SYNTHESIS, CHARACTERIZATION AND IN VITRO ANTIFUNGAL EVALUATION OF TRANSITION METAL COMPLEXES DERIVED FROM *N'*-SUBSTITUTED-4-METHYLPYPERIDINE-1-CARBOETHIOHYDRAZIDES

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ABSTRACT

Series of coordination complexes of Cr(III), Ni(II) and Zn(II) with various *N'*-substituted-4-methylpyperidine-1-carboethiohydrazides (**6a-f**) have been synthesized and characterized quantitatively and qualitatively by UV-visible spectroscopy, FTIR spectroscopy, ¹H NMR studies; microelemental analysis; electrical conductance values and magnetic susceptibility measurements. The metal complexes displayed greater antifungal activity than corresponding ligands and the order of their activity was found as [M(salmph)(Py)] > [M(fmpth)₂] > [M(talmph)₂]. The greater antifungal activity of metal complexes was found due to decrease in polarity of metal ions while coordinating with ligands during chelation process. The algicidal effect of few ligands viz. H₂salmph, Hfmpth and Htalmph and its chromium(III) complexes were also studied.

Keywords: Synthesis, Transition Metal Complexes, *N'*-Substituted-4-methylpyperidine-1-carboethiohydrazides, Antifungal Activity, Algicidal Effect.

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INTRODUCTION

Modern coordination chemistry involves various types of strategically designed and functionalized ligand systems. Among them, *N'*-substituted-4-methylpyperidine-1-carboethiohydrazides are a salient class of Schiff base ligands in coordination chemistry due to the dual coordinating sites (N and S) as potential donors.¹⁻⁵ Moreover, the coordination compounds of transition metal ions with bidentate ligands having N and S as donor sites are considered significant due to similarity with redox-active metalloenzymes.⁶⁻¹⁰ Furthermore, the potential of Schiff base ligands has urged the researchers to undertake them as an elite ligand.^{11,12}

The synthesis of Schiff base ligands and their corresponding metal complexes in a controlled manner becomes an important strategic pathway.¹³⁻¹⁶ In this study, we chose readily available, low-cost and potential organic molecules as precursors to synthesize the new Schiff base ligands and their metal complexes. The unique advantage of these Schiff base ligands is the change in their ligation behavior depending on the metallic systems and the stoichiometry.^{17,18} Therefore given above said advantages, we had synthesized, characterized the novel Schiff base ligands (*N'*-Substituted-4-methylpyperidine-1-carboethiohydrazides, (**6a-f**) and their corresponding complexes of Cr(III), Ni(II) and Zn(II) (**7a-z**). These Schiff base ligands (**6a-f**) and potential metal complexes were subjected to antifungal evaluation and algicidal effect.

EXPERIMENTAL

Materials and Methods

The chemicals and solvents were procured from Sigma-Aldrich, USA and Merck KGaA, Darmstadt, Germany and employed without any purification.

Characterization

Gouy's method was used to determine the magnetic susceptibility at room temperature. FTIR spectra were recorded in the form of KBr disc between 4000-400 cm^{-1} on Perkin-Elmer FTIR spectrophotometer. The electronic absorption spectra of complexes and ligands were recorded between 200-900 nm in ethanol or DMF. ^1H NMR spectra were obtained on Bruker 400 MHz NMR Spectrometer using TMS as an internal standard. Sulphur and halogen were estimated gravimetrically in the form of BaSO_4 and AgCl , respectively. The metal ions were estimated by standard methods.¹⁹

Synthesis of Ligands

4-Methylpiperidine-1-carbothiohydrazide (4) was synthesized using the reported method^{20,21} with few alterations (Scheme-I). The *N'*-Substituted-4-methylpiperidine-1-carbothiohydrazides (6a-f) were synthesized by refluxing an equimolar amount of 4-Methylpiperidine-1-carbothiohydrazide (4) and corresponding aldehyde/ketone (5a-f) in ethanol for 2 hours. On cooling, the resultant obtained was filtered, washed with cold ethanol and recrystallized from ethanol (Scheme-II). The physicochemical and analytical data of synthesized ligands (6a-f) are summarized in Table-1.

