

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis, Spectroscopic and Antimicrobial Studies of Manganese (II) Iron (III) Cobalt (II), Nickel (II) and Copper (II) Complexes with Oxygen Donor Chalcone Ligand.

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ABSTRACT

In the present paper, the some of first transition series metal complexes derived from (4-hydroxy-3-[3-(1H-indole-3-yl)-acryloyl]-6-methyl-2H-pyran-2-one) were synthesized from Dehydroacetic acid and Indole-2-carboxaldehyde. They correspond well with the general formula $[M(L)_2(H_2O)_2]$, where M = Mn(II), Co(II), Ni(II) and Cu(II) and $[M(L)_2(Cl)(H_2O)]$, where M = Fe(III) and L = $C_{17}H_{13}NO_4$. The ligand was characterized on the basis of elemental analysis, UV, IR, Mass, 1H NMR and antimicrobial activity. All the complexes were characterized by elemental analysis, UV, magnetic susceptibility measurements, IR, TGA-DTA & antimicrobial activity. The ligand acts as a bidentate chelate and coordinates through two oxygen atoms of ligand i.e complex formed by 1:2 (metal: ligand) ratio. The thermal stability of the complexes was studied by thermogravimetry and the decomposition schemes of the complexes are given. The ligand and its metal complexes were screened for antimicrobial activity against *Bacillus Cereus*, *Bacillus Megaterium*, *Shigellaboydii* and *Escherichia Coli* bacteria, and *Saccharomyces Cerevisiae*, *Aspergillus Oryzae* and *Penicillium notatum fungi* were studied.

Keywords: Transition metal complexes; magnetic susceptibility; Chalcone; Oxygen donar ligand; TGA-DTA; Antimicrobial activity.

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INTRODUCTION

Chalcones constitute an important class of natural products belonging to the flavonoid family, which have been reported to possess a wide spectrum of biological activities, including antibacterial, antifungal, anti-inflammatory, antitumor, insect antifeedant and antimutagenic[1-3]. Additionally, some of chalcone derivatives have been found to inhibit several important enzymes in cellular systems, such as xanthine oxidase[4] and protein tyrosine kinase[5-6]. Chalcones are also key precursors in the synthesis of many biologically important heterocycles such as benzothiazepine[7], pyrazolines[8], 1,4-diketones[9] and flavones[10]. Hence, the synthesis of chalcones has generated vast interest among organic as well as medicinal chemists.

Chalcones are one of the major classes of natural products with wide spread distribution in fruits, vegetables, spices, tea and soy based foodstuff, have been recently subjects of great interest for their interesting pharmacological activities[11]. Chalcones are belonged to the flavonoids family. A vast number of naturally occurring chalcones are polyhydroxylated in the aryl rings. The radical quenching properties of the phenolic groups present in many chalcones have raised interest in using the compounds or chalcone rich plant extracts as drugs or food preservatives [12]. Chalcones have been reported to possess many useful properties, including anti-inflammatory, antimicrobial, antifungal, antioxidant, cytotoxic, antitumor and anticancer activities. A number of chalcone derivatives, have also been found to inhibit several important enzymes in cellular systems, including xanthine oxidase [13], aldose reductase, epoxide hydrolase[14] protein tyrosine kinase [15] and quinone reductase [16].

Chalcones having an α , β -unsaturated carbonyl group are one of the important biocides and versatile synthons for various chemical transformations. Most of the chalcones are highly biologically active with a number of pharmacological and medicinal applications [17]. Chalcones have been used as anti AIDS agents [18], cytotoxic agents with antimalarials[19], antiangiogenic activity [20], antiinfective and anti-inflammatory [21] and anti-tumor agents [22]. Some chalcones were found to increase the level of the tumor suppressor protein p53 in various cancer cell lines by disrupting its complexes with the oncoprotein MDM2[23]. Chalcones are also key precursors in the synthesis of many biologically important heterocycles such as benzothiazepine [24], pyrazolines [25], 1,4-diketones and flavones. Some heterocyclic systems based on chalcone precursors are benzothiazepines, benzodiazepines, benzoxazepines, pyrimidines, pyrazoles, and oxazoles [26]. Various substituted chalcones possess antioxidant [27], radical-scavenging [28], anticancer [29], antileishmanial [30], antimetabolic [31], antitumor [32] and antibacterial [33] properties, as well as P-glycoprotein mediated multidrug resistance [34].

