



ANTIMICROBIAL STUDIES ON NOVEL Ni(II) METAL COMPLEXES WITH SALICYLOYL PYRAZOLE OXIMES: SYNTHESIS AND CHARACTERIZATION

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ABSTRACT

In this present report, five Ni(II) metal complexes with substituted salicyloyl pyrazole oxime Schiff bases were synthesized. The synthesized Ni(II) metal complexes were characterized by analytical and spectral methods. The elemental analysis data revealed that the Schiff base Ni(II) complexes have 1:2 (M:L) stoichiometry. The molar conductivity data show them to be non electrolytes. The Schiff bases are bidentate and coordinating through the imine nitrogen and phenolic oxygen of salicyloyl pyrazole oximes. Based on analytical and spectral data, four-coordinate geometry was assigned for all complexes. The electronic absorption spectra suggest the square planer geometry for the complexes. The ligand salicyloyl pyrazole oximes and their Ni(II) complexes were screened against *Bacillus subtilis*, *Staphylococcus aureus*, *Actinomyces* and *Pseudomonas aeruginosa*. Thus it can be concluded that most of the ligands and metal complexes possess moderate antimicrobial activity.

Keywords: Synthesis, Ni(II) complexes, Conductance, Absorption, Schiff base, Antimicrobial.

1. INTRODUCTION

Oximes can easily form chelate complexes with several transition metal ions [1] due to its versatile nature. 2-hydroxyoximes as ligand and their transition metal complexes have been reported as previously with their large applications in various fields [2, 3]. Transition metal complexes with oxime have been also used as cerebral and myocardial perfusion imaging agent [4, 5]. The metal complexes of oximes have been formed intramolecular hydrogen bonds and due to its packing configuration, it has important applications as biochemical model [6, 7] and semiconducting materials [8, 9]. Various Schiff bases and their metal complexes show many applications in the field of pharmaceutical, agriculture and industrial chemistry. The oxime containing Schiff base and its copper complex show catalytic effect in degrading organic dyes [10]. The oxime moiety in Schiff base and its complexes also show antimicrobial [11] and anti-cancer [12] activity. The transition metal complexes resulting from pyrazole and their derivatives are broadly used as herbicides, fungicides [13] and anti-inflammatory [14] agents.

The heterocyclic compounds containing Fluorine substitution and their similar analogues are received by enzymes as substrate because fluorine is analogous with

steric requirement to hydrogen. When fluorine substituted to molecule it enhances the activity of molecules. The Fluorine substituted compounds and their analogue of natural occurring nucleic acid are associated with a variety of biological activity such as, antiviral [15], antitumor [16, 17], antifungal [18] and antimicrobial activity [19].

The literature review suggests that, the transition metal complexes associated with pyrazole moiety, oxime group and fluorine substituent has enormous importance in the field of chemistry and huge applications in agriculture, industrial and biological fields. By taking into consideration the large applications of transition metal complexes, we intended for synthesis of Ni(II) complexes with salicyloylpyrazoleoximes.

