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Synthesis, Characterization and Pharmacological activity of complexes of Cu(II), Ni(II), Mn(II) and Co(II) from Chalcone N(4)-methyl(phenyl)thiosemicarbazone

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INTRODUCTION

The coordination chemistry of thiosemicarbazones has gained novel significance because of the latest remarks about their antibacterial, antifungal and antitumour activities. Literature survey has shown that these compounds and their complexes are industrially and biologically important. They have diverse physiological activities and have wide applications in synthetic chemistry. The biological activities of these compounds can be attributed to their ability to chelate with trace metals. Chalcones remain interesting among researchers due to their simple chemistry, ease of synthesis and a number of replaceable hydrogens to yield a large number of derivatives. They have been recognized as an interesting class of compounds with its distinctive template that exhibit several interesting and promising biological activities including anticancer, antiinflammatory, antioxidant, cytotoxic, and antimicrobial properties. They are structurally related to curcumin, a known antioxidant [1] that is being studied widely for its activity as a chemopreventive agent [2]. Among the naturally occurring hydroxy chalcones and their synthetic analogues, several compounds displayed cytotoxic activity towards cultured tumor cells. Bandgar and co-workers [3] synthesized simple methoxy chalcones by Claisen–Schmidt condensation reaction and evaluated them for their biological activities. They suggested the trimethoxy chalcone as lead compound with promising anticancer, antiinflammatory and antioxidant activities.

During the recent years, a large number of chalcone-derived thiosemicarbazones are found to have potential therapeutic applications. They possess diverse biological activities including antiinflammatory, antimicrobial and as cell growth inhibitor. Literature review revealed that no study has been done on the metal complexes of N-disubstituted thiosemicarbazones obtained from chalcones [4-6]. Hence, the main objective of the present work was to prepare transition metal complexes of chalcone N(4)-methyl(phenyl)thiosemicarbazone and to find out its binding mode in the complexes, the other objectives are to explore the antimicrobial properties and cytotoxicity of these complexes. Besides, by virtue of being the complexes of chalcone thiosemicarbazone, the targeted complexes are expected to serve as cytotoxic agents, and hence exploration of their cytotoxicity has been included as another objective of this study.

MATERIALS AND PROCEDURAL DETAILS

The standard procedures were followed to purify the commercial solvents [7] and the chemicals that were used for the synthetic purpose were of AR grade. The elemental analysis were carried out by Hitachi CHN-O rapid analyzer. The ^{1}H NMR spectra was recorded in DMSO-d_6 on a Varian 300 NMR spectrophotometer. The infrared spectra of the synthesized compounds, in the range 4000-400 cm^{-1} were recorded using KBr pellets on FTIR DR-8031 Shimadzu spectrophotometer. Electronic spectra were recorded on a Schimadzu UV – VIS – 1601 spectrophotometer. The magnetic moment measurements of the complexes were performed on a Gouy-type magnetic balance. All the measurements were done at room temperature, using $Hg[Co(NCS)_4]$ as calibrant. Diamagnetic corrections [8] using Pascal's constants were applied by adding the diamagnetic contributions of various atoms and structural units. The corrected molar susceptibility values thus obtained, were used for the calculation of effective magnetic moments.

Synthesis of the precursor, N(4)-methyl (phenyl)thiosemicarbazide

It involveed a two-step process. In the first stage, a buff coloured carboxymethyl N-methyl (phenyl)dithiocarbamate (m.p 198^{0}C) was obtained by stirring carbon disulphide, N-methyl aniline and NaOH in the presence of sodium chloroacetate on a magnetic stirrer. The dithiocarbamate obtained was heated on a water bath with 20 ml 98% hydrazine hydrate and 10 ml water for about 10 min. This crude product was then recrystallized from a mixture of ethanol and water when colorless crystals of N(4)-methyl(phenyl)thiosemicarbazide (m.p 125^{0}C) appeared. It was then filtered, washed with distilled water and dried [9].

