

Thermo gravimetric and Antimicrobial analysis of 4-hydroxy-3-(3-(4-hydroxy-3,5-dimethoxyphenyl) acryloyl)-6-methyl-2H-pyran-2-one chalcone and their metal complexes

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Abstract

In the present paper, the some of first transition series metal complexes derived from 4-hydroxy-3-(3-(4-hydroxy-3,5-dimethoxyphenyl)acryloyl)-6-methyl-2H-pyran-2-one chalcone were synthesized from Dehydroacetic acid and 4-hydroxy-3,5-dimethoxy benzaldehyde (syringaldehyde). 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. Antimicrobial activity it is found that the complexes are more active than their parent ligand.

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

INTRODUCTION

There is rising curiosity in the pharmacological virtual of natural products is chalcones compose an essential sites of natural commodity. Chalcone are made up of open chain flavonoids it contains two aromatic or heteroaromatic moiety are fused by a three carbons having α β unsaturated carbonyl structure (Balaji H. Jawale, et al., 2017; Patange, 2008). The existence of a sensitive α , β unsaturated carbonyl moiety in chalcones is well known to be accountable for its antimicrobial effects (Prasad YR, et al., 2008). In present times a number of chalcones have been investigated for its cytotoxic, insecticidal, antiviral, enzyme inhibitory, anticancer chemo preventive and mutagenic effects (Won SJ, et al., 2008; Yu DC, et al., 1982). Numerous chalcones containing (-OH) hydroxy, (-OR)alkoxy functional sets in altered place have been stated to keep anti-infectious activity (Liu XL, et al., 2008), antiulcer actions (Jeffrey JA, et al., 1996), antifungal properties (Lahtchev KL et al., 2008), antioxidant effects (Rao YK, et al., 2009), vasodilatory action (Ram VJ, et al., 2000), antimitotic activity (Khatib S, et al., 2009), antimalarial propertis (Papo N, et al., 2003), antileishmanial action in addition to prohibition of organic peacekeepers relief, prohibition of leukotriene B4, prohibition of tyrosinase and prohibition of aldose reductase effects (Balaji H. Jawale, et al., 2017; Patange, 2008). Gratitude of these results encouraged us to prepare novel chalcones as an active model for antimicrobial agents.

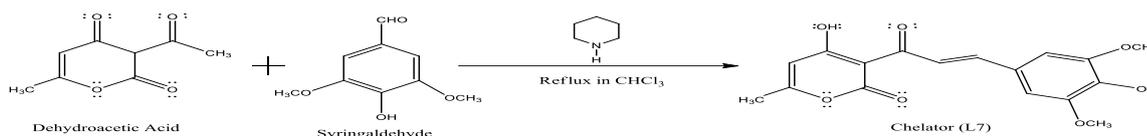
On brief investigation of literature shown that no research work has been completed on some metal in first transition series with complexing materials of the 4-hydroxy-3-(3-(4-hydroxy-3,5-dimethoxyphenyl)acryloyl)-6-

methyl-2H-pyran-2-one chalcone they are referred to Chelator derived from 4-hydroxy-3,5-dimethoxy benzaldehyde (syringaldehyde) and 3-acetyl-6-methyl-2H-pyran-2,4(3H)-dione (DHA). In this chapter, we are reveals the synthesis of novel chalcone, characterization carried out using modern tools. The transition metal [Cu (II), Ni (II), Co (II), Mn (II) and Fe (III)] complexes materials obtained from bidentate novel chalcone ligand having a carbonyl group openly connected to the α , β -unsaturated moiety derived from dehydroacetic acid and syringaldehyde.

SYNTHESIS OF CHELATOR

A chloroform solution having 0.01 mole of 3-acetyl-6-methyl-2H-pyran-2,4(3H)-dione (DHA), add few drops of piperidine base, then add alternately prepared solution 0.01 mole of 4-hydroxy-3,5-dimethoxy benzaldehyde (Syringaldehyde) in 20 ml chloroform, after this reaction mixture refluxed for 8-10 hours. After completion of reaction some of the chloroform-water azeotrope mixture separated out by purification. Crude precipitate is appearing means product are formed they separated on sluggish vaporization of the enduring CHCl_3 . The subsequent crude precipitate was filtered, then washed with ethanol and recrystallized out with CHCl_3 solvent (Patange V.N, et al., 2007; Munde A.S, et al., 2009).

