

Synthesis, characterization of Schiff base Cr(III), Fe(III) and Mn(III) macrocyclic complexes derived from oxalamide and 3,4-diphenyl-3H-pyrrole-2,5-dicarbaldehyde Schiff Base Ligand



Preeti Sharma

Research Scholar,
Department of Chemistry,
Bhagwant University,
Ajmer, Rajasthan, India



Gajendra Kumar

Associate Professor &
Corresponding Author,
Deptt. of Chemistry,
Bhagwant University,
Ajmer, Rajasthan, India

Abstract

M(III) Schiff base macrocyclic complexes of the type $[HLMX_2]$ where $M = Cr(III), Fe(III), Mn(III)$ and $X = Cl, NO_3, OAc$ have been synthesized by condensation of oxalamide and 3,4-diphenyl-3H-pyrrole-2,5-dicarbaldehyde (2:2) in the presence of divalent metal salt in methanolic medium. The complexes have been characterized with the help of elemental analysis, conductance measurements, magnetic measurements and their structural configuration have been determined by various spectroscopic (electronic, IR, 1H NMR, ^{13}C NMR, GCMS) techniques. Electronic and magnetic moments of the complexes indicate that the geometries of the metal centers are octahedral. These metal complexes were also screened for their antifungal activities against some fungi viz. *Rizoctonia sp.*, *Aspergillus sp.*, and *penicillium sp.* to assess their inhibiting potential.

Keywords: Metal complexes, Antifungal activity, Spectroscopic study, ethanebis (thioamide) and 3,4-diphenyl-3H-pyrrole-2,5-dicarbaldehyde..

Introduction

Co-ordination chemistry is considered as an additional branch of chemistry for the purpose of study and research. New possibilities have arisen in practice and research due to advancement of structure elucidation techniques like IR, UV, NMR, EPR, X-ray mass spectroscopy, the magnetic susceptibility measurements and the development of ligand field theory and application of the group theory to co-ordination chemistry. Schiff bases are typically formed by the condensation of a primary amine and an aldehyde/ketone. In which $>C=O$ group is replaced by $>C=N-R$ group. The resultant compound, $R_1R_2C=NR_3$, is called a Schiff base (named after Hugo Schiff) where R_1 is an aryl group, R_2 is hydrogen atom and R_3 is either an alkyl or aryl group. However usually compounds where R_3 is an alkyl or aryl group and R_2 is an alkyl or aromatic group are also regarded as Schiff bases. Schiff bases that contain aryl substituent are substantially more stable and more readily synthesized, while those which contain alkyl substituent are relatively unstable Schiff bases of aliphatic aldehydes are relatively unstable and readily polymerizable [1]. While those of aromatic aldehydes having effective conjugation are more stable. [2]. Schiff bases are most widely used as chelating ligand in coordination chemistry. Schiff bases are bidentate (1), tridentate (2), tetradentate (3) or polydentate (4) ligands generally capable of forming very stable complexes with transition metals. They can only act as co-coordinating ligands if they bear a functional group, usually the hydroxyl sufficiently near the site of condensation in such a way that a five or six membered ring can be formed when reacting with a metal ion.

Review of Literature

Schiff bases are used, in many field e.g., inorganic, biological, and analytical chemistry [3-4], optical and electro-chemical sensor, as well as in various chromatographic methods, to enable detection of enhanced selectivity and sensitivity [5]. Among the organic reagent actually used Schiff bases, possess excellent characteristics, structural similarities with natural biological substances relatively simple preparation procedures and

the synthetic flexibility that enables design of suitable structural properties. Complexes are a special class of compounds in which the central metal atom is surrounded by ions or molecules (called ligand) beyond their normal valency. In the modern terminology these compounds are called co-ordination compounds. Schiff bases and their structural analogues as ligating compounds containing acyclic and cyclic imine C=N bonds are of great importance in modern coordination chemistry [6]. The formation of complexes causes the d-orbitals to split into two energy sublevels, which enables many of the complexes to absorb specific frequencies of light. Thus the complexes form characteristic colored solution and compounds. Complication reactions some time enhance the relatively low solubility of some compound. So we can say that the transition metal has low ionization energies, positive oxidation states, very hard, high melting points, high boiling points, and high electrical conductivity, malleable. 5-d orbital's become more filled, from left to right on periodic table [7]. Heterocyclic compounds are widely distributed in nature and essential to many biochemical processes [8-10]. The compounds containing heterocyclic have important physiological properties ranging from anti-histamine, analgesic, anti-inflammatory, anti-hypertensive and anti-cancer. Such compounds are also used to model important bio-inorganic systems such as metalloproteinase and are finding applications as photosensitizers and catalysts [11, 12]. From the early days, the physiological properties of heterocyclic piperazines have generated interest since they are found to exert, even in small dosages, various physiological effects, including accelerated pulse, breathing and hypersensitivity to external stimuli.

