

Synthesis, Characterisation and Antimicrobial Studies of Zn(II), Ni(II) and Cu(II) Complexes of a Schiff base derived from o-Vanillin and N-Allyl Thiourea

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Abstract: In the present study a new Schiff base ligand was synthesised by condensation of o- vanillin with allylthiourea in 1:1 molar ratio. The Schiff base metal complexes of Zn(II), Ni(II) and Cu(II) were prepared using the metal salts and the synthesised Schiff base ligand in 1:1 molar ratio. The metal complexes were characterized using molar conductivity, UV-Visible and IR spectra. The ligand and its metal complexes were screened for antibacterial activity against *Klebsiella pneumonia*, *Bacillus cereus* and *Pseudomonas aeruginosa* and fungicidal activity against *Aspergillus niger*, *Candida albicans* and *Candida kefyr*. The results revealed that the synthesized compounds were more potent against all the microbes under investigation.

Keywords: Allyl thiourea, transition metal complexes, antibacterial and antifungal activities.

Introduction

Schiff bases were first reported by Schiff in 1864. The compounds containing an azomethine group (-CH=N-) are known as imines, anils or Schiff base. They result from the condensation of primary amines with ketones or aldehydes to give imines containing a C=N bond. Schiff bases derived from aromatic amines and aromatic aldehydes have a wide variety of applications in many field, eg, biological, inorganic and analytical chemistry¹⁻⁶. Among the organic reagents actually used Schiff bases possess excellent characteristic, structural similarities with natural biological substance, relatively simple preparation procedures and the synthetic flexibility that enables design of suitable structural properties.

It is well known that N and S atoms play a key role in the co-ordination of metals at the active sites of numerous metallobimolecules⁷. Schiff base metal complexes have been widely studied because they have antifungal, antibacterial, anticancer and herbicidal applications⁸⁻¹³. They serve as model for biologically important species and find applications in biomimetic catalytic reactions. Chelating ligands containing N, S and O donor atoms show broad biological activity and are of special interest, because of the variety of way in which they are bonded metal ions. It is known that the existence of metal ions bonded to biologically active compounds may enhance their activities. Allyl thiourea is used especially formerly to promote absorption of scar tissue.

Experimental

Materials and Methods:

The molar conductivities were measured with DCM 900 using the freshly prepared solution of the complexes in ethanol. The Ultraviolet-Visible spectra were recorded on a SYSTRONICS 2201 spectrometer using ethanol as solvent in the wavelength range of 400 – 800nm and the IR spectra of the synthesized compound were recorded using SHIMADZU spectrometer in 4000 – 400cm⁻¹ range, using KBr pellet.

Preparation of Schiff base ligand [HL]:

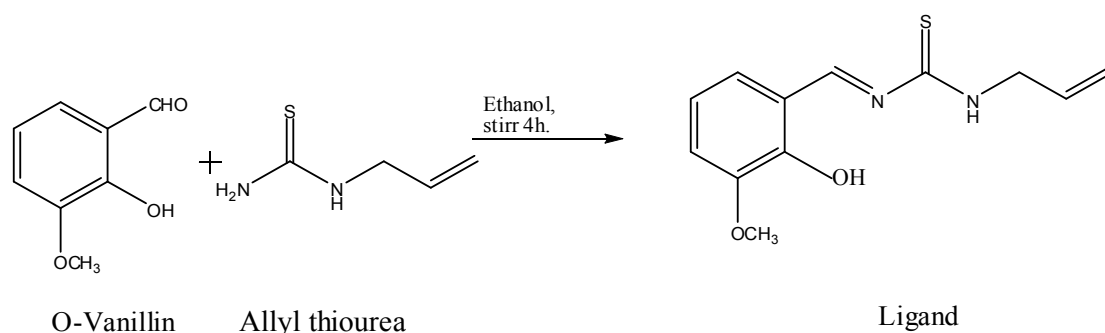
The Schiff base ligand [HL] was prepared by the following general method. An ethanolic solution of allylthiourea (0.351g, 3 mmol) was added to an ethanolic solution of o-vanillin (0.456g, 3 mmol) in 1:1 molar ratio and a few drops of sodium hydroxide solution was added. The mixture was stirred for 4h in a magnetic stirrer and the solution was turned yellow colour. The solvent was evaporated in a water bath and the Schiff base ligand was obtained as yellow oil. It was washed with ethanol and dried [Scheme 1].

