International Journal of Current Engineering and Technology
E-ISSN 2277 – 4106, P-ISSN 2347 - 5161

Available at http://inpressco.com/category/ijcet

Research Article

Synthesis and Characterization of Transition Metal Complexes along with their Antibacterial Activities

Kalpana[Á], Randhir Singh[Ḃ], Baljinder Singh[Ċ] and AvneeshKumar[Ċ*]

[Á]Department of Applied Science, Indo Global College of Engineering, Mohali, Punjab, India
[Ḃ]Department of Chemistry,GurukulaKangriVishwavidyalaya, Haridwar,India
[Ċ]Department of Biotechnology,Panjab University, Chandigarh 160014, India

Accepted 10 May 2014, Available online 01 June2014, **Vol.4, No.3 (June 2014)**

Abstract

Macrocyclic ligands are polydentate ligands containing donor atoms either incorporated or attached to cyclic backbone and showed significance in various biological studies. Tetraaza macrocyclic complexes of transition metals, Ni(II), Cu(II), Fe(III), and Mn(II) were synthesized in methanolic media using template method. These complexes were non-hygroscopic and consist of crystalline solids. Structural identification of these complexes was done using analytical techniques UV-Vis and IR Spectroscopy. The antibacterial activities of macrocyclic complexes (1-6) were screened against both Gram-negative bacteria (Escherichia coli and Vibrio cholerae) and Gram-positive bacteria (Bacillus subtilis and Staphylococcus aureus). In the present study we have reported that these synthesized complexes showed slight antibacterial activity except macrocyclic complex (6) which showed moderate antibacterial activity.

Keywords: *transition metals, macrocyclic complexes, UV-Vis and IR Spectroscopy, antibacterial activities*

Introduction

Macrocyclic complexes have received considerable attention because of their relationship to biomimetic and catalytic systems and the applications in biology, medicine and chemical techniques [M.P. Reddy *et al*, 2012,D. E. Fenton and H. Okawa,1993] The importance of macrocyclic complexes is well recognized now days. Although, Coordination chemistry of macrocyclic complexes has been a fascinating area of current research interest to the inorganic chemists all over the world [S. Chandra *et al*, 2009]. Because of their intense colors and chemical inertness, the macrocycles are of great importance as pigments and dyeing agents [S. Karabocek*et al*, 2006; K. Shankar *et al*, 2009]. Bioinorganic chemistry is an emerging area of research. Its biological significance has given rise to the studies of macrocycles and there is new trend in the study of their complexation chemistry with a vast variety of metal ions [D. Singh et al, 2010; S. Chandra *et al*, 2006]. Intrinsic structural properties of macrocyclic complexes mimic the synthetic models of metalloporphyrins and metallocorrins [E. Kubaszewski and T. Malinski 1992, R. Vaum*et al*, 1982]. The studies to achieve peripheral substitution providing points of attachments for further structural modification opens up new vistas for synthesis of more complex compounds providing possible applications in medicine [J. Eilmes, 1985; S. A. J. Collen*et al*, 1997]. The study of these synthetic model compounds plays an important role in the understanding of biological functions of these macrocycles [S. Cunha, *et al*, 2005]. Macrocyclic complexes's versatile coordination behavior, their pharmacological properties has made it a subject of attention and extensive study [E.V. Caemelbecke*et al*, 2005; E. Kimura, 1993]. In both human being and animals, antibiotics are used as an important medicinal molecule to cure infections [D. Guillemot, 1999; T. Rosu*et al*, 2006]. In the recent studies, it has been observed that if there is a regular usage of antibiotics it results in an ever increasing therapeutic problem [R. Corrêa*et al*, 1998; G. Turhan-Zitouni,*et al*, 2001]. This can be reduced with the help of antibiotic resistance inhibitors as macrocyclic complexes. Keeping the importance of the macrocyclic complexes and their antibacterial activities, the present article has been taken into account [S. Blain *et al*, 1990].