Synthesis of Chalcone

A base catalyzed Claisen-Schmidt condensation reaction was used for the synthesis of chalcone from acetophenone and benzaldehyde. Equimolar amounts of benzaldehyde (0.01 mol) and acetophenone (0.01 mol), each in 20 ml ethanol was taken in a 250 ml round-bottomed flask equipped with a magnetic stirrer. Then 20 ml of 25% NaOH solution was added drop wise to the reaction mixture keeping it in ice bath itself. Then stirring was continued for another 40 minutes, when the solution

became turbid. After a continous stirring for about 4-5h, the reaction mixture was neutralized by 1M HCl, whereby the desired peach coloured compound (m.p 142^{0}C) precipitated out with an average yield of 85%. It was filtered off, dried in air and recrystallized from rectified spirit [10].

Synthesis of ligand

To a refluxing methanolic solution of N(4)-methyl(phenyl)thiosemicarbazide (0.01 mol), chalcone (0.01 mol) dissolved in minimum amount of ethanol was added. After 10 minutes, 2 drops of glacial acetic acid was added. The mixture was then refluxed for 13h. The resulting solution was refrigerated for 3h, stirred well and filtered. The yellow solid separated was washed with 50% ethanol and dried under vacuum.

Yield: 85%. m.p 193^{0}C. Deep yellow color. Anal. Found (Calc) in %: for $C_{23}H_{21}N_3S$: C, 75.21 (74.39); H, 5.72 (5.66); N, 11.53 (11.32); S, 8.58 (8.63). IR ν_{max} cm^{-1} (KBr): 3187 ν(N-H), 3125 ν(=C-H), 1638 ν(C=N), 1621 ν(C=C), 1048 ν(N-N), 856 ν(C=S). UV-Vis (λ_{max} nm) (ε M^{-1} cm^{-1}) 289 (34602), 358 (27933). ^{1}H NMR data (δ, ppm; DMSO d6): 6.52-7.13(m, 6H); 3.42(s, 3H); 6.78(s, 1H); 7.27-7.89(m, 6H); 6.69(m, 1H); 5.56(d, 1H).

Synthesis of complexes

The complexes were prepared by following a general procedure. A hot methanolic solution of the hydrated metal chloride (0.01 mol in 20 ml) [chlorides of Mn(II), Co(II), Ni(II) or Cu(II)] was refluxed with the thiosemicarbazone in ethanol (0.01 mol in 20 ml) for about 4-5 h. The complexes formed were filtered off, washed several times with methanol and dried in vacuum.

Scheme 1 shows the synthetic procedure of the ligand and complexes. Physical characterization (yield, m.p, colour and CHNS microanalysis) were conducted for the ligand and all the complexes. They were further characterized spectroscopically by IR, UV-Vis, ^{1}H NMR and by magnetic susceptibility measurements.

All the complexes obtained in reasonable yields and are quite soluble in $CHCl_3$ and DMSO, but less soluble in ethanol and methanol. The physico-chemical properties and spectral data of the complexes of Mn(II), Co(II), Ni(II) and Cu(II) are presented below.

1. $[Mn(LH)_2Cl_2]$ Yield: 74%. m.p 262^{0}C. Yellowish orange color. Anal. Found (Calc) in %: for $C_{46}H_{42}Cl_2MnN_6S_2$: C, 62.85 (63.74); H, 4.56 (4.62); N, 9.62 (9.70); S, 7.33 (7.39); M, 6.38 (6.35). IR ν_{max} cm^{-1} (KBr): 3179 ν(N-H), 3128 ν(=C-H), 1598 ν(C=N), 1624 ν(C=C), 1058 ν(N-N), 842 ν(C=S), 524 ν(M-N), 420 ν(M-S), 320 ν(M-Cl). UV-Vis (λ_{max} nm) (ε, M^{-1} cm^{-1}) 612 (16340).