2. MATERIAL AND METHODS

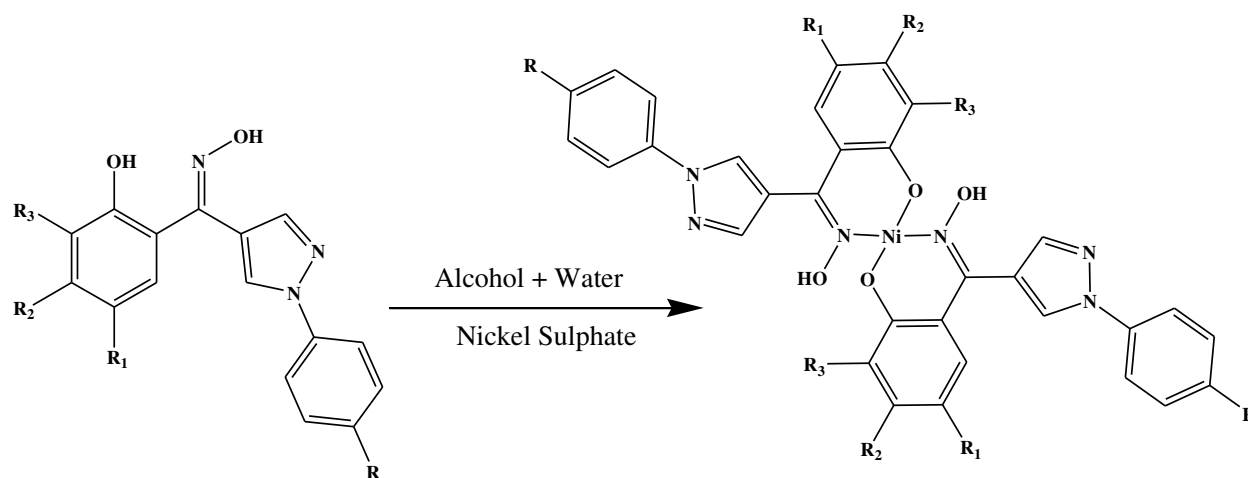
All the chemicals and solvents used for synthesis were available in research grade and purified before used. Double distilled water and distilled ethanol were used. Open capillary method was used for melting points determination and uncorrected. Electrical conductivity of metal complex was recorded in 1×10^{-3} M solution in DMF using digital conductivity meter (Elico, CM-180). The elemental analysis was performed at SAIF, Punjab

University, Chandigarh. The UV-Visible spectra in range 700-190nm were recorded on Shimadzu double beam spectrophotometer (UV-1800). The IR spectra were recorded on Shimadzu FTIR Instrument in the range 4000-450 cm^{-1} . The thermal analysis (TGA) was performed at Department of Chemistry, New Arts, Commerce and Science College, Ahmednagar (MS). The volumetric method was used for determination of percentage of metal [20]. The ligand salicyloyl pyrazole oxime was synthesized using the procedure reported in our earlier research [21].

2.1. General Procedure for Synthesis of Metal Complexes

A 0.001mole Nickel sulphate was dissolved in double distilled water and concentrated HCl was added to

acidify the solution. The resultant acidic solution of metal ion was made warmed by using hot water bath. It was then treated with alcoholic salicyloyl pyrazole oxime ligand solution (0.002 mole). The ligand solution was added slowly drop after drop. Small excess of ligand solution was added to make sure the complete complexation. The resulting mixed solution was further treated with alcoholic ammonia to make it alkaline. The solution was subsequently digested on boiling water bath where complex precipitated as coloured solid. The coloured product was first filtered on suction, washed with little hot distilled water followed by ethyl alcohol to eliminate excess of ligand. The coloured precipitates of complexes were dried under ambient conditions. The synthetic scheme for synthesis of metal complexes of salicyloyl pyrazole oxime is given in Scheme 1.



Scheme 1: Synthetic route for synthesis of Ni(II) complexes of Salicyloylpyrazoleoxime.

3. RESULTS AND DISCUSSION

All the Ni(II) complexes are synthesized by the stoichiometric reaction of the Nickel sulphate salts with new Schiff's base ligands salicyloylpyrazoleoximes in a molar ratio (M:L) of 1:2. The synthesized complexes are non-hygroscopic and air stable. The elemental analysis study was found to be in concurrence with the projected formulae and also confirmed the ML_2 composition of the complexes. All the metal complexes are coloured solids and are dissimilar than colour of free ligand. The synthesized metal complexes were found to melt with decomposition at higher temperature which is higher than free ligand this supports the complex formation. The solubility of these complexes was studied in various solvents like water, polar and non-polar organic solvents. All the synthesized complexes are soluble in dimethylformamide (DMF), dimethyl

sulfoxide (DMSO) and insoluble in water, ethyl alcohol, and other organic solvents. Solubility behavior and elemental analysis study of complexes recommend that the synthesized complexes are monomers.

