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

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ABSTRACT
Series of coordination complexes of Cr(III), Ni(II) and Zn(II) with various N'-substituted-4-methylpiperidine-1-carbothiohydrazides (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(salmpth)(Py)] > [M(fmpth)2] > [M(talmpth)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 algacidal effect of few ligands viz. H2salmpth, Hfmpth and Htalmpth and its chromium(III) complexes were also studied.

Keywords: Synthesis, Transition Metal Complexes, N'-Substituted-4-methylpiperidine-1-carbothiohydrazides, Antifungal Activity, Algacidal Effect.

INTRODUCTION
Modern coordination chemistry involves various types of strategically designed and functionalized ligand systems. Among them, N'-substituted-4-methylpiperidine-1-carbothiohydrazides 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-methylpiperidine-1-carbothiohydrazides, (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. $^1$H 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.

Scheme-I: Synthesis of 4-Methylpiperidine-1-carbothiohydrazide (4)

Scheme-II: Synthesis of $N'$-Substituted-4-methylpiperidine-1-carbothiohydrazides (6a-f)
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) | 16.64 (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 (Htalmpth, 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 (H2Salmpth, 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(H$_2$O)$_2$Cl$_2$** (LH=Hcycmpth, Hfmpth, Htalmpth, Hbenmpth,) and **CrL(H$_2$O)$_2$Cl** (LH$_2$=H$_2$salmpth, H$_2$apmpth)

An ethanolic solution of metal chloride (CrCl$_3$·6H$_2$O, 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 CaCl$_2$ (anhydrous) at room temperature.

Nickel and Zinc Metal Complexes

(a) **[ML$_2$]** (M=Ni$^{2+}$ or Zn$^{2+}$; LH = Hcycmpth, Hfmpth, Htalmpth, Hbenmpth) and **[ML(H$_2$O)$_2$Cl]** (LH$_2$=H$_2$salmpth, H$_2$apmpth)

To an ethanolic/aqueous solution of metal chloride (NiCl$_2$·6H$_2$O/ ZnCl$_2$·H$_2$O, 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 CaCl$_2$ and finally vacuum dried.

(b) **[ML(NH$_3$)$_2$]** (M=Ni$^{2+}$ or Zn$^{2+}$; LH$_2$=H$_2$salmpth, H$_2$apmpth)

An aqueous solution of metal acetate [Ni(OAc)$_2$·4H$_2$O; Zn(OAc)$_2$·2H$_2$O, 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 NH$_4$OH and pH was maintained at ≈ 9. The resulting metal complexes were collected on a filter paper, washed with aqueous ethanol and dried over anhydrous CaCl$_2$ and finally vacuum dried.

(c) **[ML(Py)]** (M=Ni$^{2+}$ or Zn$^{2+}$; LH$_2$=H$_2$salmpth, H$_2$apmpth)