2. $[CoL_2(H_2O)_2]$ Yield: 65%. m.p 254^{0}C. Yellowish brown color. Anal. Found (Calc) in %: for $C_{46}H_{44}CoN_6O_2S_2$: C, 65.91 (66.10); H, 5.24 (5.27); N, 10.09 (10.06); S, 7.67 (7.66); M, 7.08 (7.07). IR ν_{max} cm^{-1} (KBr): 3427 ν(O-H), 3120 ν(=C-H), 1596 ν(C=N), 1618 ν(C=C), 1053 ν(N-N), 795 ν(C-S), 532 ν(M-N), 468 ν(M-O), 424 ν(M-S). UV-Vis (λ_{max} nm) (ε, M^{-1} cm^{-1}) 424 (23630), 528 (18942), 1044 (9578).

3. $[NiL_2(H_2O)_2]$ Yield: 65%. m.p 258^{0}C. Dark Maroon color. Anal. Found (Calc) in %: for $C_{46}H_{44}NiN_6O_2S_2$: C, 66.16 (66.12); H, 5.23 (5.27); N, 10.04 (10.06); S, 7.65 (7.67); M, 7.07 (7.05). IR ν_{max} cm^{-1} (KBr): 3446 ν(O-H), 3126 ν(=C-H), 1598 ν(C=N), 1620 ν(C=C), 1054 ν(N-N), 789 ν(C-S), 528 ν(M-N), 472 ν(M-O), 424 ν(M-S). UV-Vis (λ_{max} nm) (ε, M^{-1} cm^{-1}) 437 (22831), 562 (16076), 734 (13624).

4. $[Cu(LH)_2Cl_2]$ Yield: 74%. m.p 270^{0}C. Dull brown color. Anal. Found (Calc) in %: for $C_{46}H_{42}Cl_2CuN_6S_2$: C, 59.47 (59.42); H, 4.56 (4.52); N, 12.04 (12.06); S, 6.87 (6.89); M, 6.79 (6.78). IR ν_{max} cm^{-1} (KBr): 3182 ν(N-H), 3130 ν(=C-H), 1597 ν(C=N), 1623 ν(C=C), 1046 ν(N-N), 835 ν(C=S), 527 ν(M-N), 423 ν(M-S), 322 ν(M-Cl). UV-Vis (λ_{max} nm) (ε, M^{-1} cm^{-1}) 642 (15564).

Biological studies

Short-term *in vitro* cytotoxic study – Trypan blue exclusion method

Chalcone N(4)-methyl(phenyl)thiosemicarbazone and its complexes were studied for short-term *in vitro* cytotoxicity using Dalton's lymphoma ascites (DLA) cells. The tumour cells were aspirated from the peritoneal cavity of tumour bearing mice and the cell capability was checked by Trypan blue exclusion method. Viable cell suspension (1x10^6 cells in 0.1 ml) was added to different drug concentrations and incubated for 3 h at 37^{0}C. The cell suspension mixed with 0.1 ml of 1% trypan blue was loaded after 2-3 minutes on a haemocytometer. The blue colour will be taken up by the dead cells while the live cells will not. The number of stained and unstained cells were counted separately and the percentage of dead cells was determined using a haemocytometer.

Antimicrobial properties

Six microbial strains (two-Gram positive bacteria; *Streptococcus, Bacillus* and two Gram negative bacteria; *Escherichia coli, Pseudomonas* and two fungi; *Fusarium* and *Aspergillus species*) were screened for the evaluation of antibacterial and antifungal activities of all the compounds, by Kirby Bauer or Disc Diffusion Method.

Antibacterial activity by Kirby Bauer method

The antibacterial activities of the compounds were ascertained by disc diffusion method [11]. Nutrient agar plates were used for keeping the culture media. Sterile filter paper discs of 3.2 mm diameter were placed on the surface of nutrient agar plates using sterile forceps. The test samples in the recommended concentrations (200 µg/ml in DMSO) were introduced into the respective wells using a micropipette. Other wells containing 2% DMSO and the standard antibacterial drug (Ciprofloxacin) served as negative and positive controls, respectively. These treated plates were incubated immediately at 37°C for 24 h. After incubation, the diameter of the inhibition zone was measured (in mm). Growth inhibition was calculated with reference to the positive control.