3.1. Solution conductivity

The solution conductivity data of all synthesized metal complexes were performed using Elico digital conductivity meter (Model CM-180) at Department of Chemistry, K. J. Somaiya College, Kopergaon (MS). A fixed amount of solid metal complex was taken into standard 25 ml volumetric flask and dissolved in DMF (10^{-3} M). The solution of metal complex was then transferred in a clean and dry 100 ml beaker and their molar conductance values were recorded at room temperature. The molar conductance values for all synthesized complexes suggest that the complexes are

non-electrolyte and covalent in nature [22]. This non-electrolyte nature of complexes supports chelating

structure in complexes. The molar conductance values are represented in Table 1.

Table 1: Physical and analytical data of Ni (II) complexes

Complex	Substituents				Colour	M. P. ($^{\circ}$ C)	% Yield	Found (Calcd.) %				ΔM ($\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$)
	R ₁	R ₂	R ₃	R				M	C	H	N	
Ni-1	Cl	H	H	F	Green	276-278	78	7.96 (8.15)	53.05 (53.37)	2.93 (2.80)	11.51 (11.67)	56.8
Ni-2	CH ₃	H	H	F	Green	278-280	81	8.45 (8.64)	60.25 (60.12)	3.97 (3.86)	12.515 (12.37)	23.7
Ni-3	Br	H	H	F	Green	>300	92	7.47 (7.25)	47.29 (47.51)	2.74 (2.49)	10.53 (10.39)	76.1
Ni-4	Cl	CH ₃	H	F	Green	290-292	86	8.01 (7.84)	54.69 (54.58)	3.36 (3.23)	11.42 (11.23)	40.2
Ni-5	Cl	H	Cl	F	Green	282-284	77	7.21 (7.44)	48.63 (48.71)	2.45 (2.30)	10.52 (10.65)	21.9

Table 2: The significant peaks in FTIR spectra of free ligand and its Ni(II) complexes.

Compound	Frequency					
	$\nu_{\text{O-H}}$	$\nu_{\text{C=N}}$	$\nu_{\text{N-O}}$	$\nu_{\text{C-O}}$	$\nu_{\text{M-O}}$	$\nu_{\text{M-N}}$
HL1	3391, 3131	1563	1232	1097	-	-
Ni-1	3145	1560	1228	1057	538	409
HL2	3350, 3134	1542	1231	1097	-	-
Ni-2	3145	1532	1228	1053	530	449
HL3	3248, 3163	1546	1282	1073	-	-
Ni-3	3146	1541	1226	1066	555	457
HL4	3327, 3157	1548	1226	1093	-	-
Ni-4	3131	1542	1212	1058	538	449
HL5	3310, 3166	1545	1242	1088	-	-
Ni-5	3139	1538	1231	1061	548	462

3.2. IR spectra

The FTIR spectral analysis studies of ligands and their metal complexes are reported and discussed with respect to assignments of band frequencies for different groups involved in complex formation, mainly from the point of view to locate coordination position in the metal complexes. The assignments of band frequencies for different groups in metal complexes corresponding to those considered for ligand spectra have been proposed on the basis of available data in the literature.

The relationship of IR spectra of ligands and its metal complexes point out that the free ligand exhibit broad band in the range 3391-3248 cm^{-1} which is assigned to free $\nu(\text{O-H})$ stretching frequency and which is absent in the spectra of metal complexes representing deprotonation followed by the development of metal oxygen bond of phenolic group [23]. The band in the range 3166-3131 cm^{-1} assignable to hydrogen bonded $\nu(\text{O-H})$ stretching frequency which shows a slight hypsochromic shift in the complexes, supportive of the coordination of