Table-1: Physico-analytical Data of Synthesized Ligands (6a-f)

Ligands	Color	Melting Point (°C)	Elemental Analysis: % Found (Calcd.)			
			C	H	N	S
4-Methylpiperidine-1-carbothiohydrazide (Hmpth, 4)	Flaky white	100	48.46 (48.55)	8.56 (8.67)	24.13 (24.27)	18.38 (18.49)
N'-cyclohexylidene-4-methylpiperidine-1-carbothiohydrazide (Hcycmpth, 6f)	Cream	149	61.47 (61.66)	10.48 (10.67)	16.44 (16.60)	12.32 (12.21)
N'-[(furan-2-yl)methylidene]-4-methylpiperidine-1-carbothiohydrazide (Hfmpth, 6a)	Cream	164	57.15 (57.37)	6.53 (6.77)	16.46 (16.73)	12.51 (12.74)
4-methyl-N'-[(thiophen-2-yl)methylidene]piperidine-1-carbothiohydrazide (Htalmph, 6b)	Cream	169	53.68 (53.93)	6.18 (6.36)	15.50 (15.73)	23.73 (23.97)
N'-benzylidene-4-methylpiperidine-1-carbothiohydrazide (Hbenmpth, 6c)	Cream	143	64.11 (64.36)	7.08 (7.27)	15.83 (15.49)	11.92 (11.86)
N'-[(2-hydroxyphenyl)methylidene]-4-methylpiperidine-1-carbothiohydrazide (H2Salmph, 6d)	White	158	60.48 (60.64)	6.62 (6.85)	14.95 (14.76)	11.31 (11.15)
N'-(2-hydroxy-1-phenylethylidene)-4-methylpiperidine-1-carbothiohydrazide (H2apmpth, 6e)	White	166	61.62 (61.85)	6.92 (6.81)	14.22 (14.43)	10.73 (10.99)

Synthesis of Metal Complexes

Chromium Complexes [CrL(H₂O)₂Cl₂] (LH=Hcycmpth, Hfmpth, Htalmph, Hbenmpth,) and [CrL(H₂O)₂Cl] (LH₂=H₂salmph, H₂apmpth)

An ethanolic solution of metal chloride (CrCl₃·6H₂O, 40-50 mL) was added an ethanolic solution of respective ligands (molar ratio - 1:1) and the reaction mixture was refluxed for 3-4 hours. The pH was maintained at ≈7-8 by adding sodium acetate solution. On cooling, the resultant metal complexes were filtered, washed with ethanol and dried over CaCl₂ (anhydrous) at room temperature.

Nickel and Zinc Metal Complexes

(a) [ML₂] (M=Ni²⁺ or Zn²⁺; LH = Hcycmpth, Hfmpth, Htalmph, Hbenmpth) and [M(LH)₂] (M = Ni²⁺ or Zn²⁺, LH₂ = H₂salmph, H₂apmpth)

To an ethanolic/aqueous solution of metal chloride (NiCl₂·6H₂O/ ZnCl₂·H₂O, 40-50 mL) was added hot ethanolic solution of appropriate ligand (1:2) slowly with continuous stirring and refluxed for 1-2 hours. On cooling, metal complexes were separated gradually. In the case of Zn(II) complexes, the complexes separated on adding an equal volume of water. The products were collected on a filter paper, washed with aqueous ethanol and dried over anhydrous CaCl₂ and finally vacuum dried.

[ML(NH₃)] (M=Ni²⁺ or Zn²⁺; LH₂= H₂salmph, H₂apmpth)

An aqueous solution of appropriate metal acetate [Ni(OAc)₂·4H₂O; Zn(OAc)₂·2H₂O, 40-50 mL] was allowed to reflux for 2 hours with 40-50 mL ethanolic solution of appropriate ligand (1:1) in the presence of 15% of NH₄OH and pH was maintained at ≈ 9. The resulting metal complexes were collected on a filter paper, washed with aqueous ethanol and dried over anhydrous CaCl₂ and finally vacuum dried.

[ML(Py)] (M=Ni²⁺ or Zn²⁺; LH₂= H₂salmph, H₂apmpth)

An aqueous solution of metal chloride (0.0015 mol, 50 mL) was treated with 3-4 mL of pyridine and the resultant solution was added in hot ethanolic solution (50 mL) of appropriate ligand (0.0015 mol) and refluxed for 1-2 hours. On cooling, the metal complexes were separated. The solid product was washed with aqueous ethanol and dried with KOH+CaCl₂. Physico-analytical data of the synthesized complexes are given in Table-2.

