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STUDY OF NOVEL METAL COMPLEXES OF THIOSEMICARBAZONES

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ABSTRACT

The reaction between thiosemicarbazide and 1-(5-chloro -1H-benzo[d] [1,2,3] triazol-1-yl)propan-2-one yielded novel heterocyclic ligand, i.e., 2-(1-(5-chloro -1H-benzo[d] [1,2,3] triazol-1-yl)propan-2-ylidene) hydrazine carbothioamide **(CBTTS)**. The reaction between novel ligand with selected Transition Metal salts yielded their metal complexes of **CBTTS**. The elemental contents, Spectral studies, metal: ligand ratio and magnetic properties of novel ligand and their metal complexes were characterized. Antibacterial and antifungal activities of ligand CBITS and its all metal complexes were studied.

KEYWORDS: Thiosemicarbazone; 5-chloro Benzotriazole; Metal complexes; spectral Study; magnetic properties and Antibacterial and antifungal activities.

INTRODUCTION

Due to various pharmaceutical as well as biological activity number of research work carried out to synthesize novel heterocyclic compounds[i]. Among them nitrogen and sulphur - containing compounds, thiosemicarbazides show importance in the field of medicinal chemistry[ii]. Many scientists have developed a variety of bio-active and pharmacological activities heterocyclic molecules which contains thiosemicarbazides and its moiety[iii]. Thiosemicarbazide (NH2-NH-CSNH2) is the simplest hydrazine derivative of thiocarbamic acid[iv]. The chemical properties of thiosemicarbazide are alike to its correspondent semicarbazide[v,vi]. Various nitrogen- and sulphur- containing heterocyclic compounds like pyrazoles, thiazoles, thiadiazoles, thiadiazines, triazoles, pyrimidines, triazines, pyrazolotriazines, and thiazolotriazines and so on synthesised from thiosemicarbazides[vii]. Thiosemicarbazides have demonstrate numerous synthetic, analytical, medicinal applications and biological activities[viii]. Thiosemicarbazides derivatives display interesting biological activities, like anti-cancer, anti-microbial, anti-HIV, anti-viral, insecticidal, anti-sclerotic and anti-parasitic activities[iii-viii]. They play an important role in the regulation of plant growth[ix]. Thiosemicarbazones generally act as chelating ligands containing which react with transition metal giving complexes[x]. Some industrially important applications like anti-corrosion and anti-fouling effects have also been reported for these derivatives. Thiosemicarbazones characterize a versatile group of Schiff based ligands having sulphur and nitrogen as donor atoms. They are frequently synthesised by the condensation reaction between aldehydes or ketones with thiosemicarbazides. During the past few decades, interest has been rapidly

growing in attainment insight into the chemistry of thiosemicarbazide derivatives due to their noticeable biological activities. Among the accumulative number of nitrogen and sulphur comprising derivatives, thiosemicarbazides are also considered by many scientists as interesting targets for synthesis novel heterocyclic compounds. The coordination compounds of thiosemicarbazone and their metal chelated were revealed different pharmaceutical and biological activities. Hence, in connection of our earlier work we synthesized thiosemicarbazone containing novel heterocyclic ligands and their metal complexes. The reaction work is summarized in following scheme-1.

EXPERIMENTAL

Laboratory grade chemicals were used. Metals and elemental contents were determined by volumetrically by Vogel's method and Thermo Finigen Flash1101 EA (Itally), respectively[v]. Infrared spectra of the synthesized Ligand and its metal complexes were recorded on Nicolet 760 FT-IR spectrometer. NMR spectrum of CBTTS (Ligand) was recorded on 60 MHz NMR spectrophotometer. LC-MS of selected samples taken on LC-MSD-Trap-SL_01046. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathio cynato cobalate (II) Hg[Co(NCS)4] was used as a calibrant. The electronic spectra of complexes in solid were recorded on at room temperature. MgO was used as reference. The antibacterial activities of the series of compounds were studied against gram +Ve and –Ve bacteria shown in Table. The evaluation of antimicrobial activity has been carried out using Broth Dilution method for antimicrobial study. Similar conditions using Amoxillin and Nystatin were used standard for comparison[iv-vii].