Material and Methods

All chemicals used in this study were of AnalaR grade. Six macrocyclic complexes were synthesized and characterized.

Synthesis of macrocyclic complexes

All complexes were synthesized using template method [B.H.M. Mruthyunjayaswamy*et al*, 2005] by condensation of acetone/diacetyl in the presence of respective metals salts (Chloride, sulphate). To a methanolic solvent (=50), o-phenylenediamine/3, 5 diamino benzoic acid with acetone/diacetyl followed by

*Corresponding author: **Avneesh Kumar**

Table 1 Elemental analysis of macrocyclic complexes

Macrocyclic Complexes/(Molecular Formula)	Color	Yield (%)	Elemental Analysis							
			C%		H%		N%		M%	
			Cal	Found	Cal	Found	Cal	Found	Cal	Found
MC-I/$C_{22}H_{26}N_4NiCl_2O_8$	Purple	45	43.72	42.0	4.30	4.0	9.27	9.10	13	12
MC-II/$C_{24}H_{25}N_4CuCl_2O_{12}$	Blue	40	41.40	41.20	3.54	3.50	8.05	8.0	11.05	11
MC-III/$C_{20}H_{22}N_4$ $CuCl_2O_8$	Blue	44	41.37	40.20	3.78	3.75	9.64	9.0	9.35	9.0
MC-IV/$C_{24}H_{25}N_4FeCl_2O_4$	Green	50	52.42	51.50	4.46	4.40	10.0	9.50	10.78	10.35
MC-V/$C_{42}H_{30}N_4FeCl_2O_4$	Pale green	42	70.98	70.80	4.22	4.0	7.78	7.75	9.02	8.9
MC-VI/$C_{22}H_{21}N_4NiCl_2O_8$	Violet	40	56.96	56.0	4.52	4.5	12.07	12.02	9.70	9.30

metal salt in ratio 2:2:1 were added in round bottom flask. Shake well and refluxing was carried out for 6-8 hours. The change in colour was appeared. The round bottom flask was kept aside for its cooling. The filtration and washing were carried out by methanol and dried in vacuum. The coloured complexes were obtained and taken for further studies [F. Rafat*et al*, 2004; N. Raman *et al*, 2008].

Characterization

All the complexes were analysed for elemental data (C, H, and N), colours and yields. The UV-Vis measurements were carried out using a spectrophotometer (Systronics UV-Vis spectrophotometer 117). Infrared spectra were recorded as KBr pellets on a Nicolet NEXUS Aligent 1100 FT-IR Spectrometer, using 50 scans and were reported in cm^{-1}. For all complexes coordination of azomethine nitrogen was supported by lowering of $\nu_{C=N}$ to 7–10 cm^{-1} as compared to free ligand in IR spectra.

Biological activity

The synthesized target compounds were evaluated for their *in vitro* antibacterial activity against bacterial culture of *Escherichia coli* and *Vibrio cholerae*, *Staphylococcus aureus* and *Bacillus subtilis*. The test isolates were taken from the MTCC (Microbial Type Culture Collection) at the Institute of Microbial Technology (IMTECH), Chandigarh, India and included *Escherichia coli* and *Vibrio cholerae*, *Staphylococcus aureus* and *Bacillus subtillus.* An Agar-diffusion method was used for the determination of the preliminary antibacterial activity. In this technique,the filter paper (Whatsmann no. 1) sterile disc of 5 mm diameter impregnated with test macrocyclic complexes (10 mg/ml of DMSO) were placed in nutrient agar plate at 37 ^oC for 12 h. The inhibition zones around the dried impregnated disks were measured after 12 hrs. The The antibacterial activity was classified as highly active (>14 mm), moderately active (10-14 mm) and slightly active (6-10 mm) and less than 5 mm was taken as inactive. The minimum inhibitory concentration (MIC) of the compounds was determined using a micro broth dilution method. In the broth dilution MIC method, various concentrations of the compounds were inoculated with a standard suspension of test bacteria. Following an overnight incubation at 37 °C, the MIC was determined by observing the lowest concentration of the compounds that would inhibit visible growth of the test bacteria. Growth was determined photometrically by measuring the optical density (OD) at 600 nm.