Table-2: Physico-analytical Data of Schiff Base Metal Complexes derived from *N'*-substituted-4-methylpiperidine-1-carbothiohydrazides (6a-f)

Complexes	Color	Elemental Analysis: % Found (Calc.)					μ_{eff} (B.M.)	Λ_M (ohm ⁻¹ cm ² mol ⁻¹)
		M	C	H	N	S		
[Cr(cycmpth)(H ₂ O) ₂ Cl ₂], 7a	Green	12.47 (12.68)	37.94 (37.81)	5.92 (5.89)	10.11 (10.24)	7.95 (7.80)	3.87	5.71
[Cr(fmpth)(H ₂ O) ₂ Cl ₂], 7b	Dark green	12.50 (12.71)	34.88 (34.73)	4.69 (4.88)	10.11 (10.26)	7.66 (7.82)	3.90	8.33
[Cr(talmpth)(H ₂ O) ₂ Cl ₂], 7c	Dark Green	12.08 (12.23)	33.67 (33.88)	4.52 (4.70)	9.68 (9.88)	14.88 (14.95)	3.89	7.15
[Cr(benmpth)(H ₂ O) ₂ Cl ₂], 7d	Dark Green	12.18 (12.38)	39.90 (39.80)	5.28 (5.17)	9.73 (9.62)	7.42 (7.61)	3.88	6.29
[Cr(salmpth)(H ₂ O) ₂ Cl], 7e	Brown	12.73 (12.98)	41.76 (41.94)	5.53 (5.34)	10.31 (10.44)	7.76 (7.69)	3.89	7.74
[Cr(apmpth)(H ₂ O) ₂ Cl], 7f	Brown	12.32 (12.54)	43.22 (43.12)	5.83 (5.73)	9.97 (9.83)	7.53 (7.72)	3.90	7.37
[Ni(cycmpth) ₂], 7g	Brown	10.46 (10.51)	55.40 (55.61)	7.23 (7.48)	14.75 (14.97)	11.18 (11.40)	Diamag.	6.53
[Zn(cycmpth) ₂], 7h	Light Yellow	11.25 (11.46)	54.88 (54.72)	7.26 (7.40)	14.65 (14.81)	11.11 (11.28)	Diamag.	5.74
[Ni(fmpth) ₂], 7i	Brown	10.38 (10.55)	51.33 (51.52)	5.57 (5.72)	14.88 (15.02)	11.26 (11.44)	Diamag.	7.45
[Zn(fmpth) ₂], 7j	Yellow	11.31 (11.50)	50.73 (50.97)	5.48 (5.66)	14.94 (14.86)	11.20 (11.32)	Diamag.	8.92
[Ni(talmpth) ₂], 7k	Brown	9.77 (9.98)	48.55 (48.73)	5.24 (5.41)	14.05 (14.21)	21.44 (21.65)	Diamag.	6.28
[Zn(talmpth) ₂], 7l	Yellow	10.63 (10.88)	48.11 (48.24)	5.17 (5.36)	14.15 (14.07)	21.30 (21.44)	Diamag.	7.54
[Ni(benmpth) ₂], 7m	Orange Red	10.08 (10.22)	58.06 (58.23)	5.71 (5.89)	14.32 (14.55)	10.86 (10.79)	Diamag.	4.90
[Zn(benmpth) ₂], 7n	Orange Yellow	10.93 (11.04)	57.51 (57.63)	5.61 (5.83)	14.26 (14.10)	10.76 (10.67)	Diamag.	10.52
[Ni(HSalmpth) ₂], 7o	Reddish Brown	9.44 (9.68)	54.97 (55.07)	5.33 (5.58)	13.58 (13.79)	10.32 (10.50)	Diamag.	6.4
[Zn(HSalmpth) ₂], 7p	Yellow	10.32 (10.56)	55.25 (55.63)	5.26 (5.52)	13.48 (13.65)	10.27 (10.40)	Diamag.	7.36
[Ni(Hapmpth) ₂], 7q	Brick Red	9.12 (9.26)	56.28 (56.51)	5.64 (5.96)	12.93 (13.18)	9.88 (10.04)	Diamag.	6.50
[Zn(Hapmpth) ₂], 7r	Yellow	9.87 (10.01)	55.74 (55.98)	6.31 (6.53)	12.87 (12.76)	9.73 (9.65)	Diamag.	7.75
[Ni(Salmpth)(NH ₃)], 7s	Red	16.63 (16.80)	47.67 (47.86)	5.48 (5.69)	15.74 (15.65)	8.96 (8.91)	Diamag.	9.63
[Zn(Salmpth)(NH ₃)], 7t	Yellow	18.03 (18.20)	47.86 (47.05)	5.47 (5.60)	15.47 (15.68)	8.68 (8.96)	Diamag.	11.31
[Ni(apmpth)(NH ₃)], 7u	Reddish Brown	15.98 (16.06)	49.14 (49.31)	5.93 (6.02)	15.17 (15.34)	8.58 (8.46)	Diamag.	10.85
[Zn(apmpth)(NH ₃)], 7v	Yellow	17.37 (17.52)	48.36 (48.51)	5.68 (5.92)	14.92 (14.99)	8.47 (8.62)	Diamag.	11.26
[Ni(Salmpth)Py], 7w	Red	14.11 (14.28)	54.98 (55.02)	5.11 (5.32)	13.34 (13.55)	7.51 (7.74)	Diamag.	8.28
[Ni(apmpth)Py], 7x	Reddish Brown	13.62 (13.81)	56.03 (56.20)	5.41 (5.62)	12.92 (13.01)	7.23 (7.49)	Diamag.	9.57
[Zn(Salmpth)Py], 7y	Light Yellow	15.33 (15.51)	54.24 (54.41)	5.09 (5.25)	13.12 (13.36)	7.45 (7.63)	Diamag.	10.12
[Zn(apmpth)Py], 7z	Yellow	14.88 (14.71)	55.20 (55.42)	5.36 (5.54)	12.64 (12.93)	7.18 (7.11)	Diamag.	6.32