The relationship between metal ions and biological activity [13] of certain systems is obvious and a subject of great interest. It has been

demonstrated through several studies that biologically inactive compounds become active and less biologically active compounds become more active [14-16] upon coordination / chelation with the some transition metal ions. The interaction between metal ions and such biologically active ligands represents an important route in designing new metal-based antibacterial and antifungal therapies against different kinds of bacteria and fungi, viruses that becomes resistant to the use of conventional drugs [17].

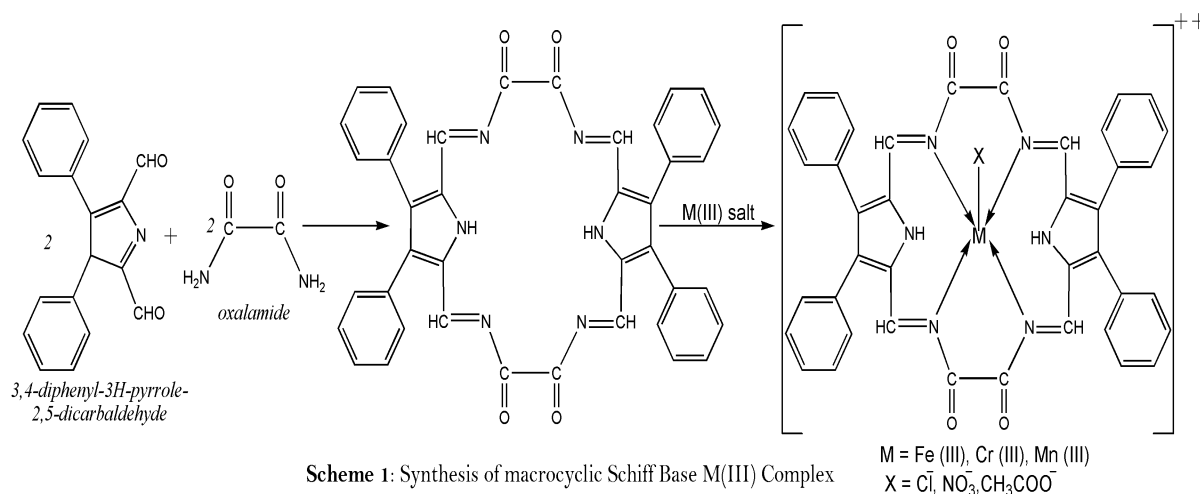
Many biologically important Schiff bases have been reported in the literature possessing antimicrobial, antibacterial, antifungal, anti-inflammatory, anticonvulsant, antitumor and anti HIV activities [18-20]. Cr (III) complexes with Schiff base ligands are potential antitumor agents. We, therefore, thought it will be worthwhile to synthesize novel metal complexes with ligands like Schiff base and their biological study that could fight more aggressively against fungal strains.

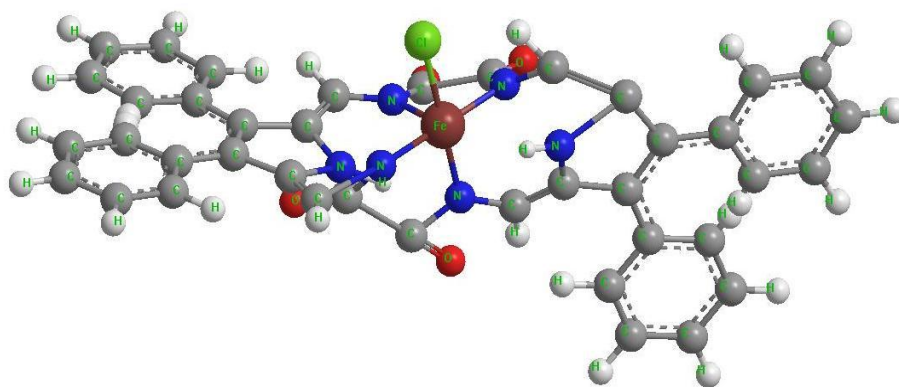
Experimental Reagents

The entire chemicals were used of the analytical grade, ethanebis(thioamide) and 3,4-diphenyl-3H-pyrrole-2,5-dicarbaldehyde purchased from S.D.-fine. Metal salts, HCl, CaCl₂, and C₂H₅OH were purchased from Merck.