REACTION



PREPARATION OF METAL COMPLEXES WITH CHELATOR

A accurately way out 0.2mole of Chelator chalcone in RBF having 30 ml of CHCl_3 solvent and Chelator liquefied absolutely. Simultaneously prepared solution of 0.01 mole of transition metal salt in 20 ml of dehydrated methanol was formerly added drop by drop to the solution of the Chelator. The reactants mixture were refluxed for 2 to 3 hours with constant stirring and then the mixture cooled to see the appearance of precipitate which infrequently initiate to the cold reaction combination, if precipitate not occurred then 10% methanolic solution of NH_3 was added drop by drop to rise the P^{H} of reaction mixture till the metal chelate crude precipitates out absolutely. The crude precipitate was digested for half an hour. Finally solid metal chelate are obtained, they are separated out on slow evaporation then filtered it in hot form. It was washed through methanol and dried out in vacuum desiccator.

REACTION



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 method³⁹. 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 method⁴⁰. 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*.

RESULT AND DISCUSSION

I) Physical And Analytical Results

The elemental evaluates indications 1:2 (metal : ligand) stoichiometry for each of the chelates. The investigative statistics of the Chelator and their transition metal chelates matched well through the general empirical formula $[\text{M}(\text{L})_2(\text{H}_2\text{O})_2]$, where M=Iron(III), Manganese(II), Cobalt(II), Nickel(II), Copper(II), L= $\text{C}_{17}\text{H}_{16}\text{O}_7$. The chelates were diverse coloured, stable in normal condition, they are insoluble in H_2O as well as common organic solvents but completely soluble in dimethylformamide and dimethylsulphoxide (Balaji H. Jawale, et al., 2017; Patange, 2008). Meanwhile a sole crystal of the every chelates could not be isolated from any common organic solvent, the probable structure was anticipated founded on investigative, modern spectral, magnetic measurements also thermal records.

Table I: Physicochemical records of Chelator and their transition metal complexes.

Ligand/ Complexes	F.W.	M.P. (°C)	Yield %	Colour	Found (Caltd.), %			
					M	C	H	O
Ligand HL $\text{C}_{17}\text{H}_{16}\text{O}_7$	332	219	82	Yellow	-	61.22 (61.44)	4.76 (4.85)	33.70
$\text{C}_{34}\text{H}_{30}\text{FeO}_{14}$	718	300<	60	Golden	7.66 (7.77)	56.80 (56.84)	4.181 (4.21)	31.07 (31.18)
$\text{C}_{34}\text{H}_{30}\text{CuO}_{14}$	726	260	35	Celadon	8.72 (8.75)	56.21 (56.24)	4.11 (4.16)	30.71 (30.85)
$\text{C}_{34}\text{H}_{30}\text{CoO}_{14}$	721	272	70	Orange	8.09 (8.17)	56.55 (56.60)	4.10 (4.19)	30.97 (31.04)
$\text{C}_{34}\text{H}_{30}\text{MnO}_{14}$	717	300<	66	Brown	7.61 (7.66)	56.80 (56.91)	4.16 (4.21)	31.20 (31.22)
$\text{C}_{34}\text{H}_{30}\text{NiO}_{14}$	721	252	58	Green Yellow	8.09 (8.14)	56.60 (56.62)	4.17 (4.19)	30.95 (31.05)