Table-3: Electronic Spectral Data of Schiff Base Metal Complexes derived from *N'*-substituted-4-methylpiperidine-1-carbothiohydrazides (6a-f)

Complexes	Electronic Bond Positions	Assignments
[Cr(cycmpth) ₂ (H ₂ O) ₂ Cl ₂]	310w, 425s, 568sbr	${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{2g}(P)$
[Cr(fmpth) ₂ (H ₂ O) ₂ Cl ₂]	325w, 440sh, 580sbr	${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{2g}(P)$
[Cr(talmpth) ₂ (H ₂ O) ₂ Cl ₂]	315w, 432s, 570sbr	${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{2g}(P)$
[Cr(benmpth) ₂ (H ₂ O) ₂ Cl ₂]	318w, 445s, 575sbr	${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{2g}(P)$
[Cr(salmpth)(H ₂ O) ₂ Cl]	320w, 452s, 582sbr	${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{2g}(P)$
[Cr(apmpth)(H ₂ O) ₂ Cl]	325w, 455s, 585sbr	${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$; ${}^4A_{2g}(F) \rightarrow {}^4T_{2g}(P)$
[Ni(cycmpth) ₂]	290ms, 440sh	$\pi-\pi^*$; ${}^1A_{1g} \rightarrow {}^1B_{1g}$
[Ni(fmpth) ₂]	375sbr, 440br, 552m	C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$; ${}^1A_{1g} \rightarrow {}^1A_{2g}$
[Ni(talmpth) ₂]	370sbr, 435br, 545m	C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$; ${}^1A_{1g} \rightarrow {}^1A_{2g}$
[Ni(benmpth) ₂]	378br, 450m, 560m	C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$; ${}^1A_{1g} \rightarrow {}^1A_{2g}$
[Ni(HSalmpth) ₂]	368b, 455mb, 565m	C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$; ${}^1A_{1g} \rightarrow {}^1A_{2g}$
[Ni(Hapmpth) ₂]	272s, 370br, 460sh, 567m	$\pi-\pi^*$; C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$; ${}^1A_{1g} \rightarrow {}^1A_{2g}$
[Ni(Salmpth)(NH ₃) ₃]	262s, 370sbr, 450sh	$\pi-\pi^*$; C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$
[Ni(apmpth)(NH ₃) ₃]	260s, 365sbr, 447sh	$\pi-\pi^*$; C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$
[Ni(salmpth)(Py) ₂]	265s, 372sbr, 450sh	$\pi-\pi^*$; C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$
[Ni(apmpth)(Py) ₂]	262s, 368sbr, 445sh	$\pi-\pi^*$; C-T; ${}^1A_{1g} \rightarrow {}^1B_{1g}$