Synthesis of Fe(III), Cr(III) and Mn(III) macrocyclic complexes

The macrocyclic Schiff base ligand have been synthesized by refluxing the reaction mixture of oxalamide (2 mmol) in ethanol (30 mL), 3,4-diphenyl-3H-pyrrole-2,5-dicarbaldehyde (2 mmol) in ethanol (20 mL) and a solution of divalent metal salt (1 mmol) in methanol (20 mL) was refluxed for 8-10h. The complex were filtered, washed with water and recrystallised from ethanol and dried under vacuum over anhydrous CaCl₂ (yield 40-45%, scheme 1).



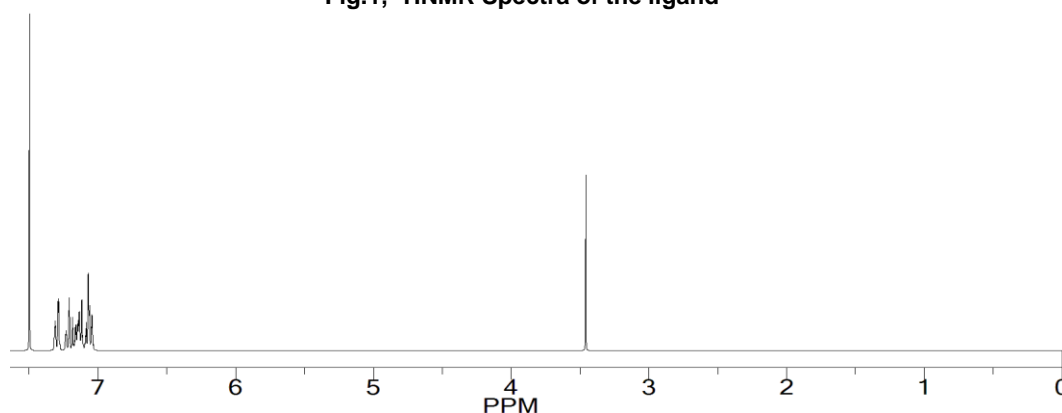


Analytical and physical measurements

The microanalysis of C, H, and N were estimated by elemental analyzer (Perkin Elmer 2400), at SAIF, CDRI, Lucknow, India and the metal contents of Cr (III), Fe (III) and Mn (III) was determined using atomic absorption spectrophotometer Perkin Elmer 5000. The conductivity was measured on digital conductivity meter (HPG system, G-3001) in DMSO at room temperature. The magnetic susceptibility measurements were carried out on Vibrating Sample Magnetometer (Model PAR 155) at room temperature. Electronic spectra (in DMSO) were recorded on a Hitachi 330 spectrophotometer ($5815\text{--}32573\text{ cm}^{-1}$). The IR spectra were performed using a FT-IR spectrophotometer Perkin Elmer 1650 in the range

$4000\text{--}200\text{ cm}^{-1}$ using Nujol Mull. ^1H NMR and ^{13}C NMR spectra (at room temperature) (in DMSO- d_6) were recorded on a Bruker AVANCE II 300 DRX or average 400 DRX spectrometer with reference to Me_4Si (0.0 ppm). The FAB mass spectra (at room temperature) were recorded on VG-70-S mass spectrometer. The purity of the Schiff base and its M(II) complexes were confirmed also by TLC [microcrystalline cellulose (E. Merck) was used for the preparation of thin layer, complete separation was achieved with the solvent system acetone/conc. HCl/water (86:8:7). R_F values increase in the following order of M(II) complexes: Cu, Ni, Co (0.52, 0.42, 0.18)].