Antifungal activity by Kirby Bauer or Disc Diffusion Method

Antifungal activity was also done by disc diffusion method [11]. The fungal cultures of *Fusarium* and *Aspergillus*, used as test organisms were maintained in Sabouraud's

dextrose broth. They were distributed homogeneously on Sabouraud's dextrose agar (SDA) plates. Sterile filter paper discs of 2.1 mm diameter were placed on the surface of SDA plates. The drug in the concentration of 200 µg/ml in DMSO was added on each disc with a micropipette. On the other discs, 2% DMSO as control and Fluconazole as the standard antifungal drug were added for the comparison of the antifungal activities of the thiosemicarbazone and its complexes. These treated SDA plates were kept at 37°C for 72 h until the fungal growth was almost complete. After incubation, the zone diameter of the fungal colony was measured and compared with that of the control.

RESULTS AND DISCUSSION

Characterization

Chalcone N(4)-methyl(phenyl)thiosemicarbazone (CHTSC) (LH)

The IR spectrum of thiosemicarbazone ligand showed a broad band of medium intensity at 3187cm^{-1}due to asymmetric ν_{NH} of the secondary –NH group. The medium intensity band at 3125 cm^{-1} may be assigned to $\nu_{=CH}$. Sharp bands at 1638 and 1621 cm^{-1} may be due to $\nu_{C=N}$ and $\nu_{C=C}$, respectively. The band at 865 cm^{-1} accounts for $\nu_{C=S}$ and indicates the presence of a thioamide (-NH-C=S) functional group in the ligand. The band at 1048 cm^{-1} has been assigned for the $\nu_{(N-N)}$ of thiosemicarbazone.

The electronic spectrum of the ligand showed an intense band at 278 nm (35936 cm^{-1}) which can be attributed to π-π* transition of the benzene rings of chalcone. Similarly, a weak band at 358 nm (27488 cm^{-1}) due to the azomethine group may be ascribed to n –π* transition in the thiosemicarbazone. It was found to be shifted in the spectra of the complexes indicating their coordination to the metal ions.

Further, the ligand structure was confirmed from the ^{1}H NMR studies. The spectrum of the ligand is characterized by the presence of a multiplet at 6.52-7.13 ppm, which is due to C_6H_5 protons attached to the terminal nitrogen atom. There is a singlet at 6.78 ppm that is attributed to the -NH protons. The multiplets that appeared at 7.27-7.89 ppm is due to C_6H_5 protons adjacent to the olefinic CH bond and the one present on the the imine group. A sharp signal appeared at 3.42 ppm is assignable to CH_3 protons adjacent to the terminal phenyl group on the nitrogen atom. The signals appeared at 6.69 and 5.56 ppm are due to the olefinic -CH protons adjacent to the phenyl- and the imine groups, respectively.

