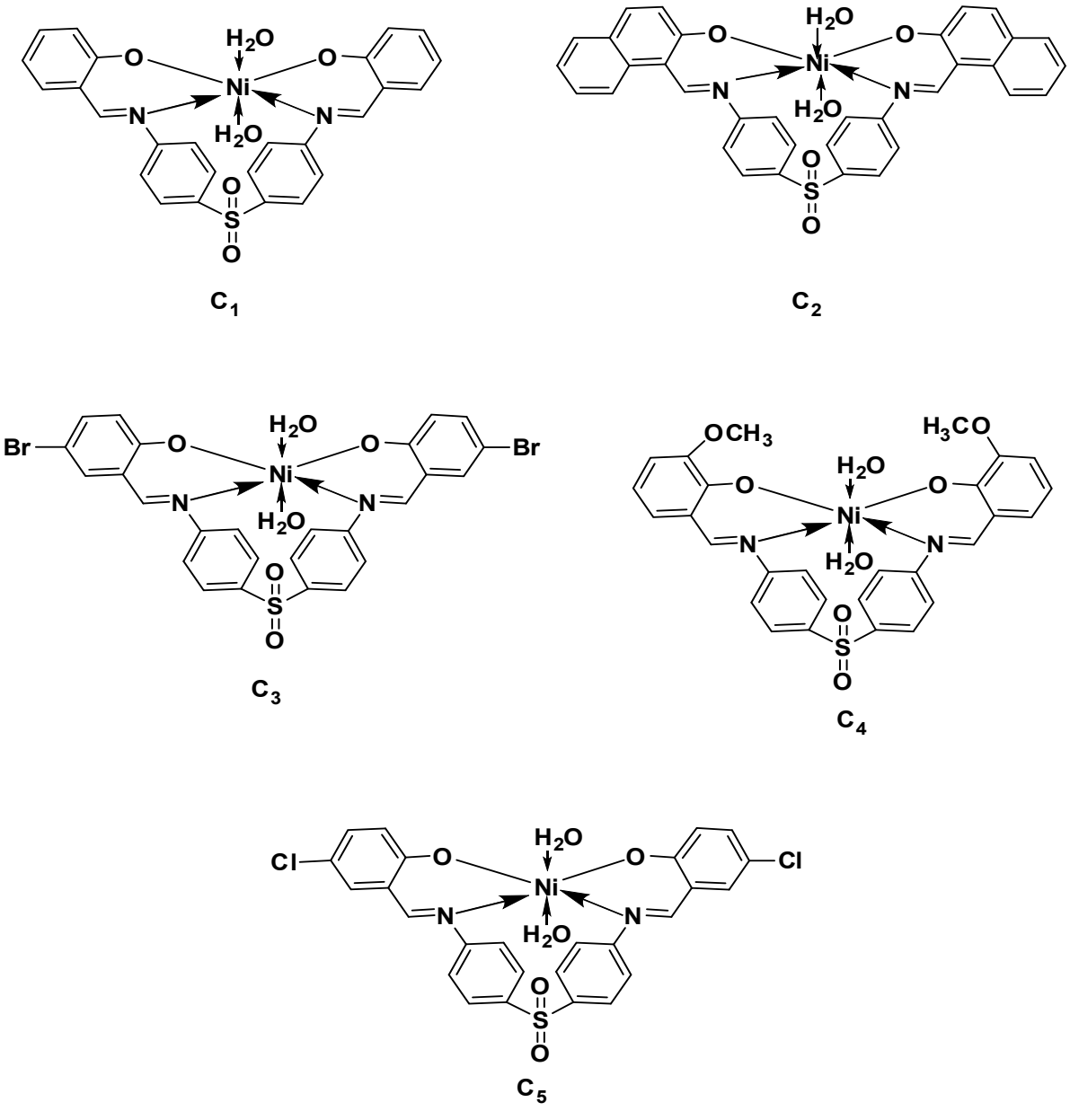

Figure 1: Proposed structure of synthesized Ni(II) complexes (C_1-C_5).

2.3. Biological evaluation

2.3.1. In vitro Antimicrobial studies

The antimicrobial activities of the synthesized Schiff base ligands and their metal complexes under study were carried out by using the agar well diffusion method. The Gram-positive pathogens *Bacillus subtilis*, *Staphylococcus aureus* and Gram-negative pathogens *Klebsiella pneumonia, Pseudomonas aeruginosa, Escherichia coli* were used in the biological potency evaluation. Antifungal activity of the compounds was tested against *Aspergillus niger* and *Candida albicans*. Standard drugs used for the study were Ciprofloxacin and Nystatin for bacterial and fungal pathogens respectively. The Muller Hinton agar plate surface was inoculated by the spread plate method with microbial inoculum over the entire agar surface.