$$\text{Percentage of growth} = \frac{\text{OD of organism grown with sample}}{\text{OD of control}}$$

Results and Discussion

The present studies described the six macrocyclic complexes (I-VI) of different metals synthesis and their antibacterial activities. These complexes were crystalline solids and non-hygroscopic. The formulae for these macrocyclic complexes were assigned on the basis of analytical data (Table 1) and enable us to predict the possible structure of the synthesized complexes.

Table 2 UV-Vis Spectral data of Macrocyclic complexes (nm)

Molecular Formula	λmax (nm)
$C_{22}H_{26}N_4NiCl_2O_8$	548.4
$C_{24}H_{25}N_4CuCl_2O_{12}$	402
$C_{20}H_{22}N_4$ $CuCl_2O_8$	374
$C_{24}H_{25}N_4FeCl_2O_4$	520
$C_{42}H_{30}N_4FeCl_2O_4$	425
$C_{22}H_{21}N_4NiCl_2O_8$	389

Electronic absorption spectral data of the complexes in dimethyl sulfoxide (DMSO) at room temperature are presented in table 2. The electronic spectra of complexes in DMSO show bands in the visible–ultraviolet region. The absorption bands below 400 nm are practically identical and can be attributed to π-π* transitions in the azomethine (-C=N) group. The Ni(II) complexes possess square-planar geometry and Cu(II) complexes possess show octahedral geometry around the central metal ions [S. Chandra and L.K. Gupta 2004; S. Chandra and S.D. Sharma 2002]. The absorption bands observed within 350-550 nm range are most probably due to the transitions of n- π* of imine group [E. Konig, 1971]. The electronic spectra of the Ni(II) and complexes show an absorption band at 380-550 nm attributed to the $2Eg \rightarrow 2T_2g$ transition, characteristic for tetragonally elongated octahedral or square planar geometry [B.N. Figgis and M.A. Hitchman, 2000; A.A.A. Emara and M.I.A. Omima, 2007]. The electronic absorption bands of the presented Ni(II) and Co(II) complexes in the visible region exhibit solvent dependence behavior. The observed red shifts in