Preparation of Schiff base transition metal complexes:

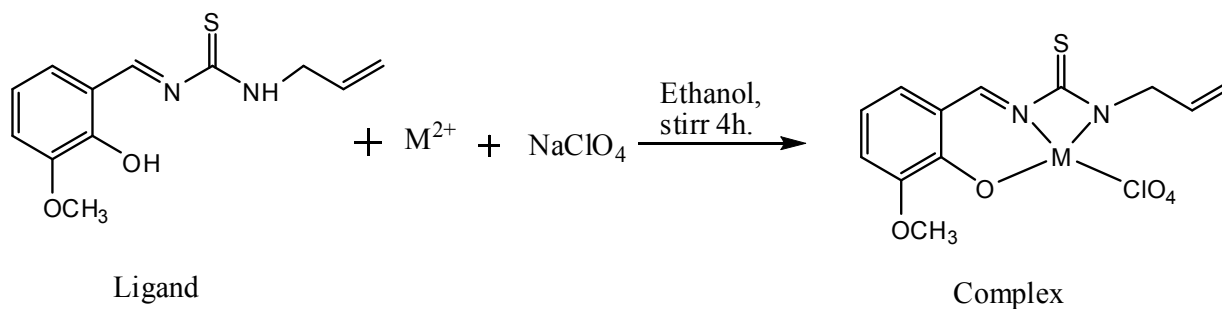
An ethanolic solution of allylthiourea (0.351 g, 3 mmol) was added to an ethanolic solution of o-vanillin (0.456g, 3 mmol) in 1:1 molar ratio and aqueous sodium hydroxide (0.12g, 3 mmol) was added. The mixture was stirred for 4h in a magnetic stirrer. The solution turned yellow colour. Then aqueous metal salts (3 mmol) (where M= Zn²⁺, Ni²⁺ and Cu²⁺) and sodium perchlorate (0.42g, 3 mmol) was added and mixture was stirred in a magnetic stirrer for 4h. The solid product was obtained was filtered, washed with ethanol and dried [Scheme2].

Test Organisms:

The bacterial species *Klebsiella Pneumoniae*, *Bacillus Cereus* and *Pseudomonas aeruginosa* and fungal species *Aspergillus niger*, *Candida kefyr* and *Candida Albicans* were used as test organisms and they are maintained on Mueller Hinton Agar solid media (MHA) and Sabouraud's dextrose (SDA) media¹⁴.



Scheme 1



Scheme 2

Where M²⁺ = Zn²⁺, Ni²⁺ and Cu²⁺

Assay of antimicrobial activity:

Agar diffusion assay was carried out to evaluate the antimicrobial activity of some synthesized compounds. The plates were incubated at 37°C for 24 hours during which activity was evidenced by the presence of a zone of inhibition surrounding the well and antibacterial and antifungal activity was expressed as mean of diameter of inhibition zones (mm) produced by the synthesised compounds when compared to controls.

Preparation of media:

Agar medium was accurately weighed and suspended in 100 ml of distilled water in a conical flask. It was heated on a water bath to dissolve the medium completely.

MHA and SDA were prepared with lawn culture using desired test organisms. The inoculated plates were kept aside for few minutes. Using well cutter 2 wells were made in those plates at required distance. In each step of well cutting, the well cutter was thoroughly wiped with alcohol. Using sterilized micropipette, 20µl of compound extract was added in to one well and in another well the same volume of corresponding control were added.

After diffusion, the plates were incubated at 37°C for 24 hours. After incubation, the inhibition of growth was analyzed and the results were recorded.

Results and Discussion

The melting point of the synthesized ligand and the transition metal complexes were measured and the results are given in table-1.

The synthesized Schiff base metal complexes were dissolved in ethanol and the molar conductivities of 10⁻³M solution at 25 ±2°C were measured. The molar conductivity values of the complexes are given in table-2.

The molar conductance of the complexes were in the range of 1-9 ohm⁻¹ cm⁻² mol⁻¹. The lower molar conductivity values indicated the non-electrolytic nature of complexes¹⁵⁻¹⁶.