(Sh = shoulder, m = medium, s= strong, sbr = strong and broad)

RESULTS AND DISCUSSION

The analytical data recorded in Table-2 were found fully consistent with the composition of the complexes synthesized. Thermogravimetric analysis shows that all the synthesized complexes are stable below 180-190 °C. The complexes are lesser soluble in ordinary organic solvents and are much soluble in DMSO, DMF and dioxane. Molar conductance of all the complexes was found in the range 5-15 $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ displaying their non-ionic nature.²² The Cr(III) complexes have magnetic moments value between 3.87-3.91 B.M. indicating their octahedral geometry. The diamagnetism of all Ni(II) complexes indicates their square planar geometry.²³ The preference for tetrahedral stereochemistry for complexes of d^{10} electronic system and observed metal-ligand stoichiometry indicate the tetrahedral structure for Zn(II) complexes, which were established as diamagnetic.²⁴

Electronic Spectral Studies

The chemical spectra of all Cr(III) complexes were obtained in DMSO. The complexes exhibited bands at 16806-18518 cm^{-1} (595-540 nm), 22831-23539 cm^{-1} (438-425 nm) and 31250-32573 cm^{-1} (320-307 nm) which may be assigned to ${}^4A_{2g}(F) \rightarrow {}^4T_{2g}(F)$ (ν_1), ${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(F)$ (ν_2) and ${}^4A_{2g}(F) \rightarrow {}^4T_{1g}(P)$ (ν_3) transitions sequentially in order of increasing energy. Out of these three spin-allowed $d-d$ transitions, the one of lowest energy is a direct measure of the crystal field splitting Δ or 10Dq. These values are in better compliance with the reported values for octahedral Cr(III) complexes^{25, 26}. The solid reflectance spectra of Ni(II) complexes below 400 nm display strong absorptions attributed to charge transfer band or ligand absorptions. A weak band or shoulder in the region 420-480 nm and 500-600 nm are attributed to ${}^1A_{1g} \rightarrow {}^1B_{1g}$ and ${}^1A_{1g} \rightarrow {}^1A_{2g}$ transitions respectively in a planner arrangement of Ni(II) atom geometry²³. The broadband of thioamide ligands was observed in the regions ≈ 365 nm and suffered a blue shift in the complexes due to thioenolization, which broadens considerably due to overlap of ligands to metal charge transfer transitions²⁷ (Table-3).

FTIR Spectral Studies

The IR spectra of ligands exhibited bands at $1625 \pm 5 \text{ cm}^{-1}$, which is due to $\nu_{\text{C=N}}$ of the azomethine group. The same band is observed at a lower frequency by 15-10 cm^{-1} as a strong band in all the complexes of Cr(III), Ni(II) and Zn(II) attributed to the coordination through azomethine nitrogen. It is further confirmed by the appearance of azine chromophore ($>\text{C=N-N=C}<$) around 1605-1600 cm^{-1} in the