II) ^1H NMR Spectrum Of Chelator

The ^1H nuclear magnetic resonance spectrum of free Chelator in deuterated chloroform at normal temperature appearances the resulting signals. δ 2.72 (singlet, due to 3H for $-\text{CH}_3$ proton in dehydroacetic acid moiety), 3.97 (singlet, due to 6H, on 2 $-\text{OCH}_3$ proton of side chain aryl moiety), 5.97(singlet, due to 1H, for C_5 -hydrogen of DHA moiety), 5.98 (singlet, due to 1H, on $-\text{OH}$ proton aryl ring), 7.28 (singlet, due to 2H, for side chain Ar-H adjacent methoxy group), 7.95 (doublet, due to 1H, β proton of $\alpha \beta$ unsaturated moiety on Chelator), 8.22 (doublet, due to 1H, α proton of $\alpha \beta$ unsaturated moiety on Chelator) and 18.17 (singlet, due to 1H, for phenolic $-\text{OH}$ proton of DHA moiety) (R.Gren, 1971; S.Forsen, et al., 1960; V.Drevenkar, et al., 1983).

III) Mass Spectra Of Chelator

Mass spectral figures confirmed the structure of the newly synthesized Chelator as showed by the mother ion peaks equivalent to its empirical mass, the mass spectrum of Chelator.

IV) Infrared Spectra Of Chelator And Its Chelates

The FTIR spectrum of free Chelator appearances specific bands at 3390cm^{-1} for ν (OH) stretching of the aromatic side chain substituted moiety, 3100cm^{-1} ν (OH) of the intramolecular phenolic O-H stretching of the DHA moiety, 1716cm^{-1} ν (C=O) stretching of lactone carbonyl in between DHA ring, 1639cm^{-1} ν (C=O) stretching of α β unsaturated carbonyl group, 1248cm^{-1} ν (C-O) stretching of phenolic in DHA moiety individually (Ramarao N., et al., 1985; Carugo O., et al., 1990; Balaji H. Jawale, et al., 2017; Patange, 2008). In the FTIR spectrum of each transition metal chelates, none of the any band was detected in the IR frequency area of $3200\text{-}3000\text{cm}^{-1}$. This indicates absence of ν (OH) of the intramolecular phenolic O-H stretching of the DHA moiety at 3100cm^{-1} proposes successive deprotonation of the phenolic functional group and chelation of phenolic oxygen to the transition metal ion. This was also sustained by an rising IR frequency in ν (C-O) stretching of phenolic in 3-acetyl-6-methyl-2H-pyran-2,4(3H)-dione (DHA) moiety (Rao P.V., et al., 2003; Balaji H. Jawale, et al., 2017; Patange, 2008) by $15\text{-}45\text{cm}^{-1}$. The ν (C=O) stretching of α β unsaturated carbonyl group was moved to lesser energy by respect to the free Chelator, signifying the contribution of the α β unsaturated carbonyl group in the complexation (Ramarao N., et al., 1985; Carugo O., et al., 1990). On the other hand a wide-ranging band representative of ν (OH) of complexation water molecules was detected in between the IR frequency region 3570 and 3200cm^{-1} . In case of Chelator and its transition metal complexes exhibited a conspicuous band in IR frequency at 1379 representative of ν (C-O-C) linkage and 994cm^{-1} *trans* -CH=CH- absorption in α β olephinic. The occurrence of different bands in the IR frequency region $600\text{-}450\text{cm}^{-1}$ can be allotted to ν (Metal-Oxygen) vibration (Balaji H. Jawale, et al., 2017; Patange, 2008; Nakamoto K., 1970).

Therefore, the all above spectral data concluded that the Chelate chelated through the transition metal ions, they acts as mono deprotonated bi-dentate and the complexation happens through the α β unsaturated carbonyl oxygen and phenolic oxygen of 3-acetyl-4-hydroxy-6-methyl-2H-pyran-2-one(enol form of DHA moiety).