nitrogen atom and presence of strong hydrogen bonding. Evidence for this coordination also come up from the small shift towards lower frequency of the band in the range 1563-1542 cm^{-1} which is assigned to azomethine linkage $\nu(\text{C=N})$ stretching and $\nu(\text{N-O})$ stretching in the range 1282-1226 cm^{-1} . The shifting of these bands in metal complexes happens because in the metal ligand complex the C=N groups becomes conjugations along with the metal-ligand bonds [24-26]. The medium to strong absorption peaks due to $\nu(\text{C-O})$ observed in the 1097-1073 cm^{-1} region. The spectra of free ligand shifted towards lower frequency in the spectra of the complexes [27]. The observed downward shift of this band on chelation supports bonding of the metal ions to the phenolic OH after deprotonation [28-29]. Further convincing evidence of the coordination of salicyloylpyrazoleoxime ligand with the metal ion was proved by emergence of weak bands in the low frequency region 555-530 cm^{-1} and 462-409 cm^{-1} which was assigned to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ respectively [30,

31]. These frequencies were observed only in the spectra of complexes and not in spectra of free ligand, thus confirming participation of the oxygen and nitrogen atoms in the coordination to the metal ion. The significant peaks in FTIR spectra of synthesized ligands and their metal complexes are summarized in Table 2.

3.3. ^1H NMR spectra

A major contribution to proton chemical shift arises from neighboring groups or atoms having an anisotropic magnetic susceptibility [32]. In transition metal complexes, there are often low lying excited electronic states and the effect of an applied magnetic field is to mix these to some extent with the ground state. The long range effect of these term, however is shielding and so protons bound to transition metal have unusually low chemical shift in general in the range 0 to -40δ ppm. As some other shifts come in this region these resonances are diagnostic and they can be studied with relatively less problems caused by overlapping peaks from other resonances [33].

^1H NMR spectra of some selected complexes was recorded in $\text{DMSO}-d_6$ as solvent and TMS as internal standard. Though due to presence of metal ion, proton resonance was not effected and gave broad peaks indicating the formation of metal complexes [34].

The ^1H NMR spectra of free ligand salicyloyl-pyrazoleoximes showed two D_2O exchangeable proton signals at $\sim 12 \delta$ ppm and 10δ ppm which is assignable to phenolic and oxime protons respectively. In ^1H NMR spectra of complexes the proton signal at $\sim 12 \delta$ ppm disappears, representing deprotonation followed by the formation of metal oxygen bond of phenolic group. The proton signals at $\sim 10 \delta$ ppm move toward higher value. But the chemical shift is smaller indicating the involvement of nitrogen atom in the formation of metal nitrogen bond and intramolecular hydrogen bonding between ligands. The aromatic protons in the metal complexes are appearing in the range 6.5 to 9δ ppm.

3.4. Powder X-ray diffraction

X-ray diffraction pattern of synthesized metal complexes were recorded in solid form. The powder XRD spectra of some selected metal complexes were scanned on Goniometer powder diffraction PW 3050/60 with Cu-K-alpha-1 radiation ($\lambda=1.5406 \text{ \AA}$). The powder X-ray diffraction patterns were measured in 2θ range between 5.0084 and 89.9744 with step

size 0.0170 . The X-ray diffractogram of all complexes showed broad peak, which indicate polycrystalline nature [35]. Although polycrystalline nature of complexes was observed they were generally not soluble in non polar solvents.

3.5. Thermal Analysis

Thermal behaviors for some selected metal complexes have been reported using Thermo gravimetric analysis air as atmosphere. The TG instrument was calibrated using $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$. In the present report, the use of TG is made to understand stoichiometry, thermal stability, the presence and nature of water molecule. In inorganic compounds, the water may present in the complexes as coordinated and lattice water. However there is no border line between these two types of water molecules. The lattice water is the water molecules trapped in the crystalline lattice either by weak bond to anion or weak ionic bond to metal or both. The coordinate water is nothing but the water molecule bonded to metal either by partial covalent bond or coordinate bond. According to Freeman and Carroll [36], the water eliminated below 150°C can be referred as lattice water and above 150°C as water coordinated to metal ion [37].