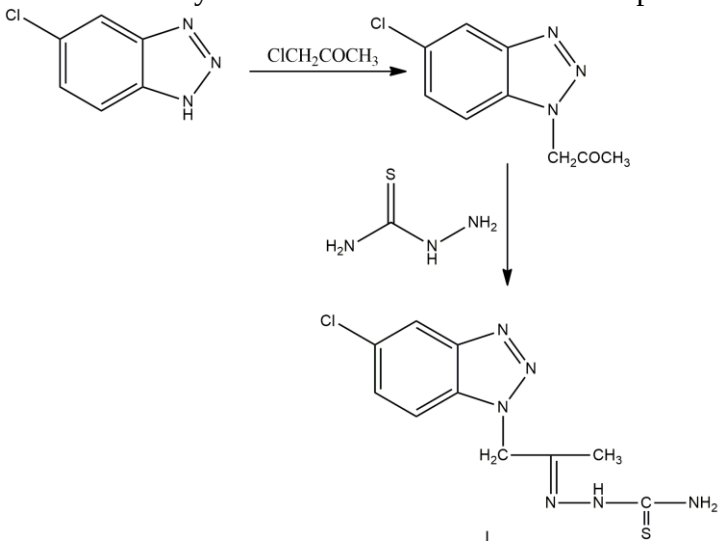


Figure-1 Reaction Scheme

Synthesis of 1-(5-chloro -1H-benzo[d][1,2,3]triazol-1-yl)propan-2-one :

In round bottom flask a mixture of 5-chloro Benzotriazole (0.01M) and chloroacetone (0.01 M) were taken. 50 mL of Dry acetone and 30 g of anhydrous potassium carbonate was added to the reaction mixture and refluxed for 7 hrs at 70°C. Filtrating the resultanting product, dried and recrystallized from ethyl acetate[viii-xv]. The purity of the compound was checked by TLC and melting point. Yield: 72 %, m.p:137-38°C, Elemental Analysis for $C_9H_8N_3OCl$ (209.5 gm/mole):Clac.%C, 51.56; %H, 3.85; %N, 20.04;%Cl,16.91; Found.%C, 51.5; %H, 3.8; %N, 20.0;%Cl,16.9.

Important IR Spectral (cm^{-1}) shows at 2932,2810,1458,1370(C-H Str.), 1631 (C=O),3067(Aromatic C-H Str.) and 1594,1503(Aromatic C-C Str.) and 785(Aromatic C-Cl).

NMR Signals (δ ppm) at 1.90-1.91(singlet, 3H, -CH3),6.91-7.50(multiplate, 3H, benzotriazole C-H) and 4.70 (singlet, 2H, -CH2-).

Table-1 Analysis of CBTTS Ligand And Its Metal Complex

Ligand and Metal Complex	Elemental analysis (%)								
	mol. wt	color	Yield %	C% Cald. Found	H% Cald. Found	N% Cald. Found	S% Cald. Found	Cl% Cald. Found	M% Cald. Found
$C_{10}H_{11}N_6SCl$	282.5	White	65	42.48 42.4	3.92 3.9	29.72 29.7	11.34 11.3	12.54 12.5	-
$C_{20}H_{22}N_{12}S_2Cl_2Cu^{2+}\cdot 2H_2O$	665.54	light blue	70	36.12 36.1	3.94 3.9	25.27 25.2	9.64 9.6	10.66 10.6	9.55 9.5
$C_{20}H_{22}N_{12}S_2Cl_2Ni^{2+}\cdot 2H_2O$	660.71	Greenish white	68	36.38 36.3	3.97 3.9	25.46 25.4	9.71 9.7	10.74 10.7	8.89 8.8
$C_{20}H_{22}N_{12}S_2Cl_2Co^{2+}\cdot 2H_2O$	660.94	reddish white	71	36.37 36.3	3.97 3.9	25.45 25.4	9.71 9.7	10.74 10.7	8.92 8.9
$C_{20}H_{22}N_{12}S_2Cl_2Zn^{2+}\cdot 2H_2O$	666.38	pale white	65	36.02 36.0	3.93 3.9	25.20 25.1	9.62 9.6	10.63 10.6	9.81 9.8
$C_{20}H_{22}N_{12}S_2Cl_2Mn^{2+}\cdot 2H_2O$	656.94	white	69	36.59 36.5	3.99 3.9	25.60 25.5	9.77 9.7	10.80 10.7	8.37 8.3