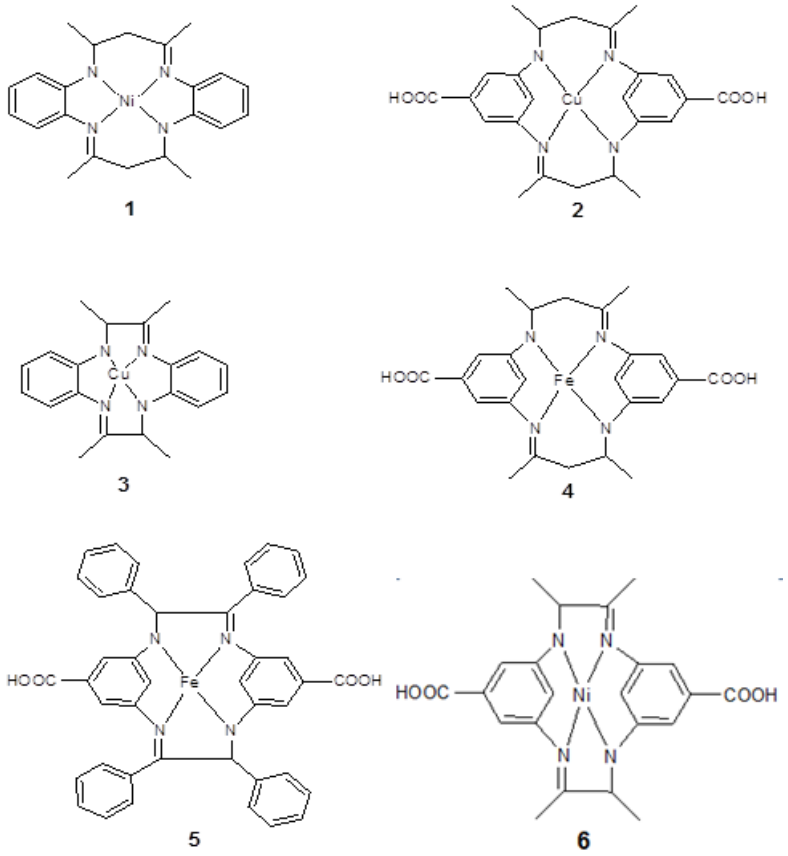

Figure 1: Proposed Structures of Dicataionic form of Macrocyclic Complexes, where 1-6 are macrocyclic complexes I-VI.

the low energy d-d band of Ni(II) and Co(II) complexes in DMSO can be interpreted in terms of weak ligand field strength [C. Preti and G.Tosi,1976].

Infrared spectra were recorded as KBr pellets on a Nicolet NEXUS Aligent 1100 FT-IR Spectrometer, using 50 scans and were reported in cm^{-1}. For all complexes coordination of azomethine nitrogen was supported by lowering of $\nu_{C=N}$ to 7–10 cm^{-1} as compared to free ligand in IR spectra. Results of IR-spectroscopy were summarized in table 3.

Table 3 Infrared Spectral data of Macrocyclic complexes (cm^{-1})

S.No.	Macrocyclic Complexes	ν (NH)	ν (ClO_4)
1	$C_{22}H_{26}N_4NiCl_2O_8$	3240s	1097(s,b) 623m
2	$C_{24}H_{25}N_4CuCl_2O_{12}$	3220s	1092(s,b) 620m
3	$C_{20}H_{22}N_4\ CuCl_2O_8$	3210m	1090(s,b) 618m
4	$C_{24}H_{25}N_4FeCl_2O_4$	3200s	1100(vs,b) 620s
5	$C_{42}H_{30}N_4FeCl_2O_4$	3210s	1100(vs,b) 620s
6	$C_{22}H_{21}N_4NiCl_2O_8$	3230s	1080(vs,b) 620s

Where s=strong, vs =very strong, b=broad, m= medium
Complex I showed IR bands near 1097 cm^{-1} together with a band at 623 cm^{-1} suggesting the presence of non-coordinated perchlorate ion. Complex II showed IR bands near 1092 cm^{-1} together with a band at 620 cm^{-1} indicated the presence of non-coordinated perchlorate ion, complex III showed IR bands near 1090 cm^{-1} together with a band at 618 cm^{-1} suggesting the presence of non-coordinated perchlorate ion. Complex IV showed IR very strong bands near 1100 cm^{-1} together with a band at 620 cm^{-1} suggesting the presence of non-coordinated perchlorate ion (Table 3). Complex V showed IR very strong bands near 1100 cm^{-1} and another band at 620 cm^{-1} suggesting the presence of non-coordinated perchlorate ion. Complex VI showed IR bands near 1080 cm^{-1} together with a band at 620 cm^{-1} suggesting the presence of non-coordinated perchlorate ion. The proposed macrocyclic complexes are **(1)** 1,4,8,11 dibenzotetraaza-tetradeca 7,14-Diene Ni(II) Macrocyclic complex, **(2)** 1,5,9,13-tetraaza dibenzoichexadeca 8,16 Cu(II) Macrocyclic complex, **(3)** 1,4,7,10-tetraaza dibenzododeca 6,12 diene Cu(II) Macrocyclic complex, **(4)** 1,5,9,13-tetraaza dibenzoichexadeca 8,16 diene Fe(III) Macrocyclic complex, **(5)** 1,5,8,12 tetraazadibenzoic 6,7,13,14 tetra benzo 7,14-duene Fe(III) Macrocyclic complex, **(6)** 1,5,8,12 tetraaza dibenzoic 6,7,13,14 tetramethyl tetradeca 7,14-diene Ni(II) Macrocyclic complex and figure 1 showed corresponding molecular structures.