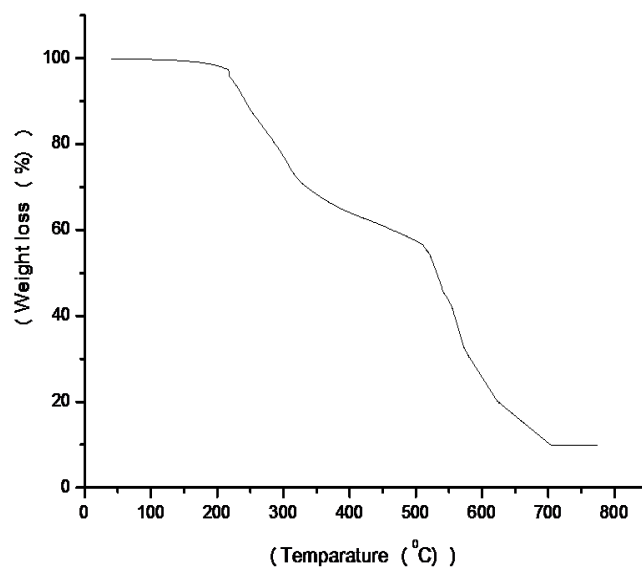


Fig.1: TGA profile of complex Ni-1 Complex.

In the present report, TGA analysis of metal complexes was made by heating the system at 10°C per minute. The weight loss of the complex was recorded as a function of time when the temperature was increased at uniform rate. The temperature range used in TGA analysis was from 30°C to 900°C . In thermograms of

complexes, Ni-1 and Ni-2 does not show any significant weight loss up to 200°C representing there is no lattice or coordinated water molecules. The TG curve for Ni-1 complex showed two steps decomposition in the temperature range 220-700 °C and for Ni-2 complex single step decomposition in the temperature range 200-670 °C was observed and suggesting loss of organic part from the complexes. Because at higher temperature, there is fast decomposition in organic part which gives to form an air stable residue of metal oxide. In Ni-1 the observed residue is 9.87% (Cal- 10.27%) and for Ni-2 complex the observed residue is 10.26 % (Cal- 10.89%). The TGA spectra are reported in Fig. 1 and Fig. 2.

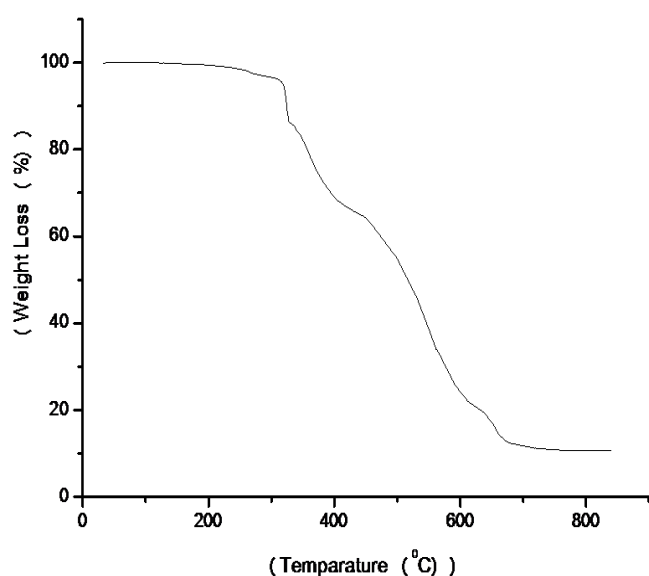
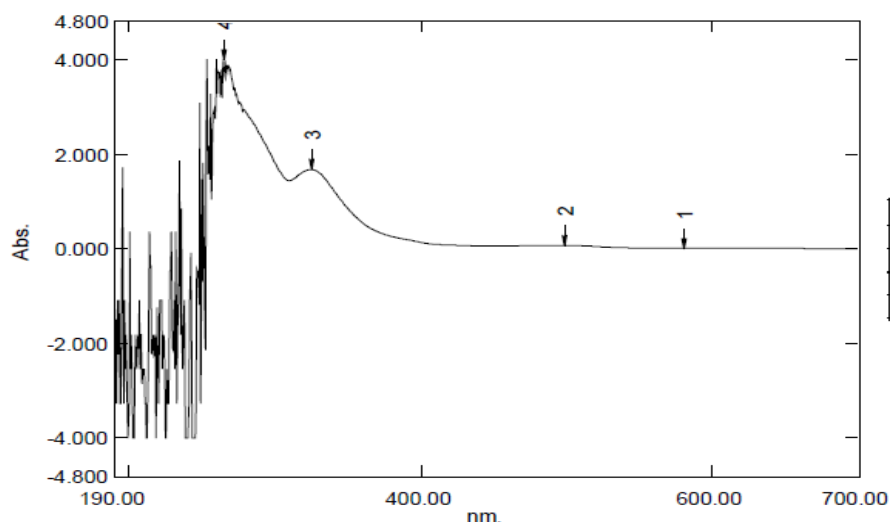