Synthesis of 2-(1-(5-chloro -1H-benzo[d][1,2,3]triazol-1-yl)propan-2-ylidene) hydrazinecarbothioamide (CBTTS) :

Thiosemicarbazone was synthesized by refluxing the solution of thiosemicarbazide (0.02mol) in ethanol and the alcoholic solution of 1-(5-chloro -1H-benzo[d] [1,2,3] triazol-1-yl)propan-2-one (0.01mol) in water bath for 6-7 hrs with continuous stirring. After cooling the compounds were filtered and recrystallized from R-spirit[vii-x]. Yield: 65%; m.p. 173-74°C. Elemental Analysis for $C_{10}H_{11}N_6SCl$ (282.5 gm/mole):Clac.%C, 42.48; H, 3.92; N, 29.72; S, 11.34; %Cl,12.54; Found.% C, 42.4; H, 3.9; N, 29.7; S, 11.3; %Cl,12.5.

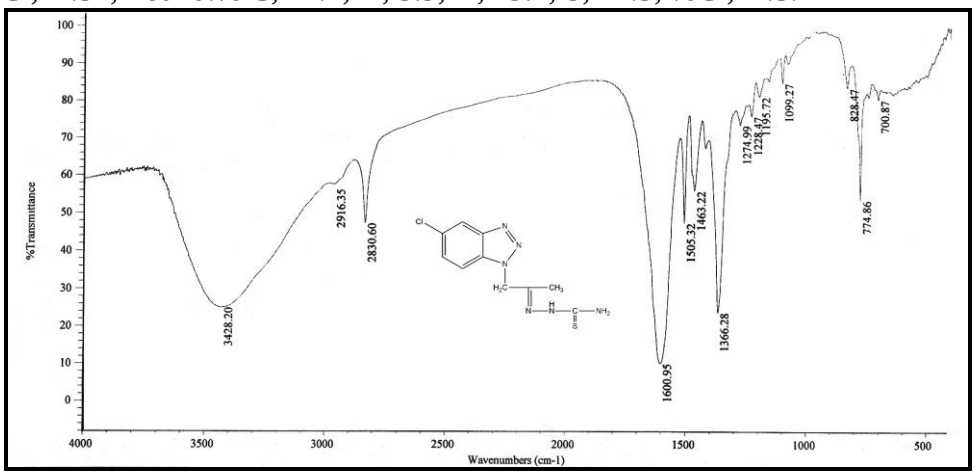


Figure-2 IR spectrum of 2-(1-(5-chloro -1H-benzo[d][1,2,3] triazol-1-yl)propan-2-ylidene)hydrazinecarbothioamide

IR Spectral (cm^{-1}) shows at 3428(N-H of NH2 and NH Str.), 2916, 2830,1505,1366(C-H Str.),1600(C=N),2830(Aromatic C-H Str.),1600, 1463(Aromatic C-C Str.) , 828(C=S) and 774(Aromatic C-Cl).

NMR Signals (δ ppm) at 1.75-1.78 (singlet, 3H, -CH3),7.57-7.93(multiplate, 3H, benzotriazole C-H),4.89-4.91(singlet, 2H, -CH2-),8.50(singlet, 1H, -NH-),3.72-3.70 (singlet, 2H, -NH2). LC-MS: M/z at 283.4 (M+).