Complexes

The vibrational spectra of the complexes were compared with that of the ligand in order to find out the bonding sites of the ligand. The presence of a characteristic band at 1638 cm^{-1} attributed to the azomethine stretching in the ligand spectrum, is shifted towards lower frequency, in the range ~ 1597 cm^{-1} in the spectra of all the complexes, indicative of the participation of the azomethine nitrogen atom in coordination [12, 13]. The medium intensity band at 3187 cm^{-1} due to the secondary –NH group stretching of the thiosemicarbazone moiety in the ligand spectrum, is found to be retained almost at the same region in the spectra of the complexes of Cu(II) and Mn(II), signifying the coordination of thioamide in the thione form. Whereas, this band is not found in the spectra of Ni(II) and Co(II) complexes indicating the loss of H atom of the tautomeric –NH, via the enolization of –NH-C=S to –N=C-SH in the presence of metal ions and their coordination through the thiolate sulphur. This is further confirmed by the appearance of a new band in the region ~790-796 cm^{-1} due to $\nu_{(C-S)}$. The broad bands at 3446 and 3427 cm^{-1} in the spectra of Ni(II) and Co(II) complexes, respectively are recognized as due to the O-H stretching modes of water molecules in them. The supportive evidence for the water molecules coordinated in the Ni(II) and Co(II) complexes, is given by the presence of bands in the low frequency region, 465–475 cm^{-1}. The bands that appeared in the very low frequency region, ~300–320 cm^{-1} may be ascribed due to $\nu_{(M-Cl)}$ in the spectra of the complexes of Mn(II) and Cu(II) [14]. The strong bands due to $\nu_{(C=S)}$ in the ligand spectrum gets shifted only by a few cm^{-1} upon the coordination through thione sulphur in the Mn(II) and Cu(II)complexes. The presence of a band between1046-1058 cm^{-1} in the spectra of ligand and complexes can be assigned to ν_{N-N}. Conclusive evidence for the bonding is the new bands in the spectra of all metal complexes in low frequency regions, 520–535 and ~ 420 cm^{-1} which are characteristic of M–N and M–S stretching vibrations, respectively. These observations show the involvement of thiolato/thione sulfur and the hydrazinic nitrogen in bonding during the complex formation. Thus, in the complexes of Cu(II) and Mn(II), LH acts as a monoanionic bidentate ligand and as a neutral bidentate one in the case of Co(II) and Ni(II) complexes. The structures of the complexes are shown in Fig 1.

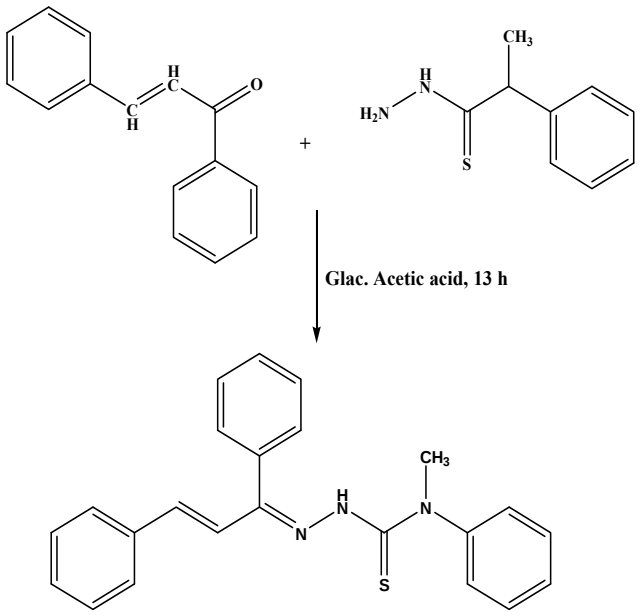
The magnetic moment- and electronic spectral data of the complexes are given in Table 1. $[Mn(LH)_2Cl_2]$ showed a magnetic moment of 5.82 B.M. which indicates its high-spin octahedral

structure. The band at 16340 cm^{-1} in its electronic spectrum may be assigned to $^6A_{1g}$ (F) $\rightarrow$$^4T_{1g}$ transition characteristic of an octahedral Mn(II) complex [15]. The Co(II) complex registered a magnetic moment of 4.89 B.M, which suggests a distorted octahedral environment around the metal ion. The three spin-allowed bands of $[CoL_2(H_2O)_2]$ at 15083,16942 and 23420 cm^{-1} may be assigned to$^4T_{1g}(F)\rightarrow{}^4T_{2g}(F)$, $^4T_{1g}(F)\rightarrow{}^4A_{2g}(F)$ and $^4T_{1g}(F)\rightarrow{}^4T_{1g}(P)$ transitions, respectively [16, 17]. A magnetic moment value of 2.78 B.M and an electronic spectrum with bands at 13275, 14657 and 22883 cm^{-1} attributed to the $^3A_{2g}(F)\rightarrow{}^3T_{2g}(F)$, $^3A_{2g}(F)\rightarrow{}^3T_{1g}(F)$ and$^3A_{2g}(F)\rightarrow{}^3T_{1g}(P)$ transitions, suggests an octahedral structure for $[NiL_2(H_2O)_2]$ [18, 19]. A magnetic moment of 1.98 B.M. for $[Cu(LH)_2Cl_2]$ indicates the presence of an unpaired electron with a very small orbital contribution and thereby, suggesting an octahedral geometry [20]. The Cu(II) complex showed a d-d band at 15564 cm^{-1} which may be assigned to the $^2E_g \rightarrow{}^2T_{2g}$ transition, usually observed for an octahedral Cu(II) ion [21].