Fig.2: TGA profile of complex Ni-2 Complex.

3.6. Electronic absorption spectral study.

Ni(II) complexes with square planar geometry does not show any significant absorption band below 1000 cm^{-1} due to large crystal field splitting. Due to this such complexes can be easily distinguished from octahedral and tetrahedral complexes. The square planar complexes of Ni(II) complexes shows low energy band frequency near 11000 cm^{-1} which is very weak and it is probably due to spin forbidden transition [38]. The square planar complexes with Ni(II) showed two absorption bands in the region 490-520nm and 550-590nm due to $d \rightarrow d$ transition and charge transfer spectra. Ni(II) complexes showed absorption band between 480-520nm are probably due to its square planer geometry [39]. This observation is supported by absorption bands in 530nm and 480nm regions assignable to ${}^1A_{1g} \rightarrow {}^1A_{2g}$ and ${}^1A_{1g} \rightarrow {}^1B_{1g}$ transitions in square planar field around Ni(II) [40]. In present investigation, the electronic absorption spectra for Ni(II) complexes was recorded in DMF solution. The electronic absorption spectra for Ni-1 complexes showed two absorption band in the range 499nm and 581nm for Ni-2 absorption bands in the range 569nm attributed to $d \rightarrow d$ transition and charge transfer spectra which supports for square planar geometry. The absorption band of ligand at λ_{max} nm due $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ for azomethine linkage group and phenolic -OH group was shifted to lower frequencies in the spectra of complexes. This suggests the participation of nitrogen atom of azomethine linkage and oxygen atom of phenolic group in coordination with metal ion. The spectra are reported in Fig. 3 and Fig. 4.



No.	Wavelength	Absorbance
1	581.00	0.012
2	499.00	0.067
3	325.00	1.675
4	265.00	4.000