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+CaCl$_2$. Physico-analytical data of the synthesized complexes are given in Table 2.
| Complexes                          | Color          | Elemental Analysis: % Found (Calc.) | μeff (B.M.) | ΛM (ohm⁻¹ cm² mol⁻¹) |
|-----------------------------------|----------------|-------------------------------------|------------|----------------------|
| [Cr(cycmpth)(H₂O)₂Cl₂], 7a       | Green          | M 12.47 (12.68) C 37.94 (37.81) H 5.92 (5.89) N 10.11 (10.24) S 7.95 (7.80) | 3.87       | 5.71                 |
| [Cr(fmpth)(H₂O)₂Cl₂], 7b         | Dark Green     | M 12.50 (12.71) C 34.88 (34.73) H 4.69 (4.88) N 10.11 (10.26) S 7.66 (7.82) | 3.90       | 8.33                 |
| [Cr(talmpth)(H₂O)₂Cl₂], 7c       | Dark Green     | M 12.08 (12.23) C 33.67 (33.88) H 4.52 (4.70) N 9.68 (9.88) S 14.88 (14.95) | 3.89       | 7.15                 |
| [Cr(benmpth)(H₂O)₂Cl₂], 7d       | Dark Green     | M 12.18 (12.38) C 39.90 (39.80) H 5.28 (5.17) N 9.73 (9.62) S 7.42 (7.61) | 3.88       | 6.29                 |
| [Cr(salmpth)(H₂O)₂Cl₂], 7e       | Brown          | M 12.73 (12.98) C 41.76 (41.94) H 5.53 (5.34) N 10.31 (10.44) S 7.76 (7.69) | 3.89       | 7.74                 |
| [Cr(apmpth)(H₂O)₂Cl₂], 7f        | Brown          | M 12.32 (12.54) C 43.22 (43.12) H 5.83 (5.73) N 9.97 (9.83) S 7.53 (7.72) | 3.90       | 7.37                 |
| [Ni(cycmpth)₃], 7g               | Brown          | M 10.46 (10.51) C 55.40 (55.61) H 7.23 (7.48) N 14.75 (14.97) S 11.18 (11.40) | Diamag.    | 6.53                 |
| [Zn(cycmpth)₂], 7h               | Light Yellow   | M 11.25 (11.46) C 54.88 (54.72) H 7.26 (7.40) N 14.65 (14.81) S 11.11 (11.28) | Diamag.    | 5.74                 |
| [Ni(fmpth)₂], 7i                  | Brown          | M 10.38 (10.55) C 51.33 (51.52) H 5.57 (5.72) N 14.88 (15.02) S 11.26 (11.44) | Diamag.    | 7.45                 |
| [Zn(fmpth)₂], 7j                  | Yellow         | M 11.31 (11.50) C 50.73 (50.97) H 5.48 (5.66) N 14.94 (14.86) S 11.20 (11.32) | Diamag.    | 8.92                 |
| [Ni(talmpth)₂], 7k                | Brown          | M 9.77 (9.98) C 48.55 (48.73) H 5.24 (5.41) N 14.05 (14.21) S 21.44 (21.65) | Diamag.    | 6.28                 |
| [Zn(talmpth)₂], 7l                | Yellow         | M 10.63 (10.88) C 48.11 (48.24) H 5.17 (5.36) N 14.15 (14.07) S 21.30 (21.44) | Diamag.    | 7.54                 |
| [Ni(benmpth)₃], 7m                | Orange Red     | M 10.08 (10.22) C 58.06 (58.23) H 5.71 (5.89) N 14.32 (14.55) S 10.86 (10.79) | Diamag.    | 4.90                 |
| [Zn(benmpth)₂], 7n                | Orange Yellow  | M 10.93 (11.04) C 57.51 (57.63) H 5.61 (5.83) N 14.26 (14.10) S 10.76 (10.67) | Diamag.    | 10.52                |
| [Ni(HSalmpth)₂], 7o               | Reddish Brown  | M 9.44 (9.68) C 54.97 (55.07) H 5.33 (5.58) N 13.58 (13.79) S 10.32 (10.50) | Diamag.    | 6.4                  |
| [Zn(HSalmpth)₂], 7p               | Yellow         | M 10.32 (10.56) C 55.25 (55.63) H 5.26 (5.52) N 13.48 (13.65) S 10.27 (10.40) | Diamag.    | 7.36                 |
| [Ni(Hapmpth)₂], 7q                | Brick Red      | M 9.12 (9.26) C 56.28 (56.51) H 5.64 (5.96) N 12.93 (13.18) S 9.88 (10.04) | Diamag.    | 6.50                 |
| [Zn(Hapmpth)₂], 7r                | Yellow         | M 9.87 (10.01) C 55.74 (55.98) H 6.31 (6.53) N 12.87 (12.76) S 9.73 (9.65) | Diamag.    | 7.75                 |
| [Ni(Salmpth)(NH₃)₃], 7s           | Red            | M 16.63 (16.80) C 47.67 (47.86) H 5.48 (5.69) N 15.74 (15.65) S 8.96 (8.91) | Diamag.    | 9.63                 |
| [Zn(Salmpth)(NH₃)₃], 7t           | Yellow         | M 18.03 (18.20) C 47.86 (47.05) H 5.47 (5.60) N 15.47 (15.68) S 8.68 (8.96) | Diamag.    | 11.31                |
| [Ni(apmpth)(NH₃)₃], 7u            | Reddish Brown  | M 15.98 (16.06) C 49.14 (49.31) H 5.93 (6.02) N 15.17 (15.34) S 8.58 (8.46) | Diamag.    | 10.85                |
| [Zn(apmpth)(NH₃)₃], 7v            | Yellow         | M 17.37 (17.52) C 48.36 (48.51) H 5.68 (5.92) N 14.92 (14.99) S 8.47 (8.62) | Diamag.    | 11.26                |
| [Ni(Salmpth)Py], 7w               | Red            | M 14.11 (14.28) C 54.98 (55.02) H 5.11 (5.32) N 13.34 (13.55) S 7.51 (7.74) | Diamag.    | 8.28                 |
| [Ni(apmpth)Py], 7x                 | Reddish Brown  | M 13.62 (13.81) C 56.03 (56.20) H 5.41 (5.62) N 12.92 (13.01) S 7.23 (7.49) | Diamag.    | 9.57                 |
| [Zn(Salmpth)Py], 7y               | Light Yellow   | M 15.33 (15.51) C 54.24 (54.41) H 5.09 (5.25) N 13.12 (13.36) S 7.45 (7.63) | Diamag.    | 10.12                |
| [Zn(apmpth)Py], 7z                 | Yellow         | M 14.88 (14.71) C 55.20 (55.42) H 5.36 (5.54) N 12.64 (12.93) S 7.18 (7.11) | Diamag.    | 6.32                 |
**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 Ω^{-1} cm^2 mol^{-1} displaying their non-ionic nature.