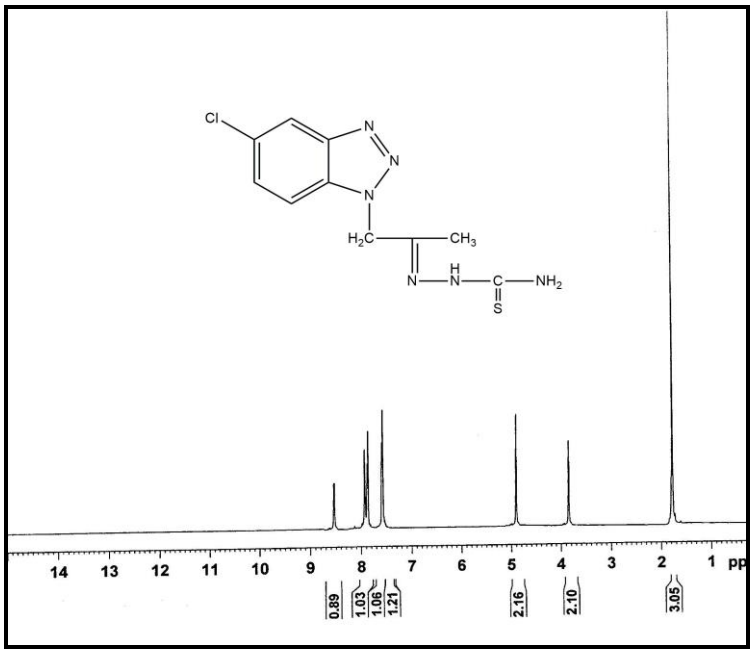
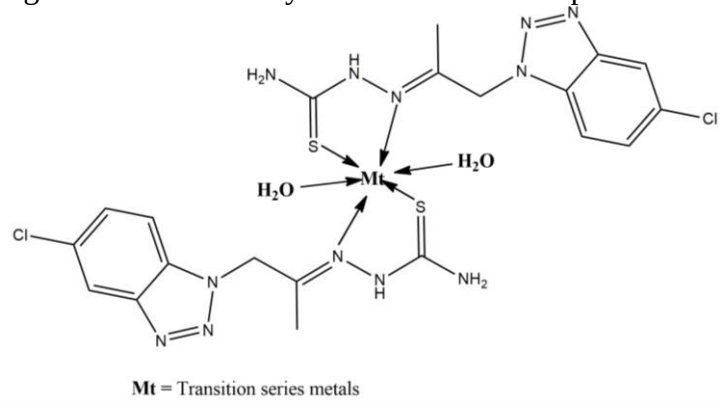


Figure-3 1H NMR of 2-(1-(6-Chloro-1H-benzo[d]imidazol-1-yl) propan-2-ylidene)hydrazine carbothioamide

Synthesis of Metal complex of 2-(1-(5-chloro -1H-benzo[d] [1,2,3] triazol-1-yl)propan-2-ylidene)hydrazinecarbothioamide(CBTTS-M) :

The metal chelates of CBTTS (i.e. of Cu^{2+}, Mn^{2+}, Zn^{2+}, Co^{2+}, Ni^{2+} ions) were prepared in similar manner. The general method for synthesis of metal Complexes is as follow.



All metal complexes were synthesized by adding of the appropriate metal salts (0.1 mol, in 20 ml ethyl acetate/water (1:1) volume to a hot solution of each thiosemicarbazone ligand (0.2 mol, in 30 ml ethyl acetate (95%)). The resulted color solutions were stirred and refluxed on a hot plate at 80°C for 1 h. The volume of the resulted solution was reduced to half volume by evaporation. One day later, the colored solid complexes formed, were filtered, the solids washed with petroleum ether and finally dried under vacuum[vii-x].

RESULTS AND DISCUSSION:

The reaction between thiosemicarbazide and 1-(5-chloro -1H-benzo[d] [1,2,3] triazol-1-yl) propan-2-one yielded 2-(1-(5-chloro -1H-benzo[d] [1,2,3]triazol-1-yl) propan-2-ylidene) hydrazine carbothioamide **(CBTTS)**. Table-1 represent the elemnetal analysis, which are consistent with the structure predicted(Scheme-1). The IR spectrum of CBTTS comprises the important bands due to thiosemicarbazide. The bands were observed at 3428 (N-H), 1600 (C=N), 828 (C=S) cm^{-1}.