Fig.1, ^1H NMR Spectra of the ligand



Biological activity

Antifungal activity. The free ligand, its metal complexes, fungicide Micronazole and the control DMSO (dimethylsulfoxide) were screened for their antifungal activity against various fungi viz. *Rizoctonia sp.*, *Aspergillus sp.*, and *penicillium sp.* These species were isolated for the infected organs of the host plants on potato dextrose agar (potato 250g+dextrose 20g+agar 20g) medium. The culture of the fungi was purified by single spore isolation technique. The solution of different concentrations $10\text{ }\mu\text{g/ml}$ of each compound (free ligand, its metal complexes and fungicides Miconazole) in DMSO was prepared for testing against spore germination [20, 21]. A drop of the solution of each concentration was kept separately on glass slides. The conidia, fungal reproducing spores (approx. 200) lifted with the help of an inoculating needle, which was mixed in every

drop of each compound separately. Each treatment was replicated thrice and a parallel DMSO solvent control set was also run concurrently on separate glass slide. All the slides were incubated in humid chambers at 25°C for 24 h. Each slide was observed under the microscope for spore germination and percent germination was finally calculated. The results were compared with a standard fungicide Micronazole at the same concentrations.

Result and Discussion.

^1H NMR

A survey of literature reveals that the NMR spectroscopy has been proved useful in establishing the structure and nature of many Schiff base ligand and their complexes. The ^1H NMR spectra of Schiff base ligand (Fig. 1) was recorded in d_6 -dimethylsulfoxide (DMSO- d_6) solution using Me_4Si (TMS) as internal standard. The ^1H NMR spectra of

the ligand shows multiplets in the region 7.12-7.56 ppm may be assigned to aromatic proton [22, 23].

^{13}C NMR of the Schiff base ligand, the signal appeared in the region 113-158 are assigned to

aromatic carbon. The signal at 198.3-185.6 and 182.8-171.2, are due to C=S and C=N respectively

Table 1. Analytical data of the trivalent Fe(III), N(III) and Co(III) complexes

Complex	Mol. wt	C	H	N	M	Colour	Yield	Conductance Λ_M
$\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4$	654.20	73.38 (73.36)	4.00 (3.98)	12.84 (12.82)				
$[\text{Fe}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)\text{Cl}]\text{Cl}_2$	816.87	58.81 (58.77)	3.21 (3.19)	10.29 (10.27)	6.84 (6.82)	Orange	58%	$135 \Omega^{-1}$
$[\text{Fe}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)\text{NO}_3](\text{NO}_3)_2$	800.53	60.01 (60.00)	3.27 (3.26)	15.75 (10.27)	6.98 (6.96)	Orange	62%	$133 \Omega^{-1}$
$[\text{Fe}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)(\text{OAc})](\text{OAc})_2$	887.64	62.24 (62.22)	3.97 (3.95)	9.47 (9.45)	6.29 (6.25)	Light Yellow	60%	$135 \Omega^{-1}$
$[\text{Cr}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)\text{Cl}]\text{Cl}_2$	813.02	59.09 (59.07)	3.22 (3.19)	10.34 (10.32)	6.40 (6.38)	Brown	65%	$140 \Omega^{-1}$
$[\text{Cr}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)\text{NO}_3](\text{NO}_3)_2$	796.68	60.30 (60.27)	3.29 (3.26)	15.82 (15.80)	6.53 (6.50)	Gray	67%	$152 \Omega^{-1}$
$[\text{Cr}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)(\text{OAc})](\text{OAc})_2$	833.80	62.51 (62.48)	3.99 (3.97)	9.51 (9.48)	5.88 (5.86)	Light gray	62%	$139 \Omega^{-1}$
$[\text{Mn}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)\text{Cl}]\text{Cl}_2$	815.96	58.88 (58.86)	3.21 (3.19)	10.30 (10.28)	6.73 (6.70)	Light Yellow	60%	$125 \Omega^{-1}$
$[\text{Mn}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)\text{NO}_3](\text{NO}_3)_2$	799.62	60.08 (60.06)	3.28 (3.26)	15.76 (15.75)	6.87 (6.85)	Reddish	64%	$147 \Omega^{-1}$
$[\text{Mn}(\text{C}_{40}\text{H}_{26}\text{N}_6\text{O}_4)(\text{OAc})](\text{OAc})_2$	886.74	62.31 (62.28)	3.98 (3.96)	9.48 (9.44)	6.20 (6.18)	Light Yellow	66%	$148 \Omega^{-1}$