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. The preference for tetrahedral stereochemistry for complexes of Ni(II) atom geometry.

**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 \( {^4}\text{A}_{2g} \rightarrow {^4}\text{T}_{2g} \) (v_1), \( {^4}\text{A}_{2g} \rightarrow {^4}\text{T}_{1g} \) (v_2), \( {^4}\text{A}_{2g} \rightarrow {^4}\text{T}_{1g} \) (v_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 \( \Delta \) 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 \( {^4}\text{A}_{1g} \rightarrow {^1}\text{B}_{1g} \) and \( {^4}\text{A}_{1g} \rightarrow {^4}\text{A}_{2g} \) transitions respectively in a planner arrangement of Ni(II) atom geometry.\(^{27}\) The broadband of thioamide ligands was observed in the regions ≈ 365 nm and suffered a blue shift in the complexes due to thienolization, which broadens considerably due to overlap of ligands to metal charge transfer transitions\(^{27}\) (Table-3).

**FTIR Spectral Studies**

The IR spectra of ligands exhibited bands at 1625 ± 5 cm^{-1}, which is due to νC=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 (νC=N-N-C=) around 1605-1600 cm^{-1} in the

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**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                      |
|----------------------|---------------------------|----------------------------------|
| \([\text{Cr(cycmpth)}]_2(\text{H}_2\text{O})_2\text{Cl}_2\) | 310w, 425s, 568sbr          | \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(P)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(F)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{2g}(P)\) |
| \([\text{Cr(fmpth)}]_2(\text{H}_2\text{O})_2\text{Cl}_2\) | 325w, 440s, 580sbr          | \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(P)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(F)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{2g}(P)\) |
| \([\text{Cr(talmpth)}]_2(\text{H}_2\text{O})_2\text{Cl}_2\) | 318w, 445s, 575sbr          | \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(P)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(F)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{2g}(P)\) |
| \([\text{Cr(benmpth)}]_2(\text{H}_2\text{O})_2\text{Cl}_2\) | 320w, 452s, 582sbr          | \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(P)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(F)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{2g}(P)\) |
| \([\text{Cr(fmpth)}]_2(\text{H}_2\text{O})_2\text{Cl}_2\) | 325w, 455s, 585sbr          | \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(P)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{1g}(F)\); \(4\text{A}_{2g}(F) \rightarrow ^4\text{T}_{2g}(P)\) |
| \([\text{Ni(mcppth)}]_2\) | 290ms, 440s               | \(\pi-\pi^*; ^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}\) |
| \([\text{Ni(talmpth)}]_2\) | 375sbr, 440br, 552m         | \(\text{C-T}; ^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}\); \(^1\text{A}_{1g} \rightarrow ^1\text{A}_{2g}\) |
| \([\text{Ni(benmpth)}]_2\) | 378sbr, 455br, 545m         | \(\text{C-T}; ^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}\); \(^1\text{A}_{1g} \rightarrow ^1\text{A}_{2g}\) |
| \([\text{Ni(fmpth)}]_2\) | 368b, 455mb, 565m           | \(\text{C-T}; ^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}\); \(^1\text{A}_{1g} \rightarrow ^1\text{A}_{2g}\) |
| \([\text{Ni(Salmpth)}]_2\) | 272s, 370br, 460sh, 567m     | \(\pi-\pi^*; \text{C-T}; ^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}\) |
| \([\text{Ni(apmpth)}]_2\) | 262s, 370br, 450s           | \(\pi-\pi^*; \text{C-T}; ^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}\) |
| \([\text{Ni(salmpth)}]_2\) | 265s, 365s, 447s           | \(\pi-\pi^*; \text{C-T}; ^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}\) |
| \([\text{Ni(apmpth)}]_2\) | 262s, 368s, 445s           | \(\pi-\pi^*; \text{C-T}; ^1\text{A}_{1g} \rightarrow ^1\text{B}_{1g}\) |