Table.II. Specific IR frequencies of Chelator and its transition metal complexes

Ligand/ Complexes	ν (OH) (side chain phenyl moiety)	ν (OH) (dehydroacetic acid moiety)	ν (C=O) (lactone)	ν (C=O) (acetyl carbonyl)	ν (C-O) (phenolic)	ν (C=C) (trans)	ν (M-O)
Ligand HL $\text{C}_{17}\text{H}_{16}\text{O}_7$	3390	$3100_{(s)}$	$1716_{(s)}$	$1639_{(m)}$	$1248_{(w)}$	$994_{(s)}$	-
$\text{C}_{34}\text{H}_{30}\text{FeO}_{14}$	3338	-	$1701_{(m)}$	$1643_{(w)}$	$1204_{(s)}$	$994_{(w)}$	$541_{(s)}$ $495_{(s)}$
$\text{C}_{34}\text{H}_{30}\text{CuO}_{14}$	3370	-	$1693_{(s)}$	$1647_{(s)}$	$1266_{(w)}$	$965_{(w)}$	$544_{(w)}$ $448_{(s)}$
$\text{C}_{34}\text{H}_{30}\text{CoO}_{14}$	3201	-	$1690_{(s)}$	$1643_{(s)}$	$1246_{(s)}$	$972_{(m)}$	$552_{(s)}$ $486_{(s)}$
$\text{C}_{34}\text{H}_{30}\text{MnO}_{14}$	3387	-	$1670_{(m)}$	$1640_{(w)}$	$1238_{(m)}$	$1000_{(s)}$	$579_{(m)}$ $534_{(s)}$
$\text{C}_{34}\text{H}_{30}\text{NiO}_{14}$	3358	-	$1699_{(s)}$	$1653_{(s)}$	$1225_{(s)}$	$999_{(s)}$	$532_{(s)}$ $519_{(s)}$