Then, a hole with a diameter of 6 to 8 mm is punched aseptically with a sterile cork borer, and the volume of the desired antimicrobial compound dissolved in DMSO with desired concentration was introduced into the well. Then, agar plates were incubated under suitable conditions depending on bacterial/fungal species requirements. The antimicrobial agents diffuse in the agar medium and inhibit the growth of the microbial strain tested. The inhibition zones exhibit around the antimicrobial compound and measured as the diameter of the zone of inhibition in millimeters (mm) [14]

2.3.2. Molecular Docking Studies

Molecular docking was originally proposed to be executed between a ligand and a protein, small molecule and target macromolecule respectively. To find possible binding modes and to predict binding affinity was the foremost goal of molecular docking Molecular docking is one of the most essential tool used in drug discovery due to its ability to predict, the conformation of small-molecule ligands within the appropriate target binding site with a substantial degree of accuracy. To find out the possible mode of action of the synthesized Schiff bases (L_1-L_5) and Ni (II) complexes (C_1-C_5) molecular docking calculations of cysteine protease human cathepsin ki.-e.CDK7 were carried out using AutoDock 4.2. Lamarckian genetic algorithm. Auto Grid was used to define the active site and the grid size was set to 46 × 54 × 56 points which cover all the active site residues [15]. The grid spacing of 0.375 Å was centered on the selected flexible residues, which are the

active sites of the CDK-7.Total of 10 runs were performed, and for each run, a maximum number of 27000 genetic algorithms (GA) generations were done on a single population of 150 individuals. The best-docked conformation among 10 conformations was obtained with the least binding energy values [16].For each complex, hydrogen bonding as well hydrophobic and other interactions has been predicted [17].

3. Results and Discussion

The elemental analysis data of synthesized Schiff bases and their complexes were found to be consistent with the expected result. The analytical and physical data of all the synthesized Schiff bases (L_1 to L_5) and their Ni(II) complexes (C_1 to C_5) are given in Table 1. Theoretical and experimentally observed values of elemental analysis of compounds are in good agreement with the molecular formula.

Table 1. Elemental analysis data of Schiff base ligands and their Ni(II) complexes

compound	Mol. Formula	Mol. Wt.	M.P. (°C)	Elemental analysis		
				C% Found (calc.)	H% Found (calc.)	N% Found (calc.)
L_1	$C_{26}H_{20}N_2O_4S$	456	231	68.43(68.41)	4.40 (4.39)	6.21 (6.14)
L_2	$C_{34}H_{24}N_2O_4S$	556	239	73.42 (73.26)	4.65 (4.48)	5.13(5.17)
L_3	$C_{26}H_{18}Br_2N_2O_4S$	614	233	50.18 (50.07)	2.93 (2.86)	4.56 (4.48)
L_4	$C_{28}H_{24}N_2O_6S$	516	249	65.16(65.12)	4.80 (4.74)	5.53 (5.48)
L_5	$C_{26}H_{18}Cl_2N_2O_4S$	524	260	60.46 (60.33)	3.48 (3.41)	5.42 (5.35)
C_1	$C_{26}H_{22}N_2O_6SNi$	548	333	57.09(56.93)	4.07(4.01)	5.35(5.10)
C_2	$C_{34}H_{26}N_2O_6SNi$	648	312	63.01(62.89)	4.10(4.04)	4.42(4.31)
C_3	$C_{26}H_{20}N_2O_6SBr_2Ni$	704	306	44.95(44.31)	2.92(2.84)	4.09(3.97)
C_4	$C_{28}H_{26}N_2O_8SNi$	608	320	56.18(55.26)	4.35(4.27)	4.76(4.60)
C_5	$C_{26}H_{20}N_2O_6SCl_2Ni$	616	340	51.17(50.64)	3.30(3.24)	4.63(4.54)

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3.1. Electronic spectral studies

Two bands in the UV-Visible region (Figure 2) analyze the absorption spectra of all synthesized Schiff base ligands (L_1-L_5) and their complexes (C_1-C_5). The observed characteristic intense band in the range 317-357 nm, in the lower energy region of the spectra of ligands, attributed to n → π* transition of azomethine group [18]. The electronic spectra of C_1- C_3complexes showed three absorption bands. The first two were in the range 243-256 nm, which are due to π → π*transition of aromatic ring and the third one was in the range 350-410 nm, which was assigned to n→ π* transition of azomethine group (C=N) of complexes. On the other hand, the UV-Visible spectrum of C_4 and C $_5$ showed two absorption bands. The first one at 240 and 243 nm in C_4 and C_5, respectively, which was attributed to π → π* transition of aromatic ring and second one at around 350 and 355 nm (in C_4 and C_5, respectively), which was assigned to n → π* transition of azomethine group(C=N) of Schiff base.