(Sh = shoulder, m = medium, s= strong, sbr = strong and broad)
complexes. The characteristic phenolic ν(O–H) band due to the presence of -OH group at ortho position of ligands (H₂Salmpth) and (H₂apmpth) was observed at 3293-3180 cm⁻¹, disappeared in the monoligated complexes of Cr(III), Ni(II) and Zn(II) having compositions [CrL(H₂O)₂Cl], [ML(Py)], [ML(NH₃)] (M=Ni²⁺ or Zn²⁺), LH₂=H₂Salmpth, H₂apmpth) suggesting the coordination by the phenolic oxygen after deprotonation. This broadband is intact in bischelates of Ni(II) and Zn(II) having compositions [ML₂] and [ML(LH₂) (LH=Hecympth, Hfmpth, Htalmpth, Hbenmpth and LH₂=H₂Salmpth, H₂apmpth) and attributed to uncoordinated –OH and involved in H-bonding. In all the aqua complexes of Cr(III) having composition [ML(H₂O)] (LH₂=H₂Salmpth, H₂apmpth) a broad bond appeared in the range of 3400-3300 cm⁻¹ showing the existence of water. The rocking band of H₂O is not observed for coordinated water which indicates the lattice nature of H₂O in the complexes. 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 2600-2500 cm⁻¹ due to ν(ν(H₂O)) 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 3300-3100 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 (935-865 cm⁻¹) from Salmpth and H₂apmpth, H₂talmpth, H₂benmpth and LH=Hfmpth disappeared in its monoligated complexes of compositions [CrL(H₂O)₂Cl], [ML(Py)] and [ML(NH₃)], (M = Ni²⁺ or Zn²⁺). 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 thioenolation) keeping the –OH free.

¹H NMR Studies
The signals due to –NH proton at δ≈11.8 ppm and phenolic –OH at δ≈12.4-13.04 ppm of ligands H₂Salmpth and H₂apmpth, react with Cr(III), Ni(II) or Zn(II) salts giving rise to monoligated complexes [CrL(H₂O)₂Cl], [ML(Py)] and [ML(NH₃)], (M = Ni²⁺ or Zn²⁺), which shows the diabasic 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 δ 11-12 ppm of ligands disappears in complexes suggesting the thioenolization and coordination through deprotonated thiol sulphur atoms. In neutral, bischelates of H₂Salmpth and H₂apmpth of Ni(II) and Zn(II) the signals due to phenolic –OH at ≈12.4-13.04 ppm remain unaffected in complexes and its downfield shift than normal phenolic –OH shows H–bonding. The chemical shift δ 7.1-7.3 ppm of aromatic protons undergoes a slight downfield shift δ 7.4-7.9 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 [M(salmpth)(Py)] and bis-ligated complexes derived from furfural [M(fmpth)₂] and thiophene-2-aldehyde [M(talmpth)₂], (M=Ni²⁺ or Zn²⁺) have been tested for antifungal activity. Antifungal activity of these compounds was evaluated by Agar-based disk-diffusion method 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(salmpth)(Py)] > [M(fmpth)$_2$] > [M(talmpth)$_2$].
The algacidal effect of CrCl$_3$, the ligands- H$_2$salmpth, Hfmpth and Htalmpth 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.

| Tested Compound | Zone of Inhibition (in mm) |
|-----------------|---------------------------|
|                 | C. albicans | A. niger |
| Hmpth, 4        | 08          | 10       |
| Hfmpth, 6a      | 10          | 12       |
| Htalmpth, 6b    | 09          | 10       |
| Hbenmpth, 6c    | 05          | -        |
| H$_2$salmpth, 6d| 12          | 10       |
| (H)$_2$apmpth, 6e| 08          | 11       |
| Hcycmpth, 6f    | 12          | 10       |
| [Ni(salmpth)Py], 7w | 17          | 19       |
| [Zn(salmpth)Py], 7y | 19          | 20       |
| [Ni(fmpth)$_2$], 7i | 14          | 11       |
| [Zn(fmpth)$_2$], 7j | 15          | 14       |
| [Ni(talmpth)$_2$], 7k | 12          | 10       |
| [Zn(talmpth)$_2$], 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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