Fig. 3: Electronic absorption spectrum of complex Ni-1

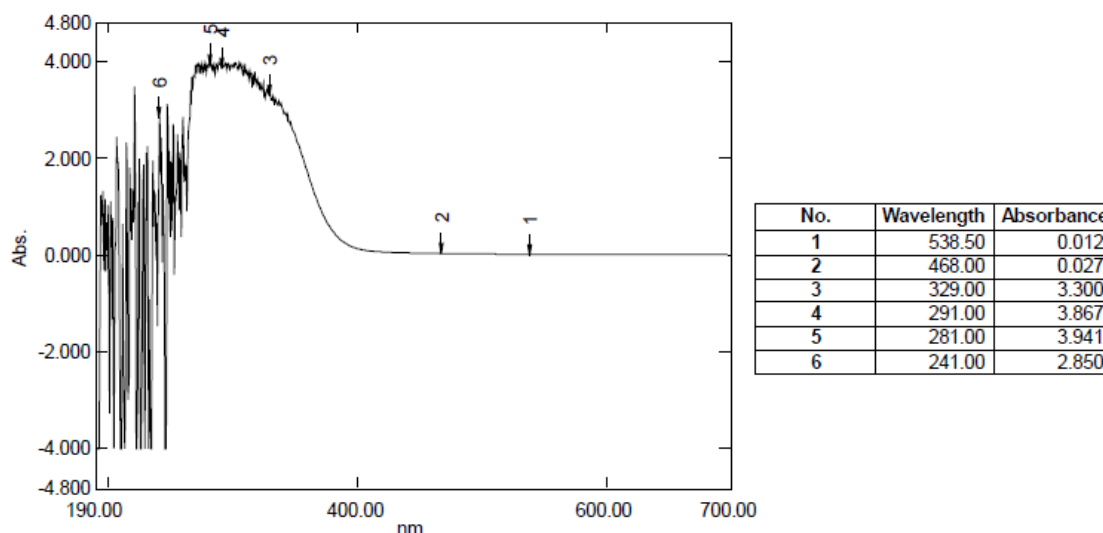


Fig. 4: Electronic absorption spectrum of complex Ni-2

Table 3: Antimicrobial activity of ligand and Ni(II) Metal complexes.

Compound	Substituents				Bacteria			
					Gram-positive		Gram-negative	
	R ₁	R ₂	R ₃	R	Sa	Bs	Am	Pa
HL1	Cl	H	H	F	23	19	13	--
HL2	CH ₃	H	H	F	--	18	14	25
HL3	Br	H	H	F	18	18	17	--
HL4	Cl	CH ₃	H	F	17	18	--	31
HL5	Cl	H	Cl	F	--	16	15	--
Ni-1	Cl	H	H	F	17	19	30	29
Ni-2	CH ₃	H	H	F	--	19	24	--
Ni-3	Br	H	H	F	12	11	17	21
Ni-4	Cl	CH ₃	H	F	12	17	--	22
Ni-5	Cl	H	Cl	F	14	13	24	23

3.7. Antibacterial activity

All the synthesized compounds were evaluated for antibacterial activity against various bacterial strains like *Bacillus subtilis*, *Staphylococcus aureus*, *Actinomyces* and *Pseudomonas aeruginosa*.

Antimicrobial studies of synthesized Schiff base metal complexes were found comparatively much more active than free ligands. The antimicrobial activity of metal complexes showed considerable zone of inhibition compared to that standard drugs. Most of the synthesized complexes showed antimicrobial activity against *Actinomyces* and *Pseudomonas aeruginosa*. After coordination with metal ion, the compounds which are biologically inactive becomes active and biologically less active compounds becomes more active [41]. Such introduction and enhancement in the activity of metal complexes were explained on the basis of Overton's concept [42] and Tweedy's chelation theory [43].

According to Overton's concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only lipid soluble materials due to which liposolubility is considered to be an important factor that controls the anti microbial activity.

The dissimilarity in the activity of the different metal complexes against different bacteria depends either on the impermeability of the cells of the microbes or difference in the ribosomes in the microbial cells. The metal complexes may also be a vehicle for activation of the ligand as a cytotoxic agent. Moreover, complexation may lead to significant reduction of drug resistant. Moreover this other factor such as solubility, conductivity and dipole moment influenced by the presence of metal ions may also be the possible reason causing enhancement of the antimicrobial activity of chelate complex as compared to free Schiff base compounds.

4. CONCLUSION

Five Ni(II) metal complexes with Salicyloylpyrazole oximes were synthesized and characterized by elemental and spectral analysis like UV-Visible, IR Spectroscopy. The four coordination geometries were assigned to all synthesized complexes. The synthesized complexes are non electrolytic in nature with square planer geometry. All the synthesized complexes showed non selective antimicrobial activity against all test bacteria. Complexes Ni-1 and Ni-2 exhibits highest antibacterial activity against *Bacillus subtilis* and *Actinomyces* than other complexes and free ligands.

5. ACKNOWLEDGEMENT

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