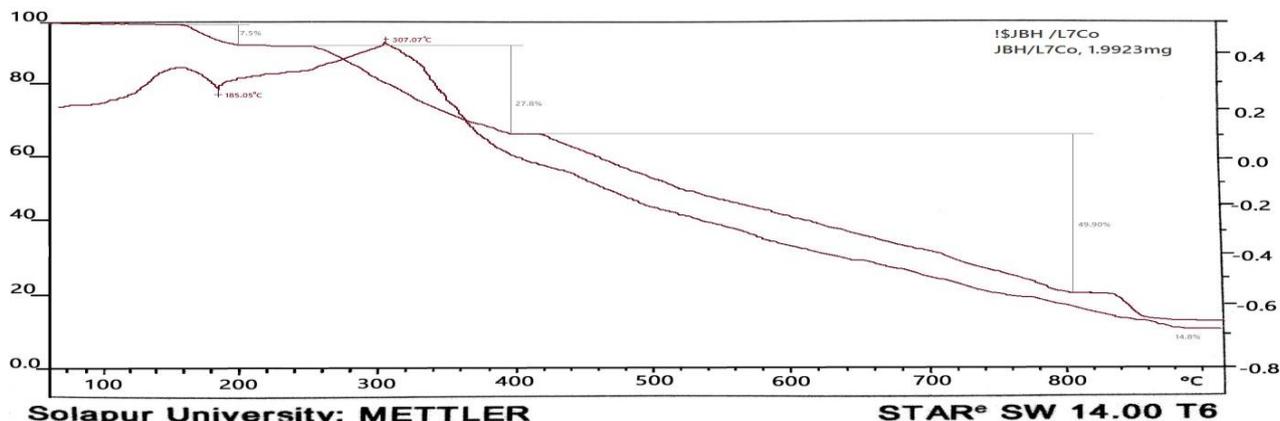
V) Magnetic Moment And UV Analysis

The UV scans of Iron(III), Manganese(II), Cobalt(II), Nickel(II), Copper(II) complexes were logged in dimethylformamide solvent. Three ${}^6A_{1g} \rightarrow {}^4T_{1g}(G)$, ${}^6A_{1g} \rightarrow {}^4T_{2g}(G)$ and ${}^6A_{1g} \rightarrow {}^4E_g(G)$ types electronic transition occurred on the basis of ultraviolet spectrum at 14465 cm^{-1} , 21317 cm^{-1} and 24252 cm^{-1} of the Iron chelate respectively, proposing an octahedral confirmation of Iron(III), which was also definite by magnetic moment ($5.92\ \mu_B$) (Balaji H. Jawale, et al., 2017; Patange, 2008; Lever A. B. P., 1968). The scans of the Copper(II) coordination compound involved of a wide-ranging band at 14219 cm^{-1} given to the ${}^2E_g \rightarrow {}^2T_{2g}$ electronic transition of a distorted octahedral configuration (Eichhorn G. L., et al., 1953). Along with this transition, the band detected at 25327 cm^{-1} arises as of INCT (intra ligand charge transfer). The UV scans of the Cobalt(II) coordination compound displayed three electronic transition at 9478 cm^{-1} given to ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, 18649 cm^{-1} signifying to ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and finally 21549 cm^{-1} which are arises to ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$, correspondingly (Balaji H. Jawale, et al., 2017; Patange, 2008), representing octahedral geometry nearby the Cobalt(II) ion. This geometry again confirmed by magnetic measurement of the Cobalt(II) coordination compound was $4.48\ \mu_B$. The UV spectrum of the Manganese(II) coordination material obtained three electronic absorption at 18351 cm^{-1} are predictable to ${}^6A_{1g} \rightarrow {}^4T_{1g}(G)$, 19759 cm^{-1} are assigned to ${}^6A_{1g} \rightarrow {}^4T_{2g}(G)$ and lastly 23151 cm^{-1} , which signifying to ${}^6A_{1g} \rightarrow {}^4T_{1g}$, ${}^4E_{1g}(4G)$ bands individually (Balaji H. Jawale, et al., 2017; Patange, 2008), showing an octahedral confirmation over the Manganese(II) coordination material. Finally we concluded the Manganese(II) coordination material are octahedral geometry on the basis of UV outcomes, supplementary definite by magnetic measurement ($5.72\ \mu_B$). The electronic absorption scans of the Nickel(II) coordination compound showed three electronic transition ${}^3A_{2g} \rightarrow {}^3T_{2g}(F)$, ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$, with respect to UV bands at 9350 cm^{-1} , 15700 cm^{-1} and 22469 cm^{-1} respectively. These electronic transition values, along with the magnetic measurement value ($3.28\ \mu_B$), suggesting an octahedral configuration of the Nickel(II) coordination compound (Lever A. B. P., 1968). The obtained values of ultraviolet scans and magnetic measurements conclude the stability of the complexes and tracks the order in terms of transition metal ions $\text{Cu(II)} > \text{Ni(II)} > \text{Co(II)}$ (Balaji H. Jawale, et al., 2017; Patange, 2008).

Table III: Magnetic and Ultraviolet-visible spectral data of Chelator and its complexes.

Ligand/ Complexes	μ_{eff}/μ_B	ν/cm^{-1}	Band assignment	Geometry
Ligand HL $\text{C}_{17}\text{H}_{16}\text{O}_7$	-	32442 40545	INCT ^a INCT	-
$\text{C}_{34}\text{H}_{30}\text{FeO}_{14}$	5.92	14465 21317 24252	${}^6A_{1g} \rightarrow {}^4T_{1g}(G)$ ${}^6A_{1g} \rightarrow {}^4T_{2g}(G)$ ${}^6A_{1g} \rightarrow {}^4E_g(G)$	Octahedral
$\text{C}_{34}\text{H}_{30}\text{CuO}_{14}$	1.98	14219 25327	${}^2E_g \rightarrow {}^2T_{2g}$ INCT	Distorted Octahedral
$\text{C}_{34}\text{H}_{30}\text{CoO}_{14}$	4.48	9478 18649 21549	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$	Octahedral
$\text{C}_{34}\text{H}_{30}\text{MnO}_{14}$	5.72	18351 19759 23151	${}^6A_{1g} \rightarrow {}^4T_{1g}(G)$ ${}^6A_{1g} \rightarrow {}^4T_{2g}(G)$ ${}^6A_{1g} \rightarrow {}^4T_{1g}$, ${}^4E_{1g}(4G)$	Octahedral
$\text{C}_{34}\text{H}_{30}\text{NiO}_{14}$	3.28	9350 15700 22469	${}^3A_{2g} \rightarrow {}^3T_{2g}(F)$ ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$	Octahedral

Evaluation:



Antimicrobial Activity

The synthesized ligand and its coordination compounds were evaluated for their *in vitro* antimicrobial activity against Gram-negative (*Shigella boydii*, *Escherichia Coli*) and Gram-positive (*Bacillus Cereus*, *Bacillus Megaterium*) bacterial strains and against *Saccharomyces Cerevisiae*, *Penicillium notatum* and *Aspergillus Oryzae* antifungal strains.