The electronic absorption spectra of the Schiff base ligands and its complexes were recorded at room temperature using ethanol as solvent and the data are presented in table-3.

Table-1 Analytical data of ligand and its Zn(II), Ni(II) and Cu(II) complexes.

Compound	Molecular Formula	Molecular Weight	Colour	Melting Point
[HL]	C ₁₂ H ₁₄ N ₂ O ₂ S	250	Yellow	80 ⁰ C
[ZnL(ClO ₄)]	ZnC ₁₂ H ₁₂ N ₂ O ₂ Cl	413	Yellow	260 ⁰ C
[NiL(ClO ₄)]	NiC ₁₂ H ₁₂ N ₂ O ₂ Cl	406	Green	260 ⁰ C
[CuL(ClO ₄)]	CuC ₁₂ H ₁₂ N ₂ O ₂ Cl	411	Dark green	260 ⁰ C

Table-2 Physical characterisation, analytical and molar conductance data of the complexes

Compound	Concentration (mol dm ⁻³)	Specific conductance (ohm ⁻¹ cm ²)	Molar conductance (ohm ⁻¹ cm ² mol ⁻¹)
[ZnL(ClO ₄)]	1.0 x 10 ⁻³	1.2 x 10 ⁻⁶	1.2
[NiL(ClO ₄)]	1.0 x 10 ⁻³	9.8 x 10 ⁻⁶	9.8
[CuL(ClO ₄)]	1.0 x 10 ⁻³	2.8 x 10 ⁻⁶	2.8

Table-3 Electronic absorption spectral data for the ligand and its metal complexes.

Compound	Solvent	Absorption (λ _{max} nm)			Geometry
		d-d	π → π* (Benzene)	n → π* (Azomethine)	
[HL]	Ethanol	-	-	353.6	
[ZnL(ClO ₄)]	Ethanol	466.28	252.92	358.4	sp
[NiL(ClO ₄)]	Ethanol	-	216.8	-	sp
[CuL(ClO ₄)]	Ethanol	437.6	-	346.4	sp

The UV-Visible spectra the band at 353.6nm in the ligand is due to the to $n \rightarrow \pi^*$ transitions of the non-bonding electrons present on the nitrogen of the azomethine group in the Schiff base¹⁷. The metal complexes showed $\pi \rightarrow \pi^*$ transitions in the range of 250 nm, $n \rightarrow \pi^*$ at 350 nm and d-d transitions at 460 nm. No d-d transition was observed for nickel complex. Based on the data a square planar geometry was suggested for all the complexes¹⁸⁻¹⁹.

The IR spectra provide valuable information regarding the nature of functional group attached to the metal atom. The ligand and metal complexes were characterized mainly using the C=N (azomethine) and OH (Phenolic) bands. The main infrared bands and their assignments are listed in table-4.

Formation of the Schiff base ligand was confirmed by the appearance of a band at 1625 cm^{-1} confirmed the formation of imine (-C=N-). Further this value is reduced during complex formation which indicated the coordination of the ligand through the metal atoms via imine group²⁰⁻²¹.

The absorption band of phenolic O-H appeared at 3340 cm^{-1} in the free ligand was shifted to the higher frequencies after complexation appeared at 3540 cm^{-1} , 3410.15 cm^{-1} and 3456.44 cm^{-1} for Zn(II), Ni(II) and Cu(II) complexes respectively, indicated the co-ordination of ligand to metal ions through azomethine nitrogen and phenolic oxygen²². The bands [$\nu_{\text{M-O}}$] observed at 518 cm^{-1} , 505.35 cm^{-1} , and 528.5 cm^{-1} for in Zn(II), Ni(II) and Cu(II) complexes respectively indicated the information of metal oxygen linkage²³. The band [$\nu_{\text{M-N}}$] observed at 441 cm^{-1} , 482.2 cm^{-1} and 447.49 cm^{-1} for Zn(II), Ni(II) and Cu(II) complexes indicated the formation of metal to nitrogen linkage²⁴⁻²⁵.

The reactivity of the synthetic products towards the biological systems is an important feature of the current research and Schiff bases of transition metal complexes play significant role in this direction. The results of the antibacterial, antifungal and larvicidal activities are given below (Table 5&6).

Table – 4 Characteristic infrared absorption frequencies (cm^{-1}) of the ligand and its complexes.