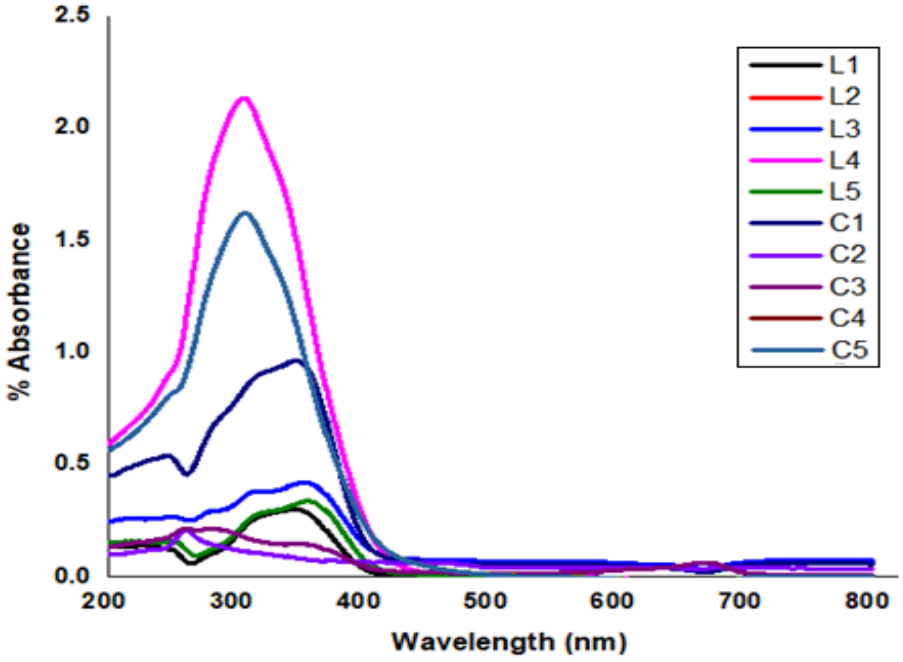

Figure 2: The UV- Vis bands Schiff bases and complexes

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3.2. FT- IR spectral studies

Significant characteristic bands in the FT-IR spectra of synthesized Schiff base ligands and their nickel complexes were observed (Table 2). The important stretching frequencies related to enolic –OH, azomethine C=N-, aromatic C=C, -C-SO_2-C- etc. groups were noticed in the FT-IR spectra. The phenolic -OH stretching vibrations of Schiff bases (Figure 3a) are observed in the range of 3427-3459 cm^{-1}. Similarly, the azomethine stretching in the ligands is an important functional entity, which was identified in the range of 1612-1627 cm^{-1}. This further confirms the formation of Schiff base ligands. In addition, the aromatic stretching frequencies were noticed around 3222-3376 cm^{-1} [19]. Further, the bands observed between 1268-1283 and 1181-1187 $cm^{-1}$are attributed to asymmetric and symmetric SO_2 moieties, respectively [20-23]. It is interesting to note that the lowering in this frequency at around 1609-1617 cm^{-1} was observed in all the Ni(II)complexes indicating the involvement of imine nitrogen atom in coordination to the metal ion [24]. In addition, the –OH stretching and bending vibrational frequencies of the substituted salicylaldehyde appeared in the region 3427-3459 cm^{-1}. The disappearance of these peaks in the spectra of all the Nickel complexes indicates that the coordination takes place via the –OH group. Furthermore, the presence of a broad band at around 3408-3334 cm^{-1} in the Ni(II) complexes suggests the presence of coordinate water molecules to the central metal ion [25, 26]. Additional evidence to the coordination of the azomethine nitrogen is the presence of ν (M-N) bands in the frequency range of 556-573cm^{-1} (Figure 3b)

Table 2: FT-IR absorption bands (in cm^{-1}) of the Schiffbases and their Ni(II) complexes.

Compound	υ(OH/H_2O)	υ(C=N)	υ(M-N)	υ(M-O)
L_1	3459	1615	-	-
L_2	3434	1619	-	-
L_3	3427	1621	-	-
L_4	3432	1612	-	-
L_5	3457	1627	-	-
C_1	3368	1618	556	510
C_2	3334	1621	569	512
C_3	3346	1611	560	515
C_4	3371	1609	573	509
C_5	3408	1623	573	507