Antibacterial activity

The antibacterial activity of macrocyclic complexes against pathogens at concentration 10mg/ml are given in table 4. The macrocyclic complexes (I-VI) showed a slight activity against all the four selected bacterial culture.

However, it was found that the macrocyclic complex-VI with Ni complex (at conc. 10 mg/mL) revealed a better activity (moderate activity) against all the four bacterial cultures. The antibacterial activity of complexes were observed in increasing order macrocyclic complex VI >macrocyclic complex V >macrocyclic complex III >macrocyclic complex IV >macrocyclic complex I >macrocyclic complex II. Antibacterial activity of the metal chelates can be explained on the basis of chelation theory[S. Chandra *et al*, 2011]. The results obtained clearly indicated that among the series of metal chelates, macrocyclic complex-VI was moderate active towards growth inhibition of Gram-negative and Gram-positive bacteria under this investigation. This might be due to delocalization of π-electrons which show broad biological activity [M.R. Ahmed *et al*, 2013] and is of special interest as the chelation tends to make the ligand more potent bacterial agent [K. Shankar *et al*, 2009].

Table 4 Antibacterial activity of Macrocyclic complexes (conc. 10 mg/mL)

Macrocyclic Complex	***E. coli***	***Bacillus subtillus***	***Staphylococcus aureus***	***Vibrio choleraei***
1	10	10	10	9
2	10	9	9	9
3	11	10	9	10
4	11	9	8	10
5	10	10	10	9
6	13	12	10	11
Ampicillin (10 µg/mL)	52	52	45	43

MIC50 (defined as the minimum concentration at which 50% of the isolates were inhibited) of macrocycliccomplexe-VI against *E. Coli* and *Vibrio cholera* were 4 mg/mL. MIC90 (defined as the minimum concentration at which 90% of the isolates were inhibited) were 17 mg/mL and 16 mg/mL respectively. MIC50 of macrocyclic complex-VI against *Staphylococcus aureus*and *Bacillus subtillus* were 4.5 mg/mL and 4.7 mg/mL, while MIC90 were 17.7 mg/mL and 18.2 mg/mL respectively.

Conclusion

The above study is a former evaluation of antibacterial activity of macrocyclic complexes. It also shows that the complexes have the capability to generate new antimicrobial metabolites. The discovery of new chemical classes of antibiotics is the result of macrocyclic complexes demonstrating antibacterial activity; which in future can be used as selective agent for maintaining human or animal health & also provides biochemical tools for the study of infectious disease.

Acknowledgement

Authors are very thankful to Dr. Pramod Kumar, Department of Chemistry, University of Delhi, Delhi for his guidance blended with invaluable suggestions and help for synthesis and characterization of macrocyclic complexes. Authors are also thankful to Dr. Baljinder Singh, Department of Biotechnology, Panjab University, Chandigarh, for providing bacterial strains for the research.

References

M.P. Reddy, R. Rondla, R.K. Edulla, H. Anren, R. Vadde, (2012). Synthesis, spectral and antibacterial studies of Copper(II) tetraazamacrocyclic complexes, *International Journal of Molecular Sciences*., **13** (4), 4982-4992.

D.E. Fenton, H. Okawa, (1993). Metal ion controlled synthesis of 16 and 18 membered by nuclear octaazamacrocyclic complexes with Co(II), Ni (II),Cu(II) and Zn(II): A comparative spectroscopic approach to DNA binding to Cu(II) complexes, *Perspectives on Bioinorganic Chemistry, JAI Press: London*, **8**.