Compound	C=N (cm^{-1})	N-H (cm^{-1})	C=S (cm^{-1})	O-H (cm^{-1})	ClO_4^- (cm^{-1})	M-O (cm^{-1})	M-N (cm^{-1})
[HL]	1635.64	-	728	3340	-	-	-
[ZnL(ClO ₄)]	1631	3448	734.88	3540	1111,1197 914	518	441
[NiL(ClO ₄)]	1625.99	3313.71	734.88	3410.15	1095.57 1222.87 968.27	505.35	482.2
[CuL(ClO ₄)]	1604.77	3170	738.74	3456.44	1232.51 1097.5 962.48	528.5	447.49

Table 5: Antibacterial activity data for the ligand and its metal complexes.

S. No	Organism	Zone of Inhibition (nm)				Ciprofloxacin
		[HL]	[ZnL(ClO ₄)]	[NiL(ClO ₄)]	[CuL(ClO ₄)]	
1	<i>Klebsiella Pneumoniae</i>	15	14	5	8	22
2	<i>Bacillus Cereus</i>	23	18	14	13	20
3	<i>Pseudomonas Aeruginosa</i>	15	13	8	11	25

Table 6: Antifungal activity data for the ligand and its metal complexes

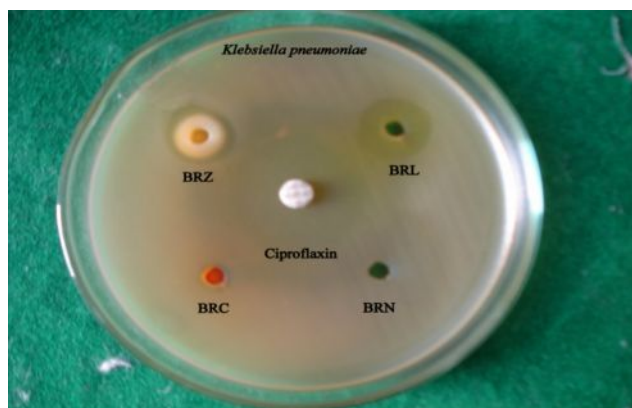
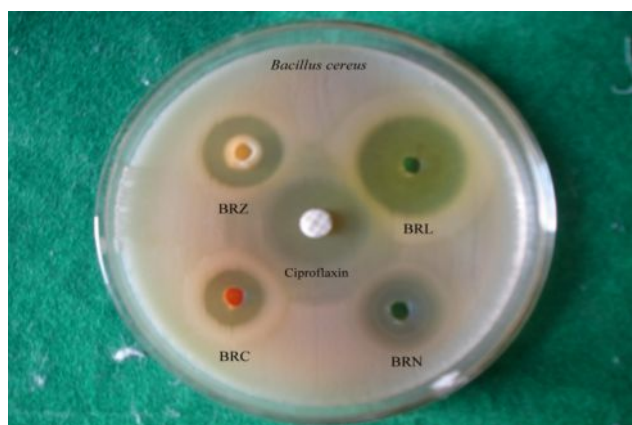
S. No	Organism	Zone of Inhibition (nm)				Ketoconazole
		[HL]	[ZnL(ClO ₄)]	[NiL(ClO ₄)]	[CuL(ClO ₄)]	
1	<i>Aspergillus Niger</i>	36	23	18	20	20
2	<i>Candida albicans</i>	34	23	27	25	19
3	<i>Candida kefir</i>	38	25	24	23	21

[HL] - Schiff base ligand ; [ZnL(ClO₄)] - [ZnC₁₂H₁₂N₂O₂Cl]
 [NiL(ClO₄)] - [NiC₁₂H₁₂N₂O₂Cl]; [CuL(ClO₄)] - [CuC₁₂H₁₂N₂O₂Cl]

In *Aspergillus niger* the free ligand and zinc(II) complex exhibited higher antifungal activity than the standard Ketoconazole. For zinc(II) and copper(II) complexes the biological activity was found to be nearly same. In *candida albicans*, the free ligand and nickel(II) complex exhibit higher fungal activity than the standard Ketoconazole. For zinc(II) and copper(II) complexes the biological activity was

found to be nearly same. In *Candida Kefyr* the free ligand and all complexes like Zn(II), Ni(II) and Cu(II) complexes were more potent than the standard Ketoconazole. Among the synthesized compounds the free ligand showed very good antifungal activity.