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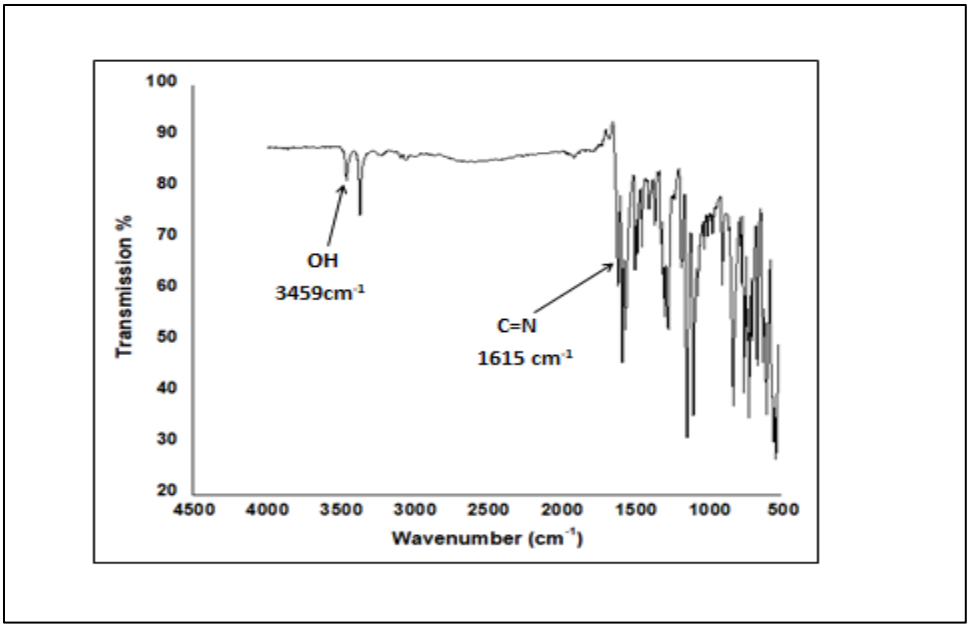
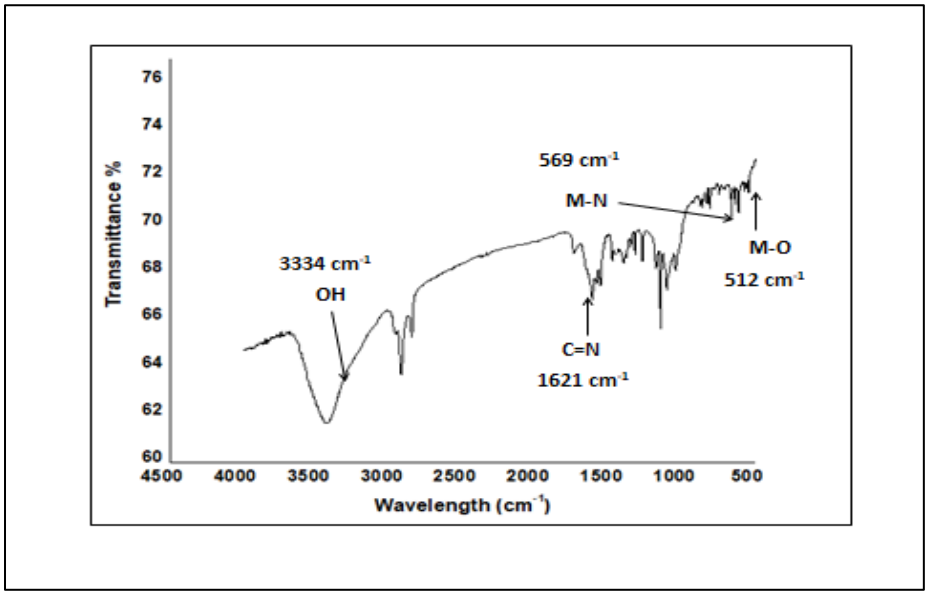


(a)



(b)

Figure 3: FT-IR spectra of L_1 and C_1 complex.

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3.3. ^{1}H–NMR spectral studies

The ^{1}H-NMR spectra of all the synthesized Schiff base ligands were recorded in DMSO solvent The ^{1}H–NMR spectra of the synthesized compounds exhibit signals due to aromatic protons as a multiplet at 6.49-8.23 ppm. In the ^{1}H–NMR spectrum of the Schiff base ligands, a singlet observed downfield around 12.56-12.92 ppm, integrating for one proton, is assigned to –OH [27]. Similarly, the azomethine proton (attached to the carbon close to the nitrogen atom) appears around 8.68-8.80 ppm as a singlet signal [28]. Representative proton ^{1}H–NMR spectra of L_4 and L_5 are shown in (Figure 4)

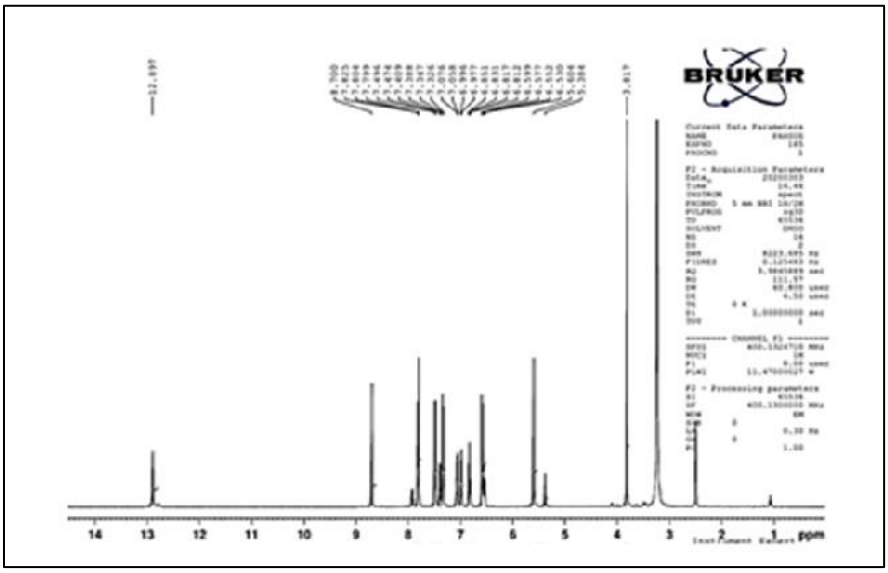

Figure 4: ^{1}H-NMR spectra of Schiff base ligand L_4.

3.4. Mass spectral studies.

The mass spectra of all the Schiff base ligands exhibit parent ion peaks, due to their respective molecular ion (M^+), corresponding to the molecular weight and confirming their molecular composition. The proposed molecular formula of these compounds was confirmed by comparing their molecular formula weights with the m/z values. The mass spectra of the Schiff base ligands are depicted in Figure 5.