Several strategies for the synthesis of the system based on the formation of carbon-carbon bond have been reported. Among them the direct aldol condensation and Claisen Schmidt condensation still occurs prominent position. The main method for the synthesis of chalcones is the classical Claisen-Schmidt condensation in the presence of aqueous alkali [35], $\text{Ba}(\text{OH})_2$ [36], ultra sound irradiation. However many of this methods suffered from harsh reaction conditions, toxic reagents, strong acidic / basic conditions, prolonged reaction time, poor yield and low selectivity. Although, several modification have been made to counter these problems. There is still a need for the development of selective and better strategies for the synthesis of α , β -unsaturated carbonyl compounds.

A search of the literature revealed that no work has been done on transition metal complexes of the chalcone derived from dehydroacetic acid and Indole-2-carboxaldehyde. The complexes of Ni(II), Cu(II), Mn(II), Co(II) and Fe(III) with this ligand were also prepared in the solid state and characterized by different physico-chemical methods.

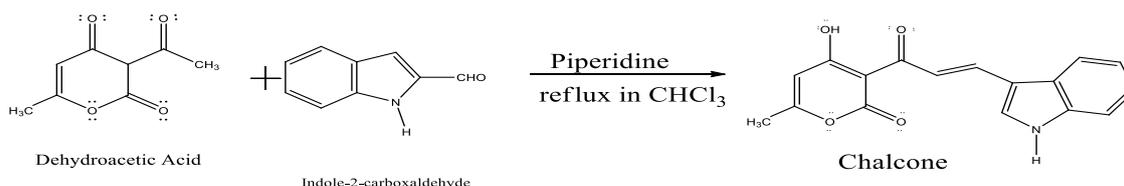
EXPERIMENTAL

Material and Methods: Dehydroacetic acid for synthesis was obtained from Merck, Germany & used as supplied. 4-isopropylbenzaldehyde of A.R. grade obtained from AVRA chemicals were used for the synthesis of the ligands. A.R. grade hydrated metal chlorides from Thomas Baker were used for the preparation of the complexes. The carbon, hydrogen & nitrogen content in each sample were measured on a Perkin Elmer (2400) CHNS Analyzer. The IR spectra (KBr), in the range of $4000\text{-}450\text{ cm}^{-1}$ were recorded on a Perkin Elmer (C-75430) IR spectrometer. The $^1\text{H-NMR}$ spectrum of the ligand was measured in CDCl_3 on Bruker instrument. The mass

spectrum of the ligand was measured in Qc-01 DAD Mass-spectrometer, thermo gravimetric analysis differential thermal analysis were realised on a METTLER-TOLEDO-DB V13.00 instruments. The Ultra-Violet visible spectra of the complexes were recorded on a Shimadzu UV-2202 Spectrophotometer. Magnetic susceptibility measurements of the complexes were performed using a Gouy balance at room temperature using $\text{Hg} [\text{Co} (\text{SCN})_4]$ as the calibrant.

General procedure for the synthesis of the ligand (HL)

A solution of 0.01 mol of Dehydroacetic acid (DHA), 8-10 drops of piperidine & 0.01 mole of 4-isopropyl benzaldelyde in 25 ml chloroform were refluxed for 8-10 hrs, 10 ml of the chloroform-water azeotrope mixture was separated by distillation. Crystal of product separated on slow evaporation of the remaining chloroform. The resulting precipitate was filtered, washed several times with ethanol & recrystallized from chloroform [37-38].



Scheme 1: Synthesis of Ligand

General procedure for the synthesis of metal complexes

To a chloroform solution (30ml) of the ligand (2mmol), methanolic solution (20ml) of metal chlorides was added with constant stirring. The PH of the reaction mixture was maintained around 7.5 by adding 10% methanolic solution of ammonia. It was then refluxed for 2hr. the resulting metal complex was filtered in hot condition & washed with ethyl acetate methanol, pet-ether & dried over calcium chloride in vacuum desiccator.