On the whole all the synthesized compounds showed a remarkable biological activity against all the three fungal species under investigation.

**Fig.1 : Antibacterial activity of the synthesised compounds against *Klebsiella pneumoniae*****Fig .2: Antibacterial activity of the synthesised compounds against *Bacillus cereus***

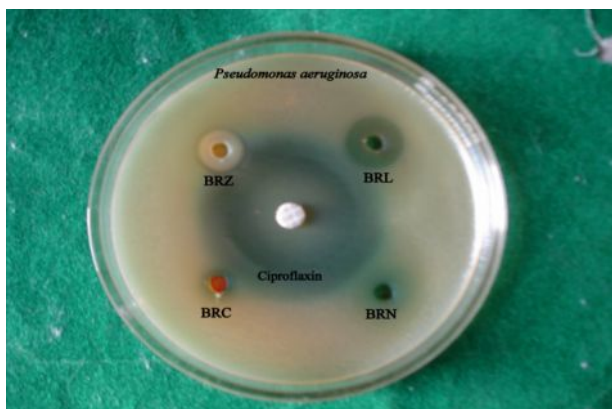


Fig.3: Antibacterial activity of the synthesised compounds against *Pseudomonas aeruginosa*

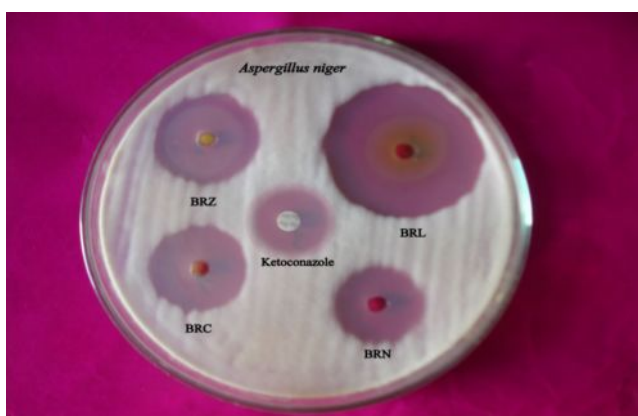


Fig.4: Antifungal activity of the synthesised compounds against *Aspergillus Niger*

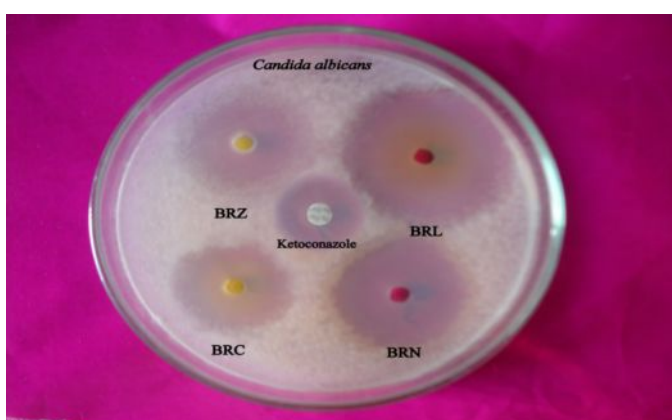


Fig.5: Antifungal activity of the synthesised compounds against *Candida albicans*



Fig.6: Antifungal activity of the synthesised compounds against *Candida kefyr*

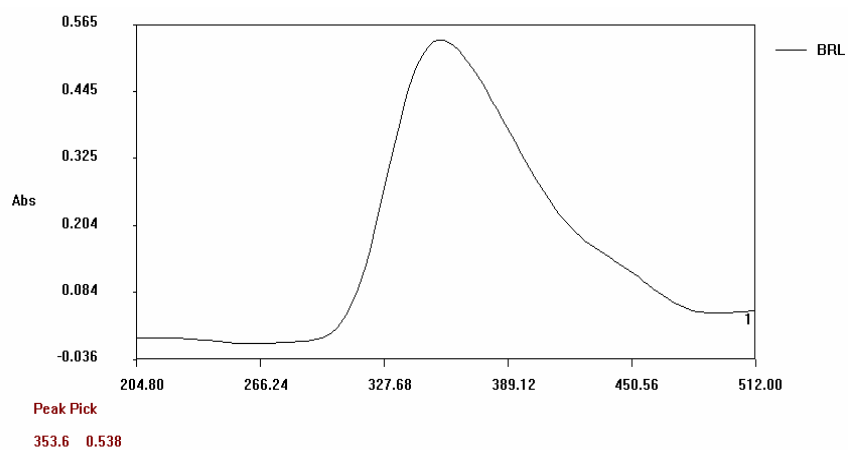


Fig.7: UV-Visible Spectrum of the Schiff base ligand [HL]