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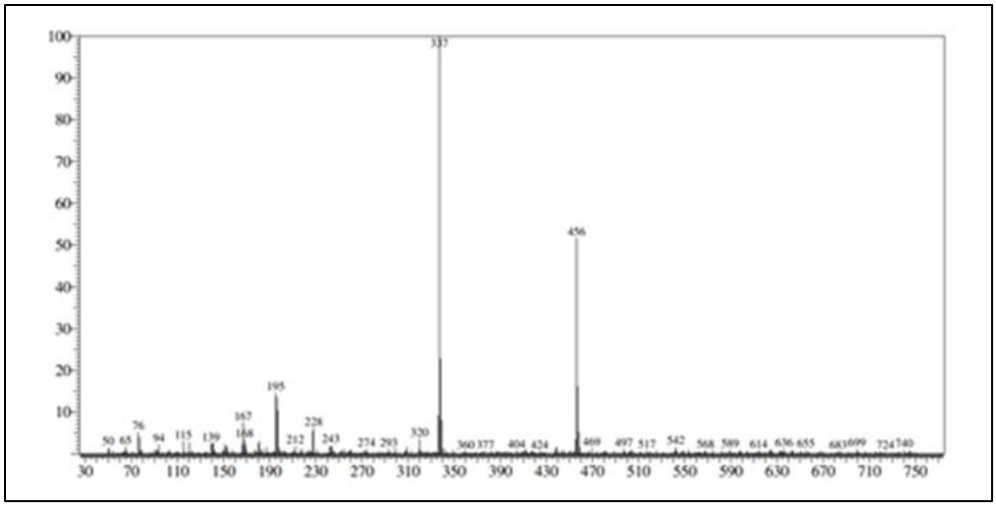

Figure 5: Mass spectra of Schiff base ligand L_1.

3.5. Antibacterial and antifungal activities

All the Schiff bases and their Ni(II) complexes showed antibacterial activity against Gram-positive and Gram-negative bacteria. (Table 3 and 4) Ciprofloxacin as a standard drug and DMSO as a control was used for all bacterial species.

The Schiff base L_4 showed the highest antibacterial activity when compared with the other ligands (Figure 6). These compounds are not only active against bacteria but also exhibit antifungal activity. Further, L_4 exhibited strong antifungal activity against *Aspergillus niger*. It showed antifungal activity more than the standard antifungal drug Nystatin. (Figure 8 A and B).

On the other hand, Ni(II) complexes were less effective against the Gram-negative bacteria viz.,*Klebsiella pneumonia* and *Pseudomonas aeroginosa.* However, complexes were acting against the Gram-positive bacteria viz., *Bacillus subtilis* and *Staphylococcus aureus*. These complexes are strongly active against fungal pathogens *Aspergillus niger* and *Candida albican.* (Figure 8 A and B). The C_4 complex showed the highest antibacterial activity when compared with the rest of the Ni (II) complexes (Figure 7).

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Table 3: Antibacterial and Antifungal activities of Schiff bases ligands

Microorganisms	**L_1**	**L_2**	**L_3**	**L_4**	**L_5**	**DMSO**	**Standard** [a]
	Zone of growth inhibition in diameter (mm)						
Gram Positive							
Bacillus subtilis	23	18	-	27	21	-	40
Staphylococcus aureus	15	14	-	17	16	-	30
Gramnegative							
Klebsiella pneumonia	-	-	14	16	12	-	36
Escherichia coli	13	15	16	18	15	-	26
Pseudomonas aeruginosa	-	14	12	18	-	-	36
Fungal pathogens							
Aspergillus niger	22	27	14	36	26	-	17
Candida albicans	16	16	12	13	18	-	30

[a] Standard used for antibacterial and antifungal activity was Ciprofloxacin and Nystatin respectively.

Table 4: Antibacterial and Antifungal activities of Ni(II) complexes.

Microorganisms	**C_1**	**C_2**	**C_3**	**C_4**	**C_5**	**DMSO**	**Standard**[a]
	Zone of growth inhibition in diameter (mm)						
Gram Positive							
Bacillus subtilis	12	14	-	20	-	-	32
Staphylococcus aureus	12	-	28	26	27	-	30
Gram Negative							
Klebsiella pneumonia	-	14	-	18	-	-	28
Escherichia coli	13	14	28	22	23	-	27
Pseudomonas aeruginosa	-	15	-	-	06	-	18
Fungal pathogens							
Aspergillus niger	-	13	36	25	37	-	28
Candida albicans	14	-	18	15	18	-	29

[a] Standard used for antibacterial and antifungal activity was Ciprofloxacin and Nystatin