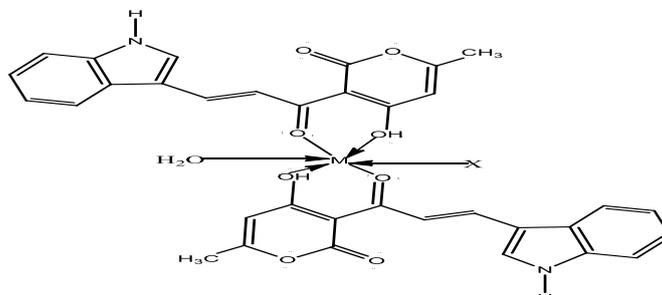


Fig. 1: Proposed structure of complex, when $X = \text{Cl}$, $M = \text{Fe(III)}$ and $X = \text{H}_2\text{O}$ $M = \text{Mn(II)}$, Co(II) , Cu(II) , Ni(II)

General procedure for the antimicrobial activity

The ligand and its metal complexes were screened for *in vitro* antibacterial activity against Gram-positive i.e. *Bacillus Megaterium*, *Bacillus Cereus* and Gram-negative i.e. *Escherichia Coli*, *Shigella boydii* by the paper disc plate method [39]. The compound were tested at concentrations of 1.0 mg ml^{-1} in DMSO (0.1ml) was placed on a paper disk (6mm in diameter) with the help of micropipette and compared with a known antibiotic, viz. *Ciprofloxacin* at the same concentrations. To evaluate the fungicidal activity of the ligands and the metal complexes, their effects on the growth of *Penicillium notatum*, *Saccharomyces Cerevisiae* and *Aspergillus Oryzae* were studied. The ligand and their corresponding metal chelates in DMSO were screened *in vitro* by the disc diffusion method [40]. The ligands and complexes were dissolved separately in DMSO to obtain concentration of $500 \mu\text{g disc}^{-1}$. The linear growth of the fungus was recorded by measuring the diameter of the colony after 96 hr. The diameters of the zone of inhibition produced by the complexes were compared with *Griseofulvin*.

RESULTS AND DISCUSSION

Elemental analyses show 1:2 (metal:ligand) stoichiometry for all the complexes (fig.1). The analytical data of the ligand and its metal complexes corresponded well with the general formula $[M(L)_2(H_2O)_2]$, where $M = Co(II), Mn(II), Cu(II), Ni(II)$, and $[M(L)_2(H_2O)(Cl)]$, where $M = Fe(III)$, $L = C_{15}H_{11}O_5$. The absence of chlorine except in the Fe(III) complex was evident from the Vol-hard test and presence of coordinated water was confirmed by thermo gravimetric analysis. Since a single crystal of the complexes could not be isolated from any common solvent, the possible structure was predicted based on analytical, spectroscopic, magnetic and TGA-DTA data.

Table I: Physical Characterization and analytical data of ligand and its metal complexes

Compound	Mr gmol ⁻¹	Colour	Yield %	M.P. in (°C)	Found (Calcd.), %			
					M	C	H	N
Ligand HL C ₁₇ H ₁₃ NO ₄	295	Yellow	62	225	-	68.09 (69.15)	4.15 (4.44)	4.52 (4.74)
C ₃₄ H ₂₈ ClFeN ₂ O ₉	699	Golden	50	260	7.86 (7.98)	57.99 (58.35)	3.91 (4.03)	3.80 (4.00)
C ₃₄ H ₃₀ CuN ₂ O ₁₀	690	Celadon	75	262	9.02 (9.21)	59.01 (59.17)	4.25 (4.38)	3.92 (4.06)
C ₃₄ H ₃₀ CoN ₂ O ₁₀	685	Orange	70	282	8.51 (8.60)	59.45 (59.57)	4.30 (4.44)	3.98 (4.09)
C ₃₄ H ₃₀ MnN ₂ O ₁₀	681	Brown	58	250	8.00 (8.06)	59.80 (59.92)	4.40 (4.44)	4.00 (4.11)
C ₃₄ H ₃₀ N ₂ NiO ₁₀	685	Green Yellow	60	>300	8.42 (8.56)	59.50 (59.59)	4.31 (4.41)	4.05 (4.09)

Mass spectra of ligand

Mass spectroscopy regard as clear and strong evidence to prove the formation of molecules via the observation of the mother ion at molecular weight equivalent value and this observed in the mass fragmentation spectra of ligand, that the mother ion appear clear band at (296 m/e), this was a good agreement for the formation of the new ligand. The mass spectra giving in the following fig. III.