S. Chandra, D. Jain, A. Kumar, P. Sharma, (2009). Coordination Modes of a Schiff Base Pentadentate Derivative of 4-Aminoantiphyrine with Co(II),Ni(II) and Cu(II) Metal ions : Synthesis, Spectroscopic and Antimicrobial Studies, *Molecules*, 2009, **14**, 174-190.

S. Karabocek, N. Karabocek, A. Armutcu, (2006). Synthesis and structural studies of 2-(hydroxyimino)-1-methylpropylideneamino-phennyiminobutan-2-one oxime, ligand and its complexes with Cu^{II} and Ni^{II}, *Transition Metal Chemistry*, **31**, 459-464.

K. Shankar, M. Ashok, P.M. Reddy, R. Rohini, V. Ravinder, (2009). Spectroscopic characterization and antibacterial activities of Mn(III) complexes containing the tetradentateaza Schiff base ligands, *International Journal of ChemTech Research*, **1**, 777-783.

D. Singh, K. Kumar, R. Kumar, J. Singh, (2010). Template synthesis and characterization of biologically active transition metal complexes comprising 14-membered tetraazamacrocyclic ligand, *Journal of the Serbian Chemical Society*, **75(2)**, 217-228.

S. Chandra, R. Gupta, N. Gupta, S.S. Bawa, (2006). Biologically relevant macrocyclic complexes of Copper.Spectral, Magnetic, Thermal and antibacterial Approach, *Transition Metal Chemistry*, **31**, 147.

E. Kubaszewski, T. Malinski, (1992). 5,7,12,14-Tetramethyldimethoxybenzo [6,1][1,4,8,11] tetraazacyclodecane, a new tumoricidal pseudo-porphyrin, *Journal of hetrocyclic Chemistry*, **29 (6)**, 1417-1422.

R. Vaum, N.D. Heindel, H.D. Burns, J. Emrich, (1982). Synthesis and evaluation of Fe(III) In-labeled porphyrin for lymph no deimaging, *Journal of Pharmaceutical Science*, 1982, **71**, 1223-1226.

J. Eilmes, (1985). Benzoylation of macrocyclic Ni (II) complex efficiently and year demetalation of Y-Y' -dibenzoylated products, *Polyhedron*, 1985, 4 (**6)**, 943-946.

S.A.J. Collen, F.M. Everaerts, F.A. Huf, (1997). Characterization of ^{60}Co Y-Radiation Induced Radical Products of Antipyrin by Means of HPLC, Mass Spectrometry, Capillary zone, Electrophoresis, Miceller Electro kinetic Capillary Chromatography and NMR Spectrometery, *Journal of Chromatography A*, 1997, **788**, 95-103.

S. Cunha, S.M. Oliveira, Jr M.T. Rodrigues, R.M. Bastos, J. Ferrari, C.M.A. De Oliveira, L. Kato, H.B. Napolitano, I. Vencato, C. Lariucci, (2005). Structural Studies of 4-Aminoantipyrine Derivatives, *Journal of Molecular Structure*, **752**, 32-39.

E.V. Caemelbecke, A. Derbin, P. Hambright, R. Garcia, A. Doukkali, A.O.K. Saoiabi, S. Fukuzumi, K.M. Kadish, (2005).

Electrochemistry of $[(TMpyP)M^{II}]^{4+}(X^-)_4$ (X^-=Cl^- or BPh_4) in N,N-Dimethylformamide Where M is one of 15 different Metal ions, *Inorganic Chemistry*, **44**, 3789-3798.

E. Kimura, (1993). Roles of Zn (II) in Zinc enzymes, *Pure Applied Chemistry*, **65**, 355.

D. Guillemot, (1999). Antibiotic use in humans and bacterial resistance, *Current Opinion in Microbiology*,**2**, 494-498.

T. Rosu, S. Pasculescu, V. Lazar, C. Chifiriuc, R. Cernat, (2006). Cu(II) Complexes with ligands Derived from 4-Amino-2,3-dimethyl-1-phenyl-3-pyrazoline-5-one, *Molecules*, **11**, 904-914.