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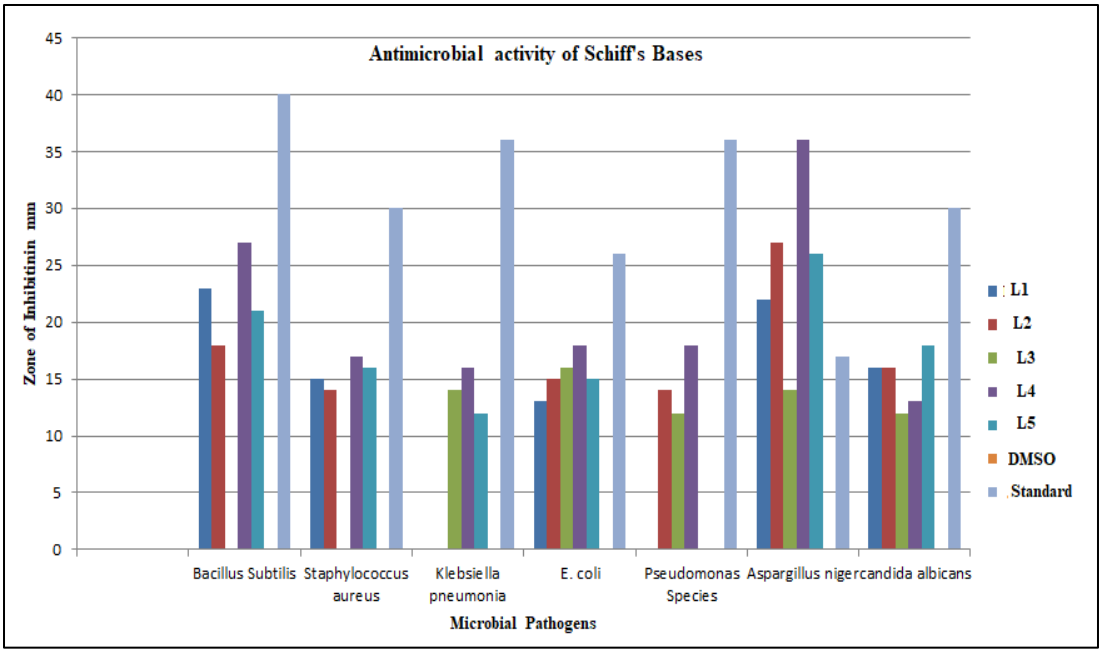

Figure 6: Graphical representation of **a**ntibacterial and antifungal activities of Schiff bases against bacterial and fungal pathogens.

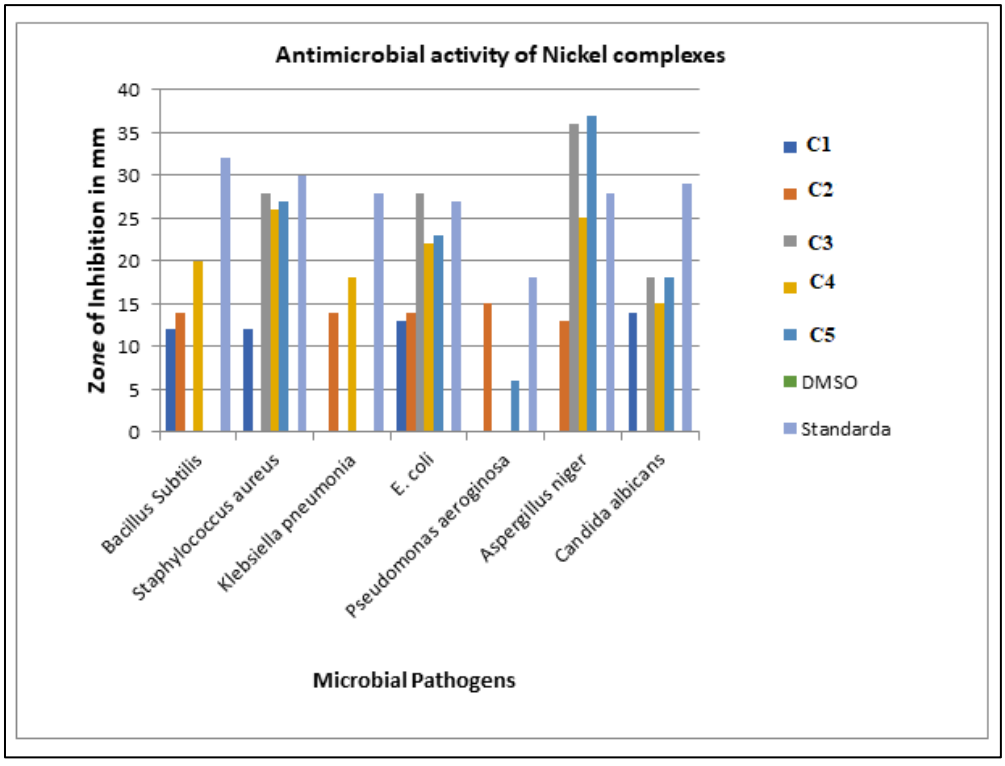

Figure 7: Graphical representation of **a**ntibacterial and antifungal activities of Ni(II) complexes against bacterial and fungal pathogens.