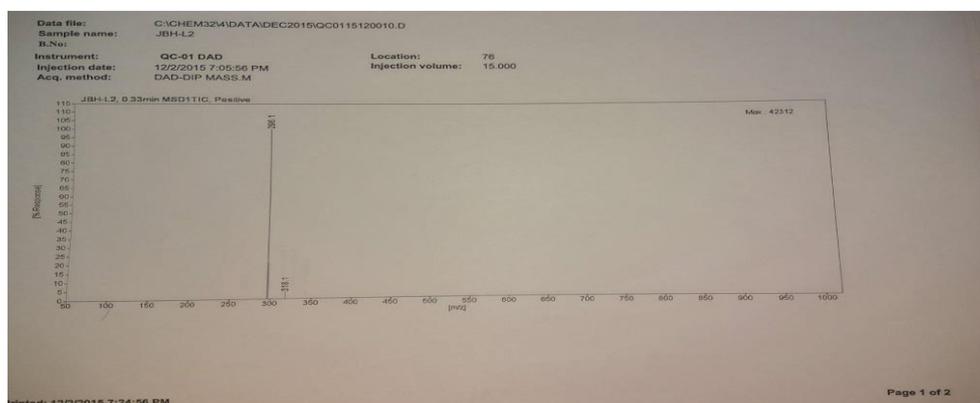


Fig. III : Mass Spectra of ligand (HL)

$C_{34}H_{28}ClFeN_2O_9$	3296 _(s)	-	1680 _(s)	1647 _(m)	1270 _(s)	972 _(s)	530 _(s) 488 _(s)
$C_{34}H_{30}MnN_2O_{10}$	3170 _(m)	-	1675 _(m)	1645 _(w)	1268 _(w)	974 _(m)	560 _(w) 462 _(s)
$C_{34}H_{30}N_2NiO_{10}$	3307 _(s)	-	1681 _(s)	1647 _(s)	1268 _(s)	972 _(s)	551 _(m) 531 _(s)

Magnetic moment and UV-Vis Spectra

The magnetic and electronic spectral data are given in Table III. The data is of relevance for the proposed structure of the complexes (Fig. 1). The electronic spectra of the Cu(II) complexes in DMF revealed one broad band at 15130 and 25226 cm^{-1} for ligand, assignable to a ${}^2E_g \rightarrow {}^2T_{2g}$ transition and charge transfer. The observed magnetic moment value for the Cu(II) complexes was in the range 1.94–2.08 μ_B . The electronic spectral data[45] coupled with the magnetic moment value suggest a distorted octahedral geometry for the Cu(II) complexes[46]. The electronic spectra of Ni(II) complexes display three bands at 9412, 15622 and 24200 cm^{-1} for ligand, assignable to ${}^3A_{2g} \rightarrow {}^3T_{2g}(F)$ (ν_1), ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ (ν_2) and ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$ (ν_3) transitions. This is in accordance with earlier reported values for octahedral Ni(II) complexes[47-48]. The reductions of the Racah parameter (B) and the nephelauxetic effect (β) from the value of the free ion suggest an appreciable amount of covalent character in the metal ligand bonds[47,49]. The calculated values the range reported for octahedral geometry. The normal magnetic moment 2.99–3.19 μ_B confirms the proposed geometry. The Co(II) complexes show three transitions at 9559, 18448 and 22665 cm^{-1} for ligand assignable to ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ (ν_1), ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ (ν_2) and ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ (ν_3) transitions[46,49]. The magnetic moment value of the Co(II) complexes (Table III) suggest octahedral geometry.

TABLE III. Magnetic And electronic absorption spectral data (in DMSO) of the compounds.

Ligand & Complex	ν / cm^{-1}	Band assignment	μ_{eff} / μ_B	Geometry
Ligand HL	32442	INCT ^a	-	-
$C_{17}H_{13}NO_4$	40545	INCT	-	-
$C_{34}H_{28}ClCoN_2O_9$	9559	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)(\nu_1)$	4.66	Octahedral
	18448	${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)(\nu_2)$		
	22665	${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)(\nu_3)$		
$C_{34}H_{30}CuN_2O_{10}$	15130	${}^2E_g \rightarrow {}^2T_{2g}$	2.08	Distorted Octahedral
	25226	INCT		
$C_{34}H_{30}FeN_2O_{10}$	14546	${}^6A_1 \rightarrow {}^4T_1(G)$	5.92	Distorted Octahedral
	21801	${}^6A_1 \rightarrow {}^4T_2(G)$		
	24449	${}^6A_1 \rightarrow {}^4E(G)$		
$C_{34}H_{30}MnN_2O_{10}$	17789	Laporte and spin forbidden	5.77	Distorted Octahedral
	19571			
	31060			
$C_{34}H_{30}N_2NiO_{10}$	9412	${}^3A_{2g} \rightarrow {}^3T_{2g}(F)(\nu_1)$	3.03	Octahedral
	15622	${}^3A_{2g} \rightarrow {}^3T_{1g}(F)(\nu_2)$		
	24200	${}^3A_{2g} \rightarrow {}^3T_{1g}(P)(\nu_3)$		