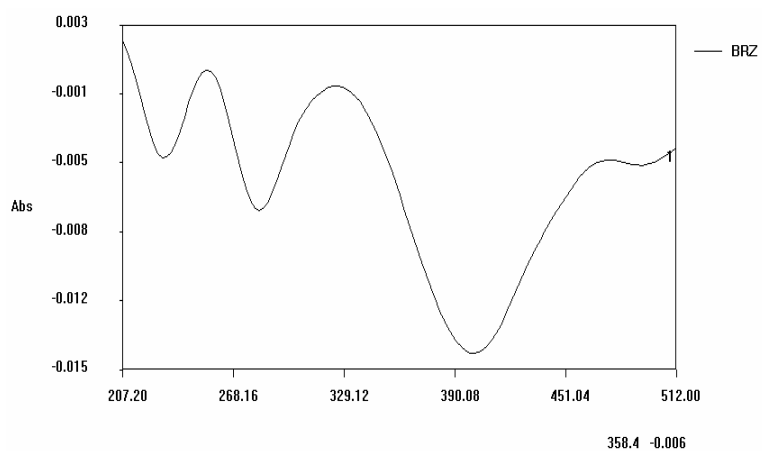


Fig.8: UV-Visible Spectrum of the Schiff base ligand [ZnL(ClO₄)]

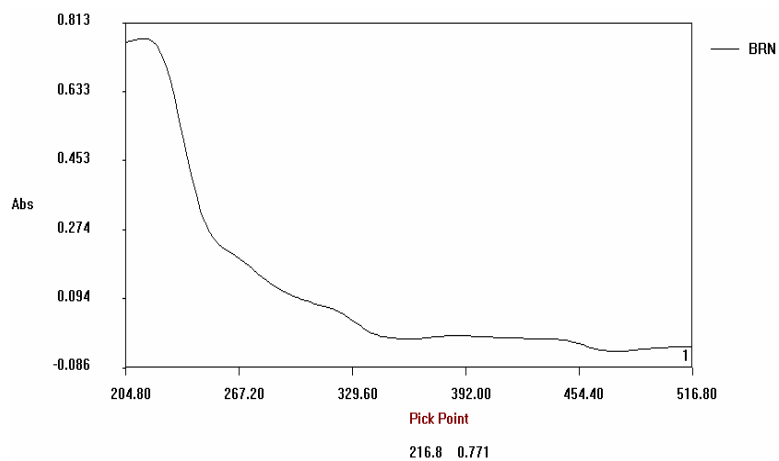


Fig.9: UV-Visible Spectrum of the Schiff base ligand [NiL(ClO₄)]

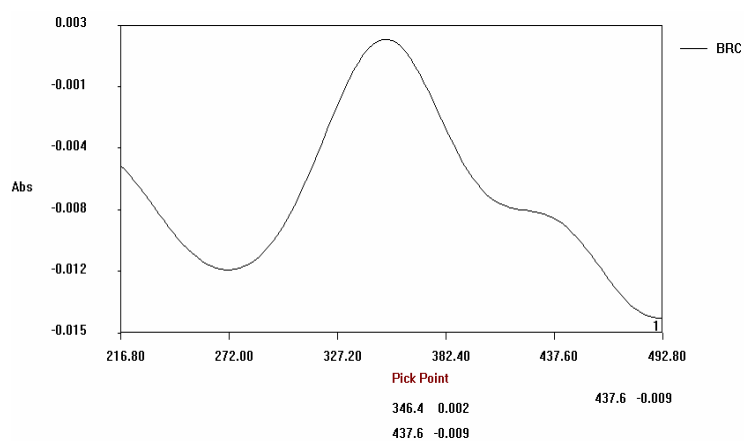


Fig.10 : UV-Visible Spectrum of the Schiff base ligand [CuL(ClO₄)]