Short-term *in vitro* cytotoxic studies of the compouds

The short-term *in vitro* cytotoxicity of thiosemicarbazone and its complexes using DLA cells showed a marked cytotoxic activity (Table 2). The free ligand showed 65%

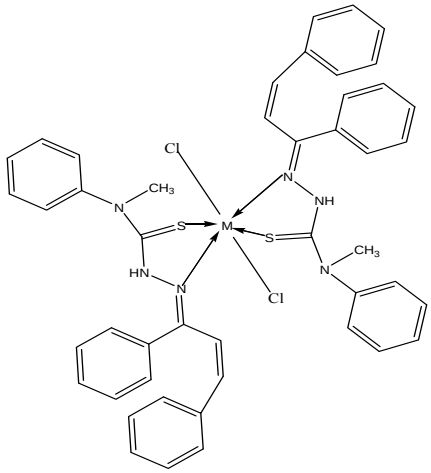
cytotoxic activity, while the Cu(II) complex showed remarkably high cytotoxic activity, with an IC_{50} value of 48 µg/ml. (Fig 2). The common feature of compounds with the carcinostatic potency is the presence of soft donor (NS) atoms. Thus, the antitumour studies carried out on chalcone N(4)-methyl(phenyl)thiosemicarbazone and its metal complexes have proven their potentiality as cytotoxic agents against EAC (Ehrlich Ascites Carcinoma) induced ascites cell lines. Though, the real pathway by which the copper(II) complex exhibits antitumour activity is not predictable, it is thought that this will be based on the structure activity relationship since in the case of *cis-platin* [22].



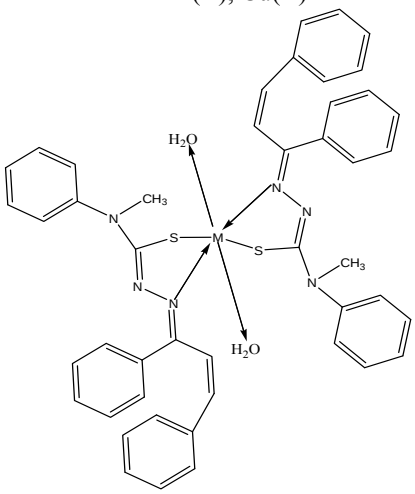
Chalcone N(4)-methyl(phenyl)thiosemicarbazone (CHTSC) (LH)

$MCl_2.xH_2O + 2LH \rightarrow [M(LH)_2Cl_2]$ (M=Mn(II) or Cu(II)) and $[ML_2(H_2O)_2]$ (M=Co(II) or Ni(II)).

Scheme 1: Synthesis of the ligand and its complexes



M= Mn(II), Cu(II)



M=Co(II), Ni(II)

Fig 1: Structure of the metal complexes of the CHTSC (LH) ligand

Table1: Magnetic moments and Electronic spectral band assignments

Complex	Band maxima (nm)	(cm^{-1})	Assignments	μ_{eff} (B.M)
$[Mn(LH)_2Cl_2]$	405 612	24691 16340	C.T $^6A_{1g}(F) \rightarrow {}^4T_{1g}$	5.82
$[CoL_2(H_2O)_2]$	427 592 663	23420 16942 15083	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$	4.89
$[NiL_2(H_2O)_2]$	437 682 753	22883 14657 13275	$^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$	2.78
$[Cu(LH)_2Cl_2]$	642	15564	$^2E_g \rightarrow {}^2T_{2g}$	1.92