The Fe(III) complexes of ligand show three bands at 14546, 21801, 24449 cm^{-1} assignable to ${}^6A_1 \rightarrow {}^4T_1(G)$, ${}^6A_1 \rightarrow {}^4T_2(G)$ and ${}^6A_1 \rightarrow {}^4E(G)$ transitions. The spectra suggest distorted octahedral geometry[46,47,50]. The electronic spectrum of Mn(II) complex of ligand displays weak bands at 17789, 19571 and 31060 cm^{-1} . These bands are both Laporte and spin-forbidden. However, due to instantaneous distortion of the octahedral structures around the metal cation, weak bands sometimes do appear[46-47].

TG-DTA Analysis

The Mn(II), Fe(III), Co(II), Ni(II) and Cu(II) complexes of ligand were chosen for a thermal study. The TG curve of the complexes of ligand shows three decomposition steps. On the TG curve of the Mn(II) complex, the first step shows a steep slope between 150–200 °C with a mass loss of 5.0 % (calculated 5.4 %), indicating the

removal of two molecules of coordinated water. An endo-thermic peak in the range 150–200 °C ($\Delta t_{\min} = 175$ °C) on the DTA curve corresponds to the dehydration step. The anhydrous compound in second step decomposes within a short temperature range from 220–330 °C, with a 37.0 % mass loss (calculated 36.3 %). An exothermic between 240 and 400 °C with a $\Delta t_{\max} = 270$ °C on the DTA curve corresponds to this mass loss. This step may be attributed to the removal of the non-coordinated part of the ligand. The third mass loss step in the range 400–790 °C corresponds to the decomposition of the coordinated part of the ligand, with a mass loss 47.0 % (calculated 47.6 %). A broad endotherm is observed for this step. The mass of the final residue corresponds to stable MnO, 14.60 % (calculated, 15.7 %).

In the thermal study of the Fe(III) complex, an inclined slope from 175–195 °C on the TG curve, with a mass loss of 7.0 % (calculated 7.9 %), indicates the removal of one molecule of water and one chloride ion. An endothermic peak in the range 180–240 °C was observed on the DTA curve ($\Delta t_{\min} = 192$ °C). The complex continues to decompose in a second step between 210 and 300 °C, with 37.0 % mass loss (calculated 35.2 %). A corresponding exothermic peak between 250–280 °C ($\Delta t_{\max} = 265$ °C) on the DTA is attributed to the removal of the non-coordinating part of the ligand. The third step corresponds to the decomposition of remaining part of the ligand with a mass loss 41.78 % (calculated 41.95 %). The mass of the final residue was 9.0 % (calculated 10.6 %), corresponding to FeO.

The thermal decomposition profile of the Co(II) complex showed no weight loss up to 140 °C. A mass loss of 5.0 % (calculated 5.4 %) was observed in the range 140–175 °C. The endothermic peak between 140–165 °C ($\Delta t_{\min} = 152$ °C) correspond to the loss of two molecules of water. The second step of decomposition was between 265 and 400 °C with a 37.0 % mass loss (calculated 36.1 %). The broad exothermic peak between 270–375 °C ($\Delta t_{\max} = 346$ °C) on the DTA curve is attributed to the removal of the non-coordinating part of the ligand. The mass loss continued with the slow decomposition of remaining part of the ligand 45.5 % (calculated 47.2 %). The mass of the final residue corresponded to CoO, 16.36 % (calculated 16.51 %).

The thermal decomposition profile of the Ni(II) complex showed a mass loss of 5.0 % (calculated 5.4 %) in the range 150–175 °C, indicating the removal of two coordinated water molecules. An endothermic peak on the DTA curve between 160–185 °C ($\Delta t_{\min} = 162$ °C) also corresponds to dehydration. The second step of the decomposition was between 190 and 325 °C with a 37.0 % mass loss (calculated 36.1 %). A broad exothermic peak between 200–350 °C ($\Delta t_{\max} = 260$ °C) on the DTA curve is attributed to the removal of the non-coordinating part of the ligand. The mass loss continued with the slow decomposition of the remaining part of the ligand up to 900 °C with a 46.0 % (calculated 47.3 %) mass loss. A broad endothermic peak between 450–850 °C was observed on the DTA curve. The mass of the final residue of 16.94 % (calculated 17.2 %) corresponds to NiO.