complexes. The characteristic phenolic $\nu_{(\text{O-H})}$ band due to the presence of -OH group at ortho position of ligands (H_2Salmph) and (H_2apmth) was observed at $3293\text{--}3180\text{ cm}^{-1}$, disappeared in the monoligated complexes of Cr(III), Ni(II) and Zn(II) having compositions $[\text{CrL}(\text{H}_2\text{O})_2\text{Cl}]$, $[\text{ML}(\text{Py})]$, $[\text{ML}(\text{NH}_3)]$ ($\text{M}=\text{Ni}^{2+}$ or Zn^{2+} , $\text{LH}_2=\text{H}_2\text{Salmph}$, H_2apmth) suggesting the coordination by the phenolic oxygen after deprotonation. This broadband is intact in bischelates of Ni(II) and Zn(II) having compositions $[\text{ML}_2]$ and $[\text{M}(\text{LH}_2)]$ ($\text{LH}=\text{Hcycmpth}$, Hfmpth , Htalmph , Hbenmpth and $\text{LH}_2=\text{H}_2\text{Salmph}$, H_2apmth) and attributed to uncoordinated -OH and involved in H-bonding. In all the aqua complexes of Cr(III) having composition $[\text{ML}(\text{H}_2\text{O})]$ ($\text{LH}_2=\text{H}_2\text{Salmph}$, H_2apmth) a broad band appeared in the range of $3400\text{--}3300\text{ cm}^{-1}$ showing the existence of water. The rocking band of H_2O is not observed for coordinated water which indicates the lattice nature of H_2O in the complexes.²⁸ Drastic conditions required to dehydrate these complexes also confirm a structure containing water molecules in these complexes. The absence of any band in the region of $2600\text{--}2500\text{ cm}^{-1}$ due to $\nu_{(\text{SH})}$ shows that all the ligands exist in thio-keto form, which is also supported by ^1H NMR studies. The IR absorption bands of ν_{NH} in the region $3300\text{--}3100\text{ cm}^{-1}$ of the free ligands disappeared in all the complexes indicating that the ligands are deprotonated in the complexes. The thioamide bands (IV) of the free ligands ($935\text{--}865\text{ cm}^{-1}$) which have a major contribution from $\nu_{\text{C=S}}$ vibration is observed at $705 \pm 20\text{ cm}^{-1}$ in all the complexes, showing the coordination with deprotonated thiol sulphur. The coordination of NH_3 in the complex $[\text{ML}(\text{NH}_3)]$ ($\text{M}=\text{Ni}^{2+}$ or Zn^{2+} , $\text{LH}_2=\text{H}_2\text{Salmph}$, H_2apmth) is indicated by the appearance of bands at $3300\text{--}3100$, 1590 , 1280 and 850 cm^{-1} assigned to ν_{NH_3} , δ_{NH_3} , ρ_{NH_3} sequentially. The pyridine ring breathing mode of vibration observed at $1025 \pm 5\text{ cm}^{-1}$ is regarded as a coordinated pyridine molecule.²⁹ The $\nu_{\text{C=N}}$ for such complexes was observed at $1595 \pm 5\text{ cm}^{-1}$. In the far-infrared region, all the complexes displayed several bands at $460\text{--}410$, $400\text{--}380$, $360\text{--}320$ and $300\text{--}230\text{ cm}^{-1}$ those are assigned to M-O , M-N , M-S , M-Cl *str* vibration, respectively.

It was observed that in slightly alkaline conditions $\text{pH} \approx 7\text{--}8$ (or 9), the ligands H_2Salmph and H_2apmth , react with Cr(III), Ni(II) or Zn(II) salts giving rise to monoligated complexes $[\text{CrL}(\text{H}_2\text{O})_2\text{Cl}]$, $[\text{ML}(\text{Py})]$ and $[\text{ML}(\text{NH}_3)]$, ($\text{M} = \text{Ni}^{2+}$ or Zn^{2+}). It behaves in a dibasic tridentate manner and bonding takes place through O, N and S. In feebly alkaline or neutral conditions these and other ligands are found to act in a bidentate monobasic way bonding through azomethine N-atom and S-atom (*via* thioenolisation) keeping the -OH free.

^1H NMR Studies

The signals due to -NH proton at $\delta \approx 11.8$ ppm and phenolic -OH at $\delta \approx 12.4\text{--}13.04$ ppm of ligands H_2Salmph and H_2apmth disappeared in its monoligated complexes of compositions $[\text{CrL}(\text{H}_2\text{O})_2\text{Cl}]$, $[\text{ML}(\text{Py})]$ and $[\text{ML}(\text{NH}_3)]$, ($\text{M} = \text{Ni}^{2+}$ or Zn^{2+}), which shows the dibasic tridentate nature of these ligands in the complexes and bonding through O, N and S atoms. In the neutral bischelates of Ni(II) and Zn(II) signals due to -NH proton at $\delta 11\text{--}12$ ppm of ligands disappears in complexes suggesting the thioenolization and coordination through deprotonated thiol sulphur atoms. In neutral, bischelates of H_2Salmph and H_2apmth of Ni(II) and Zn(II) the signals due to phenolic -OH at $\approx 12.4\text{--}13.04$ ppm remain unaffected in complexes and its downfield shift than normal phenolic -OH shows H-bonding. The chemical shift $\delta 7.1\text{--}7.3$ ppm of aromatic protons undergoes a slight downfield shift $\delta 7.4\text{--}7.9$ ppm on complexation.