Infrared Spectra

The IR spectra provide valuable information regarding the nature of functional group attached to the metal atom. The presence of a single medium band in the region $3250\text{--}3330 \text{ cm}^{-1}$ in the complexes may be assigned to N-H stretch [24]. It was noted that a pair of bands corresponding to $\nu(\text{NH}_2)$ at 3245 cm^{-1} and 3309 cm^{-1} are present in the spectra of the thiocarbohydrazide. The value of $\nu(\text{C}=\text{N})$ stretching vibration is found lower ($1520\text{--}1560 \text{ cm}^{-1}$) than the expected value ($1580\text{--}1650 \text{ cm}^{-1}$). This lower value of $\nu(\text{C}=\text{N})$ stretching may be explained on the basis of a drift of lone pair density of azomethine nitrogen towards the metal atom [25] indicating that coordination takes place through nitrogen of (C=N) groups. The bands present in the range $3020\text{--}3040 \text{ cm}^{-1}$ may be assigned due to (C-H) stretching vibrations of benzil and naphthalene ring [26]. The C-N stretch in the range $1000\text{--}1300 \text{ cm}^{-1}$. The band near 780 cm^{-1} in thiocarbohydrazide may be assigned as being due to free $\nu(\text{C}=\text{S})$. The band at $3292\text{--}3438 \text{ cm}^{-1}$ is due to the presence of OH group in the complexes. This band is also present in the spectra of all the complexes, which indicate that sulphur is not coordinating to the metal atom [27]. The far infrared spectra show bands in the region $420\text{--}450 \text{ cm}^{-1}$ corresponding to $\nu(\text{M-N})$ vibrations [28]. The presence of bands in all complexes in the region $420\text{--}450 \text{ cm}^{-1}$ originates from the (M-N) azomethine vibrational modes and identifies coordination of azomethine nitrogen [29]. The bands present at $290\text{--}310 \text{ cm}^{-1}$ may be assigned due to $\nu(\text{M-Cl})$ vibrations [30].

The appearance of two characteristic bands in the ranges $1561\text{--}1559 \text{ cm}^{-1}$ and $1370\text{--}1367 \text{ cm}^{-1}$ in the case of complexes was attributed to $\nu_{\text{asym}}(\text{COO}^-)$ and $\nu_{\text{sym}}(\text{COO}^-)$, respectively, indicating the participation

of the carboxylate oxygen in the complexes formation. The mode of coordination of carboxylate group has often been deduced from the magnitude of the observed separation between the $\nu_{\text{asym}}(\text{COO}^-)$ and $\nu_{\text{sym}}(\text{COO}^-)$. The separation value, $\Delta\nu(\text{COO}^-)$, between $\nu_{\text{asym}}(\text{COO}^-)$ and $\nu_{\text{sym}}(\text{COO}^-)$, in these complexes were more than 190 cm^{-1} ($191\text{--}193 \text{ cm}^{-1}$) [22].

Magnetic measurements and electronic spectral studies

The electronic spectra of Cr (III) complexes showed absorption band in the region $8950\text{--}9310$, $13150\text{--}13520$, $17550\text{--}18450$ and $27380\text{--}27780 \text{ cm}^{-1}$ attributed to ${}^4\text{B}_{1g} \rightarrow {}^4\text{E}_{1g}$, ${}^4\text{B}_{1g} \rightarrow {}^4\text{B}_{2g}$, ${}^4\text{B}_{1g} \rightarrow {}^4\text{A}_{2g}$ and ${}^4\text{B}_{1g} \rightarrow {}^4\text{E}_g$. The spectral bands are consistent with that of five coordinated Cr (III) complexes [31]. On the bases of spectral studies of these complexes, a five coordinated square pyramidal geometry and C_{4v} symmetry may be assigned for these complexes [32,33]. The magnetic moment value for this complex was found to be 3.68-4.93 B.M. at room temperature which is close to the predicted values for three unpaired electrons in the metal ions [34].

The absorption spectral bands of manganese (III) complexes showed three spin allowed transitions: ${}^5\text{B}_{1g} \rightarrow {}^5\text{A}_{1g}$, ${}^5\text{B}_{1g} \rightarrow {}^5\text{B}_{2g}$, ${}^5\text{B}_{1g} \rightarrow {}^5\text{E}_g$ appearing in the ranges $12250\text{--}12550$, $16150\text{--}18860$ and $35450\text{--}35720 \text{ cm}^{-1}$, respectively consistent with a five coordinated square pyramidal geometry and C_{4v} symmetry for Mn (III) complexes [33,34]. The magnetic moment values for these complexes were found in the range 4.92-5.74 B.M expected for square pyramidal manganese complexes [50].