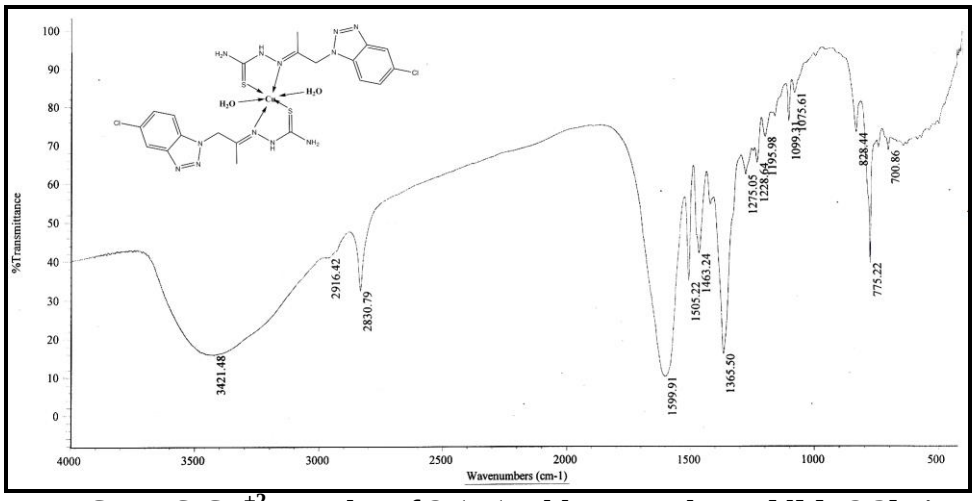


Figure-4 IR-CBTTS-Cu^{+2} complex of 2-(1-(5-chloro -1H-benzo[d] [1,2,3]triazol-1-yl) propan-2-ylidene)hydrazinecarbothioamide

The NMR spectrum of CBTTS indicates that the singlet of 2 H and 1H at 3.72-3.70 and 8.50 for NH of thiosemicarbazide. The methylene proton shows singlet at 4.89-4.91 δ. Thus the structure of CBTTS is confirmed as shown in Figure-1.

The metal and C, H, N contents of metal complexes of CBTTS(Table-I) are also consistent with the predicted structure. The results show that the metal: ligand (M:L) ratio for all divalent metal complex is 1:2[xv-xvii].

The presence of band characteristic of metal-nitrogen and metal-Sulphur group of parent CBTTS in the infrared spectra of all the complexes suggest the formation of the entire metalocyclic compound. The other bands are almost at their respective positions as appeared in the spectrum of parent-CBTTS ligand.

The observed μ_{eff} values in the range 2.36-5.56 B.M are consistent with the above moiety.The value of magnetic moments and reflectance spectral data of each complexes co-relates with structure assigned as the octahedral geometry[xii-xvii]. The data of electronic transitions and magnetic moments of metal complexes are summarized in Table-2.

Table– 2 Spectral Features and Magnetic Moment of CBTTS- metal chelates

Metal Chelates	**μ_{eff} (BM)**	**Electronic spectral data(cm^{-1})**	**Transition**
CBTTS-Cu^{2+}	2.36	14962 24619	CT $^2B_{1g} \rightarrow {}^2A_{1g}$
CBTTS-Ni^{2+}	3.45	22307 15721	$^3A_{2g} \rightarrow {}^3T_{1g}$ (P) $^3A_{2g} \rightarrow {}^3T_{1g}$ (F)
CBTTS-Co^{2+}	4.50	24940 19889 8418	$^4T_{1g}(F) \rightarrow {}^6T_{2g}(\square_1)$ $^4T_{1g}(F) \rightarrow {}^4A_{2g}(\square_2)$ $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$
CBTTS-Mn^{2+}	5.56	23777 18415 16726	$^6A_{1g} \rightarrow {}^6A_{1g}(^4E_g)$ $^6A_{1g} \rightarrow {}^4T_{2g}(^4G)$ $^6A_{1g} \rightarrow {}^4T_{1g}(^4G)$
CBTTS-Zn^{2+}	D	-	-

D*=Diamagnetic

Thermogravimetric analysis of CBTTS and its metal chelates was investigated by conducting thermogravimetric analysis (TGA) shown in Table-3. TGA was carried out in a slow stream of air at 10°C/min. heating rate. Du point thermogravimetric analyzer (TC-10ATA-3000) was used for TGA.