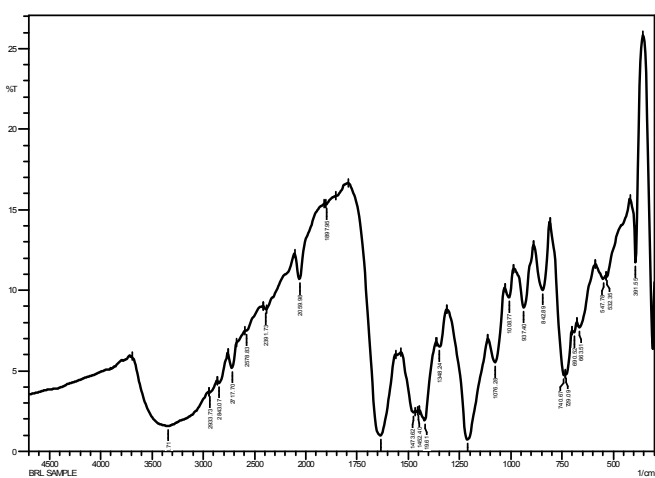


Fig.11: Infrared spectrum of the Schiff base ligand [HL]

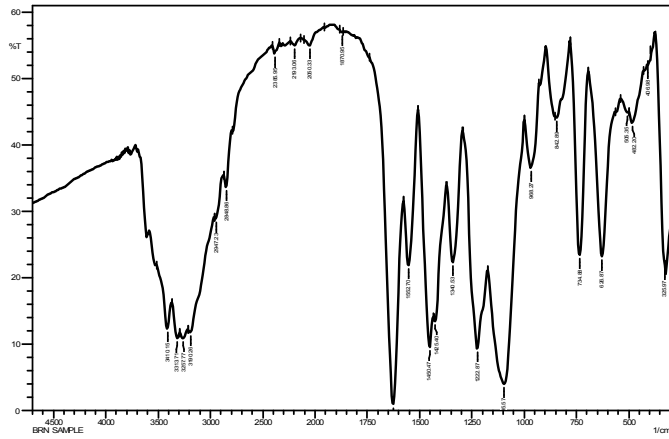


Fig.12: Infrared spectrum of the [NiL(ClO₄)]

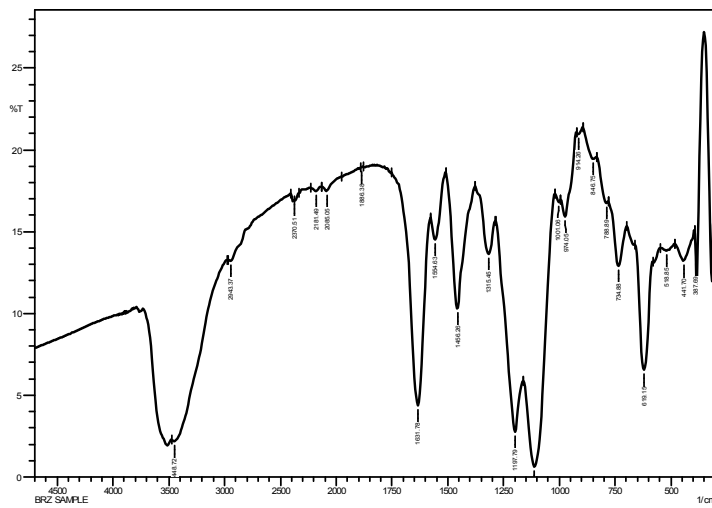


Fig.13: Infrared spectrum of the [ZnL(ClO₄)]