The electronic spectra of the iron (III) complexes gave two bands at $9850\text{--}9980$, and $27650\text{--}27760 \text{ cm}^{-1}$, which could be assigned to the transitions ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}$ and ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}$, respectively,

suggesting a five coordinated square pyramidal geometry of Fe (III) complexes [34,35] this idea also supported the C_{4v} symmetry for these complexes. The complexes show magnetic moment values in the range 5.20-5.45 B.M [35].

Antifungal activity.

For the experimental data Table 2, it has been observed that the ligand as well as its complexes shows a significant degree of antifungal activity against *Aspergillus sp.*, *Rizoctonia sp.* and *Penicillium sp.* DMSO control has showed a negligible activity as compare to the metal complexes and ligand. However, the metal complexes are show better activity than the ligand [35]. The complexes are highly effective against *Aspergillus sp.* HLCr(OAc)₂ is the only complex to show 78% activity against

Table 2. Fungicidal screening data of the ligand and their corresponding metal complexes

Compound	% Inhibition of spore germination								
	Aspergillus sp. (mg/ml)			Penicillium sp. (mg/ml)			Rizoctonia sp. (mg/ml)		
	1.0	1.5	2.0	1.0	1.5	2.0	1.0	1.5	2.0
C ₂₂ H ₂₆ N ₁₀ O ₄	28	36	41	09	17	22	30	35	39
[Fe(C ₄₀ H ₂₆ N ₆ O ₄)Cl]Cl ₂	60	70	76	53	60	68	46	51	63
[Fe(C ₄₀ H ₂₆ N ₆ O ₄)NO ₃](NO ₃) ₂	43	53	70	46	51	63	41	42	50
[Fe(C ₄₀ H ₂₆ N ₆ O ₄)(OAc)](OAc) ₂	71	65	79	58	61	71	51	53	66
[Cr(C ₄₀ H ₂₆ N ₆ O ₄)Cl]Cl ₂	66	60	78	56	60	72	50	57	56
[Cr(C ₄₀ H ₂₆ N ₆ O ₄)NO ₃](NO ₃) ₂	53	60	71	45	51	63	43	45	53
[Cr(C ₄₀ H ₂₆ N ₆ O ₄)(OAc)](OAc) ₂	72	75	80	64	68	77	61	62	71
[Mn(C ₄₀ H ₂₆ N ₆ O ₄)Cl]Cl ₂	63	69	71	56	59	61	50	55	58
[Mn(C ₄₀ H ₂₆ N ₆ O ₄)NO ₃](NO ₃) ₂	54	57	62	46	50	58	47	50	51
[Mn(C ₄₀ H ₂₆ N ₆ O ₄)(OAc)](OAc) ₂	70	72	81	56	61	64	49	39	55
Miconazole (standard)	59	71	100	65	78	83	76	82	94

Conclusion:

The analytical data show the presence of one metal ion per ligand molecule and suggest a mononuclear structure for the complexes. The electronic spectral data is in the favor of octahedral geometry of the complexes. The ligand and its Fe(III), Cr(III) and Mn(III) complexes were tested for antifungal activity against some fungi. Antifungal study reveals that, metal complexes have more biological activity than free ligand. Complex (6) [Cr(C₄₀H₂₆N₆O₄)(OAc)](OAc)₂ show best biological action.