Table 2: *In vitro* cytotoxicity of CHTSC* and its metal complexes

Drug Concentration (µg/ml)	Percentage Cytotoxicity of Complexes				Ligand
	Mn	Co	Ni	Cu	(CHTSC*)
10	4	9	6	23	4
20	8	17	13	38	11
50	21	32	30	49	26
100	32	52	47	65	43
200	48	70	59	89	65
*Chalcone N(4)-methyl(phenyl)thiosemicarbazone					

Table 3: *In vitro* antimicrobial activity of the schiff base and its complexes						
Compound	Antibacterial activity				Antifungal activity	
	Diameter of Inhibition zone (millimeters)				Diameter of Inhibition zone (millimeters)	
	Strepto	Bacillus	Pseud	E.coli	Fusarium	Aspergillus
CHTSC	9	11	8	8	7	-
Mn(II)	21	17	19	22	15	13
Co(II)	12	9	13	15	9	-
Ni(II)	13	19	15	16	12	14
Cu(II)	16	16	18	21	15	12
Ciprofloxacin	27	25	24	25		
Ketoconazole					23	25

Antibacterial activity of chalcone N(4)-methyl(phenyl)thiosemicarbazone and its complexes

The antibacterial activity of the compounds was tested against a set of clinically important species of two - Gram positive and two - Gram negative bacteria by disc diffusion method. After incubation, the diameter of zone of inhibition was measured in millimeter and the results obtained are presented in Table 3 and Fig 3. A comparative study indicates that the metal complexes exhibit higher activity than the free ligand.

Antifungal activity of chalcone N(4)-methyl(phenyl)thiosemicarbazone and its complexes

The antifungal activity of the ligand and its metal complexes was tested against two species, *Fusarium, and Aspergillus* by disc diffusion method. After incubation, the compounds yielded clear zone of inhibition around the discs. The results are as shown in Table 3 and Fig 4.

The studies revealed that the compounds are active towards the four bacterial strains in different manners. Accordingly, the complexes are found to have maximum bactericidal activity with zone of inhibition in the range 15-22 mm. The complexes of Mn(II), Ni(II) and Cu(II) showed moderate activity against the fungal species. The mode of higher biological activity of the complexes can be explained on the basis of Tweedy's chelation theory [23, 24]. According to this theory, the polarity of the metal ion is reduced considerably due to chelation. This is because of the partial sharing of the positive charge of the metal ion with the donor group and due to p-electron delocalization over the whole chelate ring. This inturn enhances the lipophilic character of the chelates. The higher lipophilicity is expected to enhance the antimicrobial properties as well. Thus the lipophilic cell wall with lipids and polysaccharides as some of the essential constituents, favours the passage of metal chelates into the cells. This leads to the blocking of the metal binding sites in the microbial enzymes and thereby interfering with the normal cell metabolic processes and thus restricts further growth of the organism. The inhibitive action of these metal chelates on the growth of the tested microorganisms is due to the presence of highly liposoluble azomethine groups as donor sites. Moreover, the form of inhibitive action of the complexes may involve the hydrogen bond formation through the coordinated anions and azomethine group with the active centers in the cell [23, 24].