R. Corrêa, Z. Vaz, J.B. Calixto, R.J. Nunes, T.R. Pinheiro, A.D. Andricopulo, R.A. Yunes, (1998). Further studies on analgesic activity of cyclic imides. *II Farmaco*, **53**(1), 55-57.

G. Turhan-Zitouni, M. Sivaci, F.S. Kilic, K. Erol, (2001). Synthesis of Some Triazolyl-antipyrine Derivatives and Investigation of Analgisic Activity, *Europian Journal Medicinal Chemistry*, **36**, 685-689.

S. Blain, P. Appriou, H. Chaumeil, H. Handel, (1990). Application of a tetraazamacrocycle immobilized on an organic polymer to the determination of trace amounts of Mn in sea water, *Analytical Chemistry Acta*, **232**, 331.

B.H.M. Mruthyunjayaswamy, O.B. Ijare, Y. Jadegoud, (2005) Synthesis, Characterization and Biological Activity of Symmetric Dinuclear Complexes Derived from a Novel Macrocyclic Compartmental Ligand, *Journal of Brazilian Chemical Society*, **16**,783-789.

F. Rafat, M.Y. Siddiqi, K.S. Siddiqi, (2004). Synthesis and Characterization of Ni(II),Cu(II) and Co(III) complexes with polyamine-containing macrocycle bearing an aminoethyl pendant arm, *Journal of Serbian Chemical Society*, **69**, 641-649.

N. Raman, J.D. Raja, A. Sakthivel, (2008). Template Synthesis of novel 14- membered tetraazamacrocyclic transition metal complexes: DNA cleavage and antimicrobial studies, *Journal of the Chilean Chemical Society*,**53** (3), 1568-1571.

S. Chandra and L.K. Gupta, (2004). Spectroscopic characterization of tetradentatemacrocyclic ligand: it's transition metal complexes, *SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy*, **60** (12), 2767-2774.

S. Chandra and S.D. Sharma, (2002). Template synthesis of copper (II) complexes of two twelve-membered tetradentate nitrogen donor macrocyclic ligands, *Journal of the Indian Chemical Society*, **79** (6), 495-497.

E. Konig, (1971). Structure and bonding, *Springer: Berlin*, 9, 175.

B.N. Figgis and M.A. Hitchman, (2000). Ligand field theory and its applications.Vol. 158.*Wiley-Vch: New York*.

.A.A. Emara and M.I.A. Omima, (2007). Synthesis and spectroscopic studies of new binuclear transition metal complexes of Schiff bases derived from 4, 6-diacetylresorcinol, *Transition Metal Chemistry*, **32**(7), 889-901.

C. Preti, and G. Tosi, (1976). Coordination Compounds of Mn (II) with Tetrahydro-1, 4-thiazin-3-one and Thiazolidine-2-thione, *Australian Journal of Chemistry*,**20**, 543-546.

S. Chandra, M. Tyagi and S. Agarwal, (2011). Spectral and antimicrobial studies on tetraazamacrocyclic complexes of Pd^{II}, Pt^{II}, Rh^{III} and Ir^{III} metal ions, *Journal of Saudi Chemical Society*, **15**(1), 49-54.

M.R. Ahmed, I.E. Yousif, A.H. Hasan, and J.M. Al-Jeboori, (2013). Metal complexes of macrocyclic Schiff base ligands; Preparation,characterization and biological activity, *The Scientific world Journal*, **2013**, Article ID 289805.

K. Shankar, R. Rohini, V. Ravinder, P.M. Reddy and Y.P. Ho, (2009). Ru(II) complexes of N_4 and N_2O_2macrocyclic Schiff base ligands: their antibacterial and antifungal studies, *SpectrochimicaActa Part A: Molecular and BiomolecularSpectroscopy*, **73**(1), 205-211.