Table-3 Thermogravimetric analysis of MBTTS and its metal chelates

Ligand/ Metal complexes	**% Weight loss at different temperature(°C)**						
	100	**200**	**300**	**400**	**500**	**600**	**700**
CBTTS	-	8.82	9.26	23.46	28.17	31.45	34.17
CBTTS-$Cu^{+2}.2H_2O$	0.01	5.54	11.68	26.38	31.48	33.38	34.25
CBTTS-$Ni^{+2}.2H_2O$	2.62	15.3	18.18	36.45	52.74	65.64	68.16
CBTTS-$Co^{+2}.2H_2O$	1.73	12.58	24.41	38.23	52.32	64.62	67.4
CBTTS-$Zn^{+2}.2H_2O$	6.61	15.23	31.05	36.52	55.39	66.06	69.55
CBTTS-$Mn^{+2}.2H_2O$	2.35	9.9	13.62	34.25	53.18	66.08	68.5

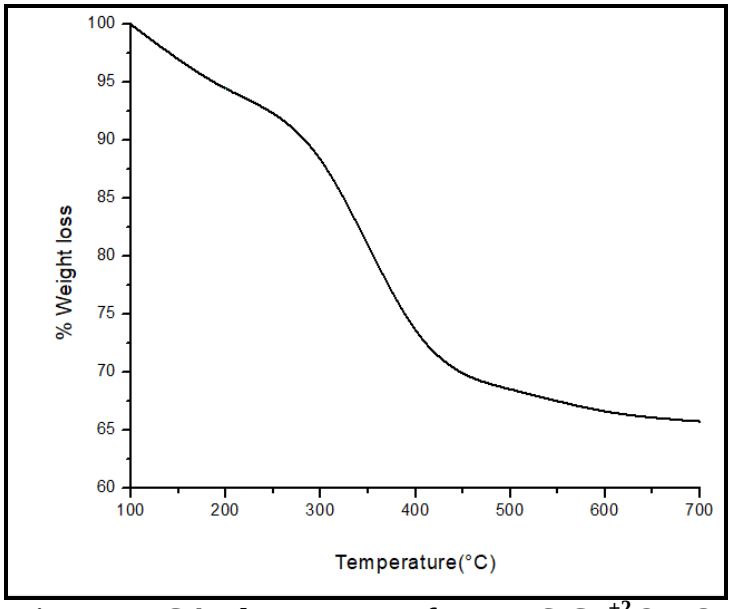


Figure-5 TGA Thermogram of MBTTS-Cu^{+2}.$2H_2O$

The screening of antibacterial and antifungal activity of CBTTS ligand and its all complexes (Table-4 and 5) reveals that the ligand is moderately toxic against bacterial and fungi, while all the complexes are more toxic than ligand. Among all the complexes the Cu^{+2} complex is more toxic against fungi.

Table:-4 Antibacterial Activity of CBTTS Ligand and Its Metal Chelates

Compounds	**Minimum Inhibitory Concentration (MIC, µgmL^{-1})**			
	Gram positive		**Gram negative**	
	Bacillus subtilis	***Staphylococcs aureus***	***Klebsiella promioe***	***E.coli***
CBTTS	125	125	150	150
CBTTS-Cu^{2+}	**25**	**25**	**12.5**	**12.5**
CBTTS-Ni^{2+}	75	100	100	70
CBTTS-Co^{2+}	75	50	50	25
CBTTS-Zn^{2+}	25	50	100	110
CBTTS-Mn^{2+}	75	75	75	125
Amoxillin	250	150	250	200