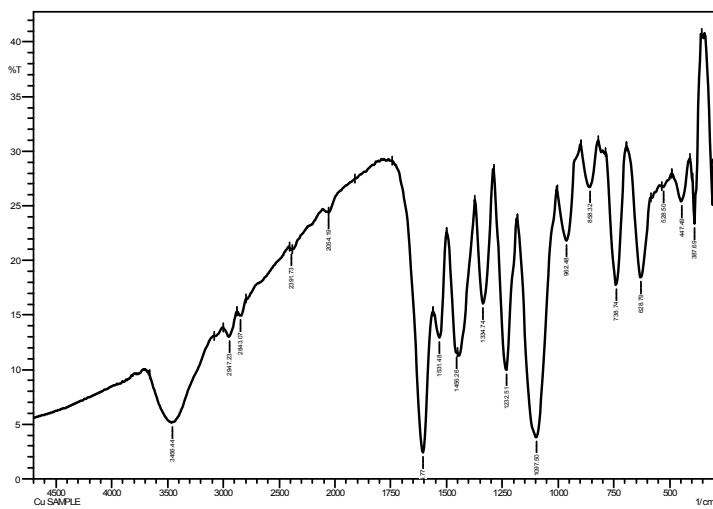


Fig.14: Infrared spectrum of the [CuL(ClO₄)]

Conclusion

The molar conductivity values of all the synthesized complexes were corresponds to non-electrolytic nature of the complexes.

The UV and IR spectral data suggest that the ligand behaves as monobasic with N₂, O donor

atoms. From the UV-Visible spectra a square planar geometry was suggested for Zn(II), Ni(II), and Cu(II) complexes. The results revealed that the synthesized compounds were more potent against all the microbes under investigation.

References

- Schiff, H. Ann. Chem. Suppl., 1864, 3, 343.
- B. T. Thankar, K.R. Surati, P. Patel, Journal of Iranian Chemical Society, 2006, Vol.3, No.4, 371-377.
- Cimerman Z ;Miljanic S; and Galic N, Croatica chemical acta, ,2000, 81-95.
- Elmali A; Kabak M and ElermanY, "J Mol Struct", 2000, 477, 151.
- Perry B F; Beezer A E; Miles R J; smith B W; Miller J and Nascimento MG, "Microbios", 1988, 45-181.
- Julija Matijerica, Marijana Vinkovic, Vikic, Croatica Chemica Acta ,2006, 79(3), 489-495.
- Singh, K.; Barwa, M.S.; Tyagi, P. Eur. J. Med. Chem , 2007, 42, 394-402.
- Santha Lakshmi S, Syed Tajudeen S and Kannapan Geetha , Journal of Pharmacy Research, , 2011, 4(5), 1531-1532.
- Syed Tajudeen S, Santha Lakshmi S and Kannapan Geetha 3(11), Journal of Pharmacy Research, , 2010, 2759-2760.
- Malaty Sony S.M, Saraboji K, Crys. Res. Technol., 2004, 39, No.2, 185-192.
- Singh, K.; Barwa, M. S.; Tyagi, P. Eur.J. Med. Chem., 2006, 41,1.
- Pannerselvam, P.; Nair, R. R.; Vijayalakshmi, G.; Subramanian, E. H.; Sridhar, S. K. Eur. J. Med. Chem., 2005, 40,225.
- Xun Fen, Z.Kristallogr., 2007, NCS 222 ,129-130.
- Jayabalakrishnan C and Natarajan K, Transition Met. Chem., 2002, 27, 75.
- Geary W J, "Co. ord Chemistry", 1971, 81-122.
- Rober K; Bogges and David A, "J. of chemical education", 1975, 649-665.
- Compolte E and Kaya M J, Co-Ord. Chemistry , 2004, 1217-1223.
- EL-ajaily, M.M.; Mainub, A.A.; Hudese, S.S.; Ben-Saber, S.M., Asian J. of chem., 2006, 18(14), 2427-2430.
- Hamil, A.M.; Khalifa, K.M.; AL-Houni,A.; and EL-ajaily, Rasayan, J.chem., 2009, 2, No.2 261-266.
- Iskanden M R; Ei – syed L and Ismail K Z, "Trans Met Chemistry", 1979, 225.
- Raman, N.; Sobha, S.; Thamarachelvan, A. Spectrochimica Acta Part A; Molecular & bio molecular Spectroscopy, 2011, 78, 888-898.
- Patwardhan H A; Gopinathan S and Gopinahan C, "Indian of Chemistry", 1978, 224.
- Percy G, "Spectrochem. Acta", 1961, 1287.
- Nakamota K; "Infrared and Raman Spectral of Inorganic Co-ordination Compounds", 3rd edn. , John Wiley, New York, 1978 .
- Thomas M; Nair M K M and Radhakrishnan R K, "Synth Rad Inorg.Chem", 1995, 25-47.