On the TG curve of the Cu(II) complex, the mass loss commences at 120 °C with an inclined slope from 155–185 °C with a mass loss of 6.0 % (calculated 5.4 %), indicating the removal of two molecules of coordinated water. An endothermic peak in the range 150–200 °C ($\Delta t_{\min} = 158$ °C) on the DTA curve also corresponds to the dehydration. The second step of the decomposition continues on the TG curve from 275 up to 375 °C, with a mass loss of 37.0 % (calculated 35.7 %) and the exothermic peak ($\Delta t_{\max} = 299$ °C) on the DTA curve may be attributed to the removal of the non-coordinated part of the ligand. The third step in the range 420–880 °C with a mass loss of 46.0 % (calculated 47.0 %) corresponds to the decomposition of the coordinated part of the ligand. A broad endotherm was also observed for this step. The mass of the final residue corresponded to stable CuO, 15.9 % (calculated 16.1 %).

Antimicrobial Activity



Bacillus Megaterium



Bacillus Cereus



Escherichia Coli



Shigella boydii



Fig.V : Antimicrobial activity of ligand & its complexes

Antimicrobial activity was assayed by paper disc plate method by measuring inhibition zones in mm. in vitro antimicrobial activity of all synthesized compounds and standard have been evaluated against four strains of bacteria which include *Bacillus Megaterium*, *Bacillus Cereus* and Gram-negative i.e. *Escherichia Coli*, *Shigella boydii* and against three fungal strains like *Penicillium notatum*, *Saccharomyces Cerevisiae* and *Aspergillus Oryzae*. The standard used was *Ciprofloxacin* and *Grysofulvin*.

Compound	Inhibition zone of bacterial & fungal growth in mm						
	Antimicrobial activity				Antifungal activity		
	<i>Bacillus Megaterium</i>	<i>Bacillus Cereus</i>	<i>Escherichia Coli</i>	<i>Shigella boydii</i>	<i>Penicillium notatum</i>	<i>Saccharomyces Cerevisiae</i>	<i>Aspergillus Oryzae</i>
	Conc ⁿ ,1mg/ml	Conc ⁿ ,1mg/ml	Conc ⁿ ,1mg/ml	Conc ⁿ ,1mg/ml	Conc ⁿ ,0.5 mg/ml	Conc ⁿ ,0.5 mg/ml	Conc ⁿ ,0.5 mg/ml
Ligand HL C ₁₇ H ₁₃ NO ₄	10	08	08	12	04	-	02
C ₃₄ H ₂₈ ClCoN ₂ O ₉	22	12	19	13	12	10	10
C ₃₄ H ₃₀ CuN ₂ O ₁₀	24	14	24	23	14	12	14
C ₃₄ H ₃₀ FeN ₂ O ₁₀	20	16	08	12	10	-	-
C ₃₄ H ₃₀ MnN ₂ O ₁₀	26	20	10	16	11	18	16
C ₃₄ H ₃₀ NiN ₂ O ₁₀	16	14	18	18	12	20	18
<i>Ciprofloxacin</i>	36	54	32	30	-	-	-
<i>Grysofulvin</i>	-	-	-	-	34	40	42

From the results of antimicrobial activity of ligand and complex it is clear that the complexes shows enhance activity than the ligands. The increase in antimicrobial activity is due to faster diffusion of metal complexes as a whole through the cell membrane or due to the combined activity of the metal and ligand[51].

CONCLUSION

The analytical data shows 1:2 metal to ligand stoichiometry, we have proposed distorted octahedral geometry for Cu(II), Mn(II) & Fe(III), other Ni(II), Co(II) are octahedral geometry. Antimicrobial activity it is found that the complexes are more active than their parent ligand. A thermal study revealed that the complexes are thermally stable.

ACKNOWLEDGEMENTS

The authors thankful the Director, Instrumentation Centre, Solapur University, Solapur(MH), for providing necessary instrumental facilities. Also authors are wish to thank Dr. Desai, Head, Department of Microbiology, Sub-campus Dr. B.A.M.University, Osmanabad, for his cooperation in determining the antimicrobial activity of the synthesized compounds. Lastly I specially thankful to my Guide, Dr. S.D.Salunke, Principal, R.S.M. Latur, because of his broad and profound knowledge, his precious

instruction and constructive criticism has helped me to gain tremendous knowledge. His encouragement made my work possible.

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