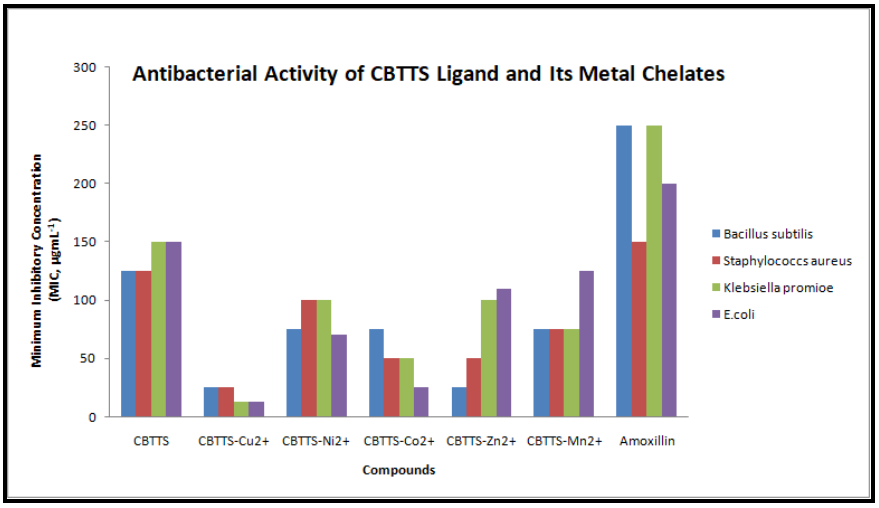


Figure-6 Antibacterial Activity of CBTTS Ligand and Its Metal Chelates

Table– 5 Antifungal activity of CBTTS ligand and its metal chelates

Compounds	**Minimum Inhibitory Concentration (MIC, µgmL^{-1})**			
	Aspergillus niger	***Botrydepladia Thiobromine***	***Nigrospora Sp.***	***Fusarium oxyporium***
CBTTS	100	75	75	100
CBTTS-Cu^{2+}	**25**	**25**	**12.5**	**12.5**
CBTTS-Ni^{2+}	75	50	75	75
CBTTS-Co^{2+}	100	75	75	50
CBTTS-Zn^{2+}	50	25	50	50
CBTTS-Mn^{2+}	50	50	75	50
Nystatin	**300**	**200**	**250**	**200**

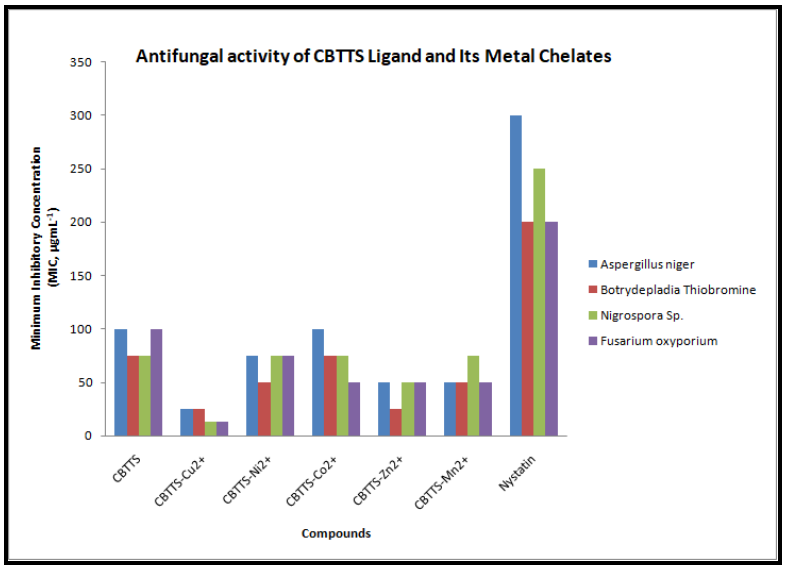


Figure-7 Antifungal Activity of CBTTS Ligand and Its Metal Chelates

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