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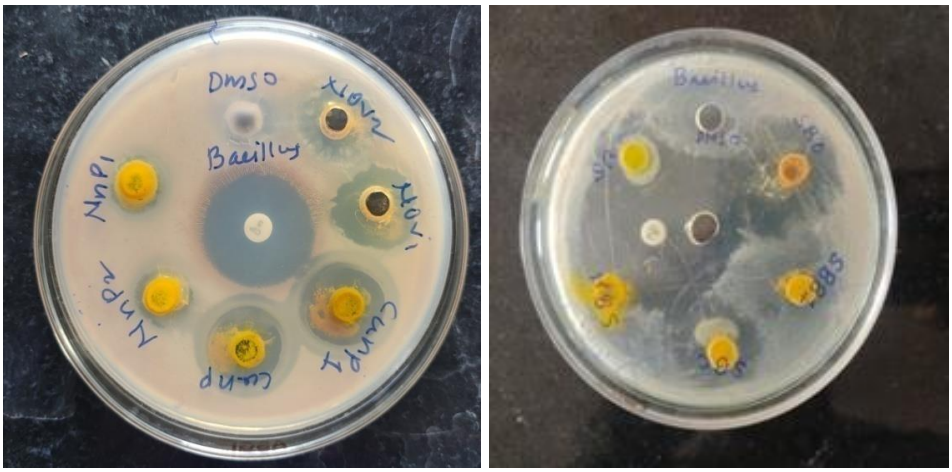
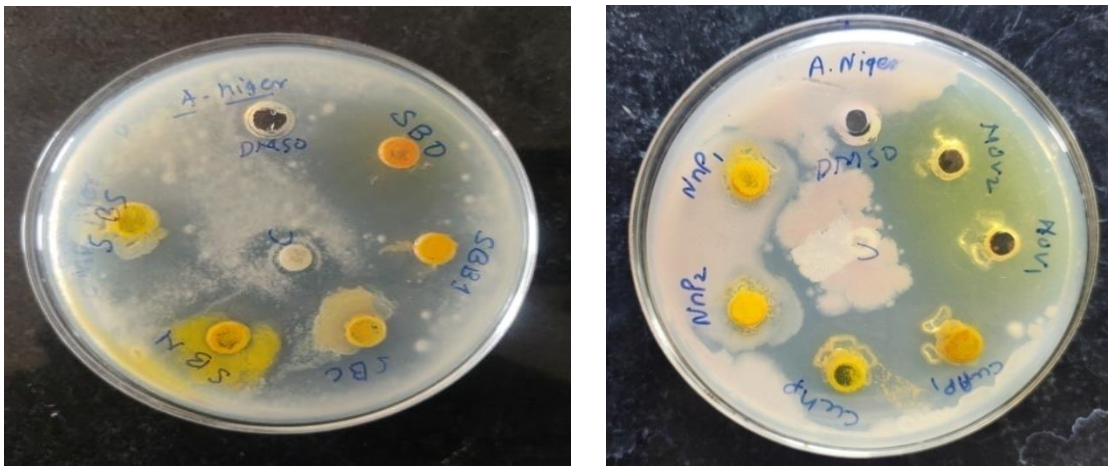


Antibacterial activity against *Bacillus subtilis*

Figure 8 A: Zone of inhibition of Schiff base ligands (L_1- L_5) and their Ni(II) complexes against *Bacillus subtilis*



Antifungal activity against *Aspergillus niger*

Figure 8 B: Zone of inhibition of Schiff base ligands (L_1- L_5) and their Ni(II) complexes against *Aspergillus niger*

3.6. Molecular docking studies

To know the most preferred conformation of all Schiff base ligands with protein PDB ID :1au2, we performed the dockingstudy of each ligand for 10 confirmations. The best-docked conformation among 10 conformations was obtained with the least binding energy. The Binding values are -9.25 kcal/mol, -9.40 kcal/mol, -9.12 kcal/mol, -7.11 kcal/mol, +285.63 kcal/mol, for ligands CDK-7-L_1, CDK-7-L_2, CDK-7-L_3, CDK-7-L_4 and CDK-7-L_5, respectively (Table 5).Further, the best-docked complexes were analyzed for hydrogen bonding interactions and hydrophobic interactions [29-30].

Compound L_2 has the highest binding affinity followed by L_1, L_3 and L_4, whereas compound L_5 has the lowest affinity among all the docked ligands which is 285.63 K. Cal/ Mol. Further, L_2 molecule and its interaction with amino acids like ARG188, TYR190, and PHE156 and hydrophobic and other interactions with, LUE158, LEU134, ARG136, ASP137, THR175, ARG176, ARG179, and PHE162. The highest binding affinity of L_2 than the other Schiff bases is mainly due to the involvement of ARG188 in hydrogen bonding interaction and TYR190, LEU134, ARG136, ASP137, LEU158, THR175, ARG176, ARG179, and PHE162 in hydrophobic and other interaction with amino acid.

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The docking investigation results of Ni (II) complexes revealed that ARG188, TYR190, and ARG136 residues of cysteine protease human cathepsin are involved inhydrogen bonding interactions. Compound C_2 has the highest binding affinity. The highest binding affinity of C_2 than the other Ni(II) complexes is mainly due to the involvement of ARG188 in hydrogen bonding interaction and TYR190, ARG136 MET189, LEU134, ILE55, PHE162, PRO165, in hydrophobic and other interaction with amino acid (Figure 9)