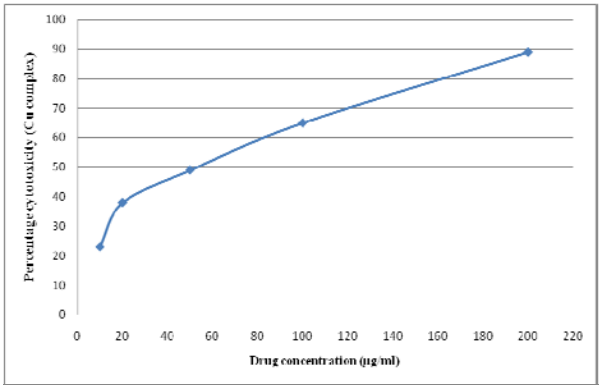


Fig 2: Cytotoxic action of the copper complex of chalcone N(4)-methyl(phenyl) thiosemicarbazone

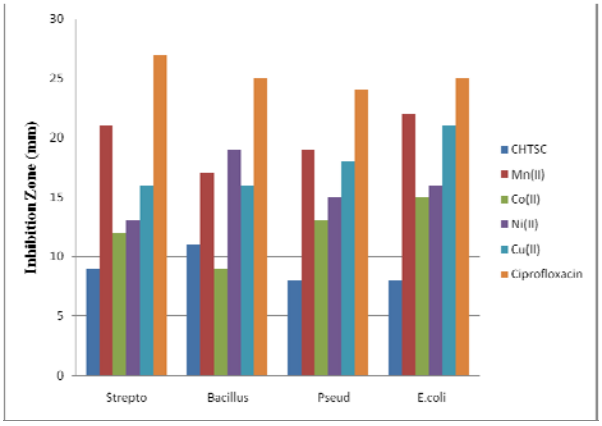


Fig 3: Antibacterial activity of CHTSC and its complexes

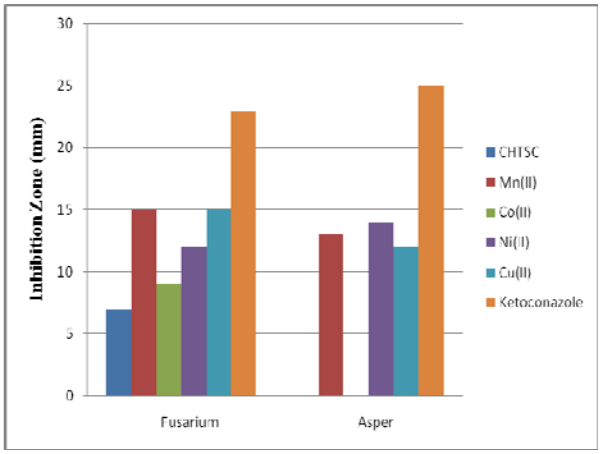


Fig 4: Antifungal activity of CHTSC and its complexes

CONCLUSION

A Novel ligand, chalcone N(4)-methyl(phenyl)thiosemicarbazone and its mononuclear complexes of Cu(II), Co(II), Mn(II) and Ni(II) were synthesized and characterized. Based on the elemental analysis and spectral data, the nature of coordination of the ligand in these metal(II) complexes was determined. The spectral data revealed the bidentate behaviour of the ligand, bonding to the metal ion using the iminic C=N nitrogen and thiolato/thione sulphur atom. The mononuclear octahedral complexes corresponding to the general formulae $[M(LH)_2Cl_2]$ (M: Mn(II) or Cu(II)) and $[ML_2(H_2O)_2]$ (M:Co(II) or Ni(II)) were formed. The *in vitro* cytotoxic studies of the compounds revealed their potentiality as anticancer agents. It was found that the metal complexes were more cytotoxic than the free ligand against EAC cell line. The free thiosemicarbazone showed 65% cytotoxic activity. The IC_{50} for the copper(II) complex was 48µg/ml. The metal complexes exhibited moderate to strong antibacterial activity than the free ligand, but less active than Ciprofloxacin (positive control). Comparing their activity, we found that Mn(II) complex exhibited a higher activity towards bacterial species than the other metal complexes. The Mn(II), Ni(II) and Cu(II) complexes appeared to have moderate antifungal activity against *Fusarium sp*. when compared with the ligand and the Co(II) complex. Hence the current work indicates that chalcone N(4)-methyl(phenyl)thiosemicarbazone ligand and its metal(II) complexes can be considered as novel and promising ones in the medicinal and biological fields.

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