Table IV: Antibacterial effect of Chelator and its transition metal chelates

Test Compound	Inhibition zone diameter (mm)							
	<i>Bacillus Megaterium</i>		<i>Bacillus Cereus</i>		<i>Shigella Boydii</i>		<i>Escherichia Coli</i>	
	Concentration, 0.5mg ml ⁻¹	Concentration, 1mg ml ⁻¹	Concentration, 0.5mg ml ⁻¹	Concentration, 1mg ml ⁻¹	Concentration, 0.5mg ml ⁻¹	Concentration, 1mg ml ⁻¹	Concentration, 0.5mg ml ⁻¹	Concentration, 1mg ml ⁻¹
Chelator C₁₇H₁₆O₇	08	09	11	13	07	09	07	08
C ₃₄ H ₃₀ FeO ₁₄	09	11	15	16	11	13	-	-
C ₃₄ H ₃₀ CuO ₁₄	11	13	20	22	-	-	12	14
C ₃₄ H ₃₀ CoO ₁₄	07	09	16	18	13	15	11	13
C ₃₄ H ₃₀ MnO ₁₄	-	-	19	21	11	12	10	12
C ₃₄ H ₃₀ NiO ₁₄	08	10	-	-	10	12	-	-
Ciprofloxacin	34	36	50	54	28	30	30	32

The antibacterial record tells that transition metal chelates displayed enriched actions equaled to the free chalcone chelator. Such improved antibacterial effects of transition metal coordinated compound can be elucidated on the origin of chelation theory⁴⁵ in addition to overtone's conception⁴⁴.

Table V: Antifungal Effects of Chelator and its transition metal chelates.
[Yield of Mycelial dry weight in mg (% inhibition)]

Compound	Aspergillus Oryzae		Saccharomyces Cerevisiae		Penicillium Notatum	
	250 ppm	500 ppm	250 ppm	500 ppm	250 ppm	500 ppm
Chelator C₁₇H₁₆O₇	36(14)	22(16)	62(10)	48(12)	66(10)	52(12)
C ₃₄ H ₃₀ FeO ₁₄	48(18)	18(19)	71(12)	52(14)	72(16)	69(18)
C ₃₄ H ₃₀ CuO ₁₄	14(24)	08(26)	32(16)	22(18)	32(18)	21(20)
C ₃₄ H ₃₀ CoO ₁₄	18(16)	12(18)	27(14)	24(16)	47(14)	32(16)
C ₃₄ H ₃₀ MnO ₁₄	22(18)	14(20)	43(14)	36(15)	48(12)	39(13)
C ₃₄ H ₃₀ NiO ₁₄	52(16)	44(18)	54(12)	32(14)	77(10)	65(12)
Griseofulvin	40	42	39	40	32	34

The inhibition of growing of trial fungous detected for all chelates was not caused by any transition metal ions or chalcone ligand only, however was by reason of increasing result of equally transition metal ion as well as chalcone ligand in the chelates.

CONCLUSION

It was detected that in mass outcomes mother ion equivalent to the empirical mass of Chelator seem strong band at (333 m/e), this was a strong sign for the formation of the Chelator. Melting points of the coordination compounds are comparatively high, proposing good thermal stability at room temperature. TG/DSC analysis of the selected coordination compounds provides information about decay form and also supports existence of complexation and lattice water molecules in metal coordination compounds. The complexes are biologically active and exhibit enhanced antifungal activities compared to their parent ligands, hence further study of these complexes in agriculture could lead to interesting results.

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