Thus, based on the above studies, the following tentative structures (Fig. 1.) have been proposed for the synthesized complexes.

Antifungal Evaluation

4-Methylpiperidine-1-carbothiohydrazide (4), *N'*-substituted-4-methylpiperidine-1-carbothiohydrazides (6a-f), monoligated pyridine complexes of *N'*-substituted-4-methylpiperidine-1-carbothiohydrazides derived from salicylaldehyde $[\text{M}(\text{salmph})(\text{Py})]$ and bis-ligated complexes derived from furfural $[\text{M}(\text{fmpth})_2]$ and thiophene-2-aldehyde $[\text{M}(\text{talmph})_2]$, ($\text{M}=\text{Ni}^{2+}$ or Zn^{2+}) have been tested for antifungal activity. Antifungal activity of these compounds was evaluated by Agar-based disk-diffusion method³⁰ against fungal strains *C. albicans* and *A. niger* using Griseofulvin as a standard drug. The results are

shown in Table-4. All the tested compounds were found to possess moderate to significant antifungal activity. The complexes were found more active than ligands and the order of their activity was found as $[M(\text{salmph})(\text{Py})] > [M(\text{fmpth})_2] > [M(\text{talmph})_2]$.

The algacidal effect of CrCl_3 , the ligands- H_2salmph , Hfmpth and Htalmph and their chromium complexes were studied on the growth of green algae- *chlorella*. The ligands and complexes were found less toxic than metal chloride. The lesser algacidal effect of ligands and complexes concerning metal ions may be attributed to their larger size.

Fig. -1: Tentative Structures of the Complexes synthesized. Where $X = \text{Py}$ or NH_3 ; $M = \text{Ni}^{2+}$ or Zn^{2+} . The parts involving O, N and S atoms in the above structures represent the donor system of the ligands

Table-4: Antifungal Activity of 4-Methylpiperidine-1-carbothiohydrazide (4), N' -Substituted-4-methylpiperidine-1-carbothiohydrazides (6a-f) and Schiff base metal complexes (7w, 7y, 7i, 7j, 7k, 7l)

Tested Compound at a Concentration of 100 $\mu\text{g/ml}$	Zone of Inhibition (in mm)	
	<i>C. albicans</i>	<i>A. niger</i>
Hmpth, 4	08	10
Hfmpth, 6a	10	12
Htalmph, 6b	09	10
Hbenmpth, 6c	05	-
H_2Salmph , 6d	12	10
$(\text{H}_2\text{apmpth})$, 6e	08	11
Hcycmpth, 6f	12	10
$[\text{Ni}(\text{Salmph})\text{Py}]$, 7w	17	19
$[\text{Zn}(\text{Salmph})\text{Py}]$, 7y	19	20
$[\text{Ni}(\text{fmpth})_2]$, 7i	14	11
$[\text{Zn}(\text{fmpth})_2]$, 7j	15	14
$[\text{Ni}(\text{talmph})_2]$, 7k	12	10
$[\text{Zn}(\text{talmph})_2]$, 7l	14	10
Griseofulvin	22	25

CONCLUSION

Three bidentate N, S donor type N' -Substituted-4-methylpiperidine-1-carbothiohydrazides (**6a-f**) were synthesized using cyclohexanone, thiophene-2-aldehyde, benzaldehyde, salicylaldehyde, furfural and 2-hydroxyacetophenone. These ligands were complexed with transition metals to produce their metal complexes. Physico-analytical data including spectral data and elemental analysis of ligands & their metal(II) complexes were shown as per proposed structures. Potential ligands & their metal complexes

were tested for antifungal and algacidal potential. Results showed that metal complexes have greater antifungal activity in comparison to corresponding ligands. The greater antifungal activity of metal complexes was shown due to the chelation phenomenon, which coordinates the metal ion with ligands and makes a reduction in its polarity.

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