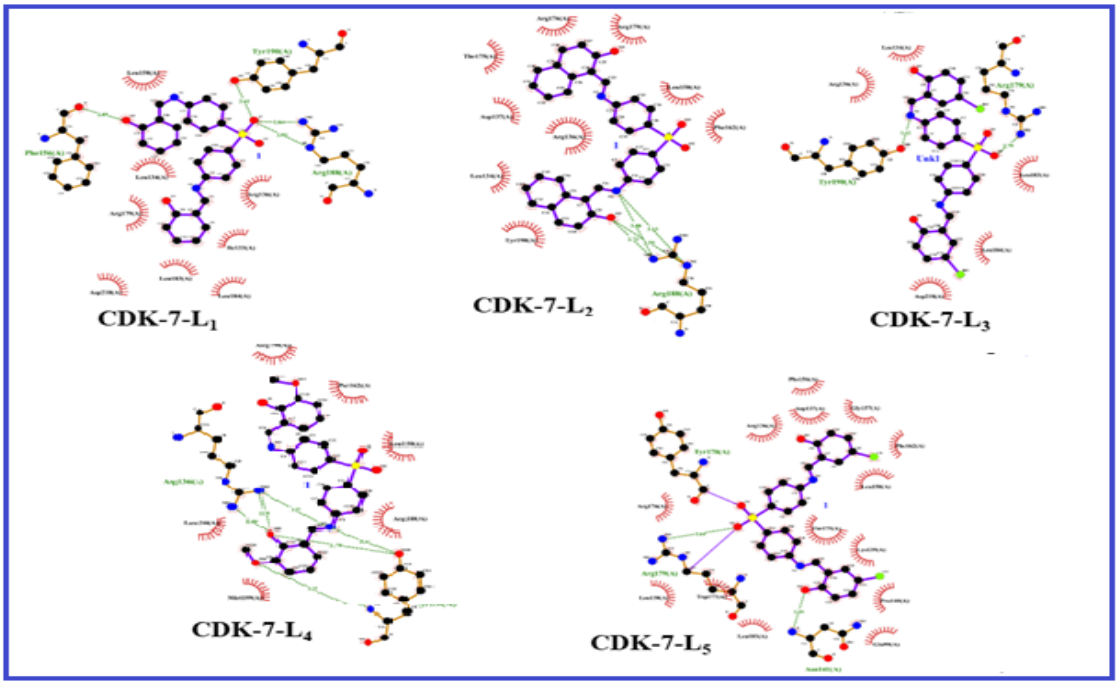

Figure 9: Docking interactions of Schiff base ligands (L_1-L_5) with amino acid

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Table 5: The Binding values of Schiff base ligands and Ni (II) complexes with CDK-7 protein.

Compound	**Lowest Binding affinity (kcal/mol)**	**RMSD from reference structure(Å)**	**Hydrogen bond interaction**	**Hydrogen Bond length in Å**	**Hydrophobic and Other interactions**
CDK7-L_1	-9.25	42.421	PHE136	2.85	LEU158, LEU134, ARG179, LEU183, ILE133, ARG136, LEU184, ASP218
			ARG188	2.81 2.84	
			TYR190	2.61	
CDK7-L_2	-9.40	35.068	ARG 188	2.59 2.73 3.08 3.13	TYR190, LEU134, ARG136, ASP137, LEU 158, THR175, ARG176, ARG179, PHE162
CDK7-L_3	-9.12	37.191	ARG179	2.79	LEU134, ARG136, LEU 183, LEU184, ASP218
			TYR190	3.02	

CDK7-L_4	-7.11	43.983	ARG136	2.89 2.95 3.27	ARG179, PHE162, LEU158, ARG188, MET189, LEU134
			TYR190	3.27 2.6	
CDK7-L_5	+285.63	35.985	ARG179	2.64	GLU99, LYS139, PRO140, TRP177, THER175, ARG176, ARG136, LEU183, LEU138, LEU158, GLY157, PHE162
			ASN141	3.05	
CDK7-C_1	-4.65	43.369	ARG188	2.94 2.63	LEU158, ILE55, PHE162, MET189, LEU134,
			TYR190	3.24	
CDK7-C_2	-4.98	42.047	ARG136	2.654 3.04	MET189, LEU134, ILE55,

			ARG188	2.92	PHE162, PRO165
			TYR190	2.86 2.90	
CDK7-C_3	-4.20	38.504	TYR190	3.11 3.24	GLY191, TRP132, VAL192, LEU134, ILE133, ARG136, LEU158, ILE55
CDK7-C_4	-3.34	41.037	ARG179,	2.95	MET189, LEU134, PHE162, ILE55, ARG136, ASP137, LEU183
			TYR190	2.93	
CDK7-C_5	-3.10	41.39	ARG188	2.47	MET189, PHE162, ILE55, GLY163, PRO165
			TYR190		

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4. Conclusions

The synthesized Schiff bases act as a tetradentate ligand and coordinated to the Nickel (II) ion through imine nitrogen and phenolic oxygen atoms. The binding of ligand to a metal ion is confirmed by elemental analysis, spectral studies UV-Visible and FT-IR. The Nickel (II) complexes are found to exhibit octahedral geometry. All the Schiff bases (L_1-L_5) and their Nickel (II) complexes showed moderate to good antimicrobial activities against the tested microbial species. Further, the molecular docking results revealed that ARG188, TYR190, and ARG136 residues of cysteine protease human cathepsin are involved in hydrogen bonding interactions. All the synthesized compounds shows good to excellent consequence in comparision with standardised drugs for biological screening.

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