References

- Hine J, Yeh C.Y. (1967) Equilibrium in formation and conformational isomerization of imines derived from isobutyraldehyde and saturated aliphatic primary amines, *J. Am. Chem. Soc.*, 89, 2669-2676.
- Fessenden R.J., Fessenden J.S. (1998) *Organic Chemistry*, Brooks/Cole Publishing Company, USA, 1998.
- Kumar G., Devi S., Kumar D., (2016) Synthesis of Schiff base 24-membered trivalent transition metal derivatives with their anti-inflammation and antimicrobial evaluation, *Jou. of Mole. Str.*, 1108, 680-688.
- Elmali A., Kabak M., Elerman Y. (2000) Keto-enol tautomerism conformational structure of N-(2-hydroxy-5-methoxy phenyl), 2-hydroxy benzaldehyde imine, *J. Mol. Struct.*, 477, 151-158.
- Valcarcel M., Laque de Castro M.D. (1994) *Flow through Biochemical Sensors*, Elsevier, Amsterdam.
- Petering H. G., Buskirk H. H., Underwood G.E. (1964) The Anti-Tumor Activity of 2-Keto-3-ethoxybutyraldehyde Bis(thiosemicarbazone) and Related Compounds, *Cancer Res.*, 24, 367-372.
- Du X., Guo C., Hansel E., Doyle P. S., Caffrey C. R., Holler T. P., Mckerrow J. H., Cohen F. E., (2002) Synthesis and structure-activity relationship study of potent trypanocidal thio semicarbazone inhibitors of the trypanosomal cysteine protease cruzain, *J. Med. Chem.*, 45, 2695-2707.
- Ball R. G., Graham W. A. G., Heinekey D. M., Hoyano J. K., McMaster A. D., Mattson B. M., Michel S. T. (1990) Synthesis and structure of dicarbonylbis(eta.-pentamethylcyclopentadienyl)diiridium., *Inorg. Chem.*, 29, 2023-2025.
- Chang S., Jones L., Henling C. M., Grubbs R. H. (1998) Synthesis and characterization of new ruthenium-based olefin metathesis catalysts coordinated with bidentate Schiff-base ligands, *Organometallics*, 17, 3460-3465.
- Z. Jiang, M. S. Lebowitz and H. A. Ghanbari (2006) Neuroprotective activity of 3-aminopyridine-2-carboxaldehyde thiosemicarbazone (PAN-811), a cancer therapeutic agent. *CNS Drug Rev.*, 12, 77-90.
- West D. X., Gebremedhin G. H., Butcher R. J., Jasinski J. P. (1995) *Molecular structure and*

- spectral properties of bromo(2-acetylpyridine⁴-N-methylthiosemicarbazonato) copper(II), *Transition Met. Chem.*, 20, 84-87.
12. Jasim M. A., Karawi A., (2009) Synthesis and characterization of a new N₂S₂ Schiff base ligand and its complexes with nickel(II), copper(II) and cadmium(II) including the kinetics of complex formation, *Transition Met. Chem.*, 2009, 34, 891-897.
 13. Jack K., David C., Bary J., Gloe K., Jolliffe K. A., Lawrance G. A., Lindoy L. F., Meehane G. V., Wenzelb M. (2008) Synthetic, structural, electrochemical and solvent extraction studies of neutral trinuclear Co(II), Ni(II), Cu(II) and Zn(II) metallocycles and tetrahedral tetranuclear Fe(III) species incorporating 1,4-aryl-linked bis-b-diketonato ligands, *Dalton Trans.*, 12, 1331-1340.
 14. Bryan A.M., Merril W.A., Reiff W.M., Fettinger J.C., Power P.P., (2012) Synthesis, structural, and magnetic characterization of linear and bent geometry cobalt(II) and nickel(II) amido complexes: evidence of very large spin-orbit coupling effects in rigorously linear coordinated Co²⁺, *Inorg. Chem.*, 2012, 51(6), 3366-3373.
 15. Fatima A. de, Pereira C.P., Olimpio C.R.S.D.G., Oliveira B.G.F., Franco L.L., Silva P.H.C., (2018) Schiff bases and their metal complexes as urease inhibitors—A brief review, *Journal of Advanced Research*, 13, 113-126.
 16. Achar G., Shahini C.R., Patil S.A., Budagumpi S. (2017) Synthesis, structural characterization, crystal structures and antibacterial potentials of coumarin-tethered N-heterocyclic carbene silver (I) complexes, *Jou. of Organometallic Chemistry*, 833, 28-42.
 17. Halli M. B., Patil V. B., (2011) Synthesis, spectral characterization and DNA cleavage studies of Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes with benzofuran-2-carbohydrazide schiff bases, *Indian J. Chem.*, 50(A), 664-669.
 18. Kumar G., Kumar A., Shishodia N., Garg Y.P., Yadav B.P. (2011) Synthesis, Spectral characterization and antimicrobial evaluation of Schiff base Cu(II), Ni(II) and Co(II) novel macrocyclic complexes, *E-Journal of chemistry*, 8, 1872-1880.
 19. Kumar G., Devi S., Johari R. (2012) Synthesis and Spectral Characterization of Schiff Base Cr(III), Mn(III), and Fe(III) Novel Macrocyclic Complexes Derived from Thiocarbonylhydrazide and Dicarbonyl Compound, *E-Journal of Chemistry*, 9, 2255-2260.
 20. Chen Y., Ruppel J.V., Zhang X.P. (2007) Cobalt-catalyzed asymmetric cyclopropanation of electron-deficient olefins. *J. Am. Chem. Soc.* 129, 12074-12075.
 21. Kumar G., Kumar D. (2013) Monitoring of base catalyzed ethanolysis of *Jatropha curcas* oil by reversed phase high performance liquid chromatography assisted by ultrasonication, *Journal of Environmental Chemical Engineerin*, 1, 962-966.
 22. Rahman A., Choudhary M.I., Thomsen W.J. (2001) Bioassay Techniques for Drug Development, Harwood Academic Publishers, The Netherlands, pp. 16.
 23. Bain G.A., West D.X., Krejci J., Martinez J.V., Ortega S.H., Toscano R.A., (1997) Synthetic and spectroscopic investigations of N(4)-substituted isatin thiosemicarbazones and their copper(II) complexes, *Polyhedron*. 16 (1997) 855-862.
 24. Lodeiro C., Basitida R., Bertolo E., Macias A., Rodriguez R. (2003) Synthesis and characterization of four novel NxOy Schiff base macrocyclic ligands and their metal complexes. *Transition Met. Chem.* 28 (2003) 388-394.
 25. Mikhailov O.V., Kazymova M.R., Shumilova T.A., Solovieva S.S., (2004) Template synthesis in the M(II)-thiocarbonylhydrazide-diacetyl triple system, *Transition Met. Chem.* 29, 732-736.
 26. Chandra S., Thakur S. (2004) Electronic, e.p.r., cyclic voltammetric and biological activities of copper(II) complexes with macrocyclic ligands, *Transition Met. Chem.* 29 (2004) 925-935.
 27. Shakir M., Islam K.S., Mohamed A.K., Shagufa M., Hasan S.S. (1999) Macrocyclic complexes of transition metals with divalent polyaza units, *Transition Met. Chem.* 24 (1999) 577-580.
 28. Rana V.B., Singh P., Singh D.P., Teotia M.P. (1982) Trivalent chromium, manganese, iron and cobalt chelates of a tetradentate N₆ macrocyclic ligand, *Transition Met. Chem.* 7, 174-177.
 29. Khan T.A., Hasan S.S., Varkey S.P., Rather M.A., Jahan N., Shakir M. (1997) Template synthesis and spectroscopic studies of highly conjugated tetraiminetetraamide macrocyclic complexes from 1,2-diphenylethane-1,2-dione dihydrazone, *Transition Met. Chem.* 22, 4-8.
 - J.S. Wood (1972) Stereochemical electronic structural aspects of five-coordination, *Prog. Inorg. Chem.* 16, 227-486.
 30. D.P. Singh, V.B. Rana (1995) Binuclear chromium(III), manganese(III), iron(III) and cobalt(III) complexes bridged by diaminopyridine, *Polyhedron* 14, 2901-2906.
 31. D.P. Singh, R. Kumar, J. Singh (2009) Synthesis and spectroscopic studies of biologically active compounds derived from oxalyldihydrazide and benzil, and their Cr(III), Fe(III) and Mn(III) complexes, *Eur. J. of Med. Chem.* 44, 1731-1736.
 32. B.N. Figgis, J. Lewis (1965) The Magnetic Properties of Transition Metal Complexes, *Prog. Inorg. Chem.* 6, 37-239.
 33. D.P. Singh, R. Kumar, C. Sharma (2010) New 14-membered octaazamacrocyclic complexes: Synthesis, spectral, antibacterial and antifungal studies, *Eur. J. of Med. Chem.* 45, 1230-1236.
 34. Yoon T.P., Jacobsen E.N. (2003) Privileged Chiral Catalysts, *Science*, 299, 1691-1693.
 35. Nagar R. (1990) Syntheses, characterization, and microbial activity of some transition metal complexes involving potentially active O and N donor heterocyclic ligands, *J. Inorg. Biochem.* 40, 349-356.