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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDIES OF SELECTED TRANSITION METAL COMPLEXES DERIVED FROM BENZOTRIAZOLE RING WITH THIOSEMICARBAZONES

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ABSTRACT
The novel ligand, (2-(1-(1H-benzo[d][1,2,3]triazol-1-yl)propan-2-ylidene) hydrazine carbo thioamide(BTTS) was synthesised from thiosemicarbazide and 1-(1H-benzo[d][1,2,3]triazol-1-yl)propan-2-one. 1-(1H-benzo[d][1,2,3]triazol-1-yl)propan-2-one was synthesised from Benzotriazole and chloroacetone. The reaction between novel ligand with selected Transition Metal salts (Cu(II), Co(II), Ni(II), Mn(II) and Zn(II)) yielded their metal complexes of BTTS. The characterization like elemental contents, Spectral studies, metal: ligand ratio and magnetic properties of novel ligand and their metal complexes were carried out. Antibacterial Activity of ligand BTTS and its all metal complexes were studied.

KEYWORDS: Benzotriazole; Thiosemicarbazone: Metal complexes; Spectral Study; Magnetic properties and Antibacterial activities.

INTRODUCTION
Due to various pharmaceutical as well as biological activity number of research work carried out to synthesis novel heterocyclic compounds[i]. Among them nitrogen and sulfur -containing compounds, thiosemicarbazides show importance in the field of medicinal chemistry[ii].
Hence, 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 sulfur- containing heterocyclic compounds like pyrazoles, thiazoles, thiadiazoles, thiadiazines, triazoles, pyrimidines, triazines, pyrazolotriazines, and thiazolotriazines and so on synthesised from thiosemicarbazide[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,vii]. 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[vii]. 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, we thought to synthesis thiosemicarbazone containing novel heterocyclic ligands and their metal complexes. The whole reaction work is summarised in following scheme-1.

EXPERIMENTAL

Laboratory grade chemicals were used. 1H-benzotriazole synthesised by reported method[xiii] 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 BTTS (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 activity was measured at a conc, 50µg/ml by agar-cup plate method[iv-vii]. Similar conditions using Amoxillin as a control was used standard for comparison. The Zone of Inhibition measured in mm. Antifungal activity of all the samples was monitored against various fungi, following the method reported in literature[iv-vii].

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

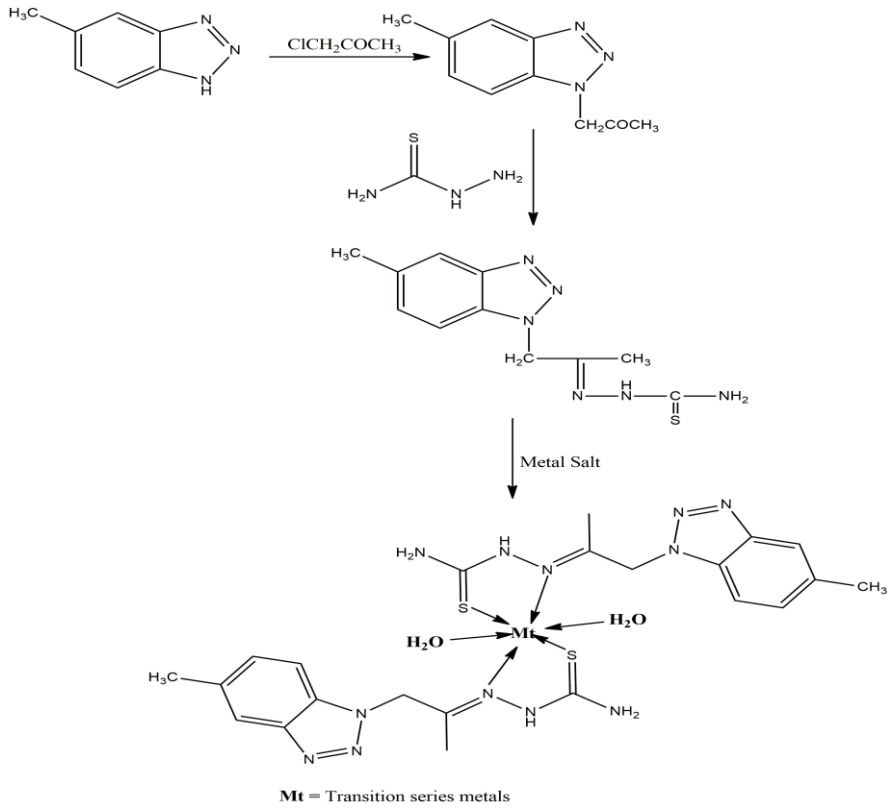
Mixture of Benzotriazole (0.01M) and chloroacetone (0.01 M) were taken into a 250 mL round bottom flask. 150 mL of dry acetone and 30 g of anhydrous potassium carbonate was added and the reaction mixture was refluxed for 6 h at 75°C. Filtrate the product, dried and recrystallized from acetone. The purity of the compound was checked by TLC and melting point. Yield: 79 %, m.p:125°C, Elemental Analysis for $C_9H_9N_3O$(175 gm/mole):Clac.%C, 61.70; %H, 5.18; %N, 23.99; Found.%C, 61.6; %H, 5.1; %N, 23.9. IR Spectral Features (cm^{-1}) shows at 2874,1480,1390(C-H Str.),1620(C=O),2990(Aromatic C-H Str.) and 1580,1475(Aromatic C-C Str.). NMR Signals (δ ppm) at 2.15(singlet, 3H, -CH3),7.45-8.00(multiplate, 4H, benzotriazole C-H) and 4.90-4.92 (singlet, 2H, -CH2-).

Synthesis of (2-(1-(1H-benzo[d][1,2,3]triazol-1-yl)propan-2-ylidene) hydrazine carbo thioamide(BTTS)[vii-x]:

Thiosemicarbazone was synthesized by refluxing the solution of thiosemicarbazide (0.02mol) in ethanol and the alcoholic solution of 1-(1H-benzo[d][1,2,3]triazol-1-yl)propan-2-one (0.01mol) in water bath for 6 hrs with continuous stirring. After cooling the compounds were filtered and recrystallized from R-spirit. Yield: 72%; m.p. 170°C. Elemental Analysis for $C_{10}H_{12}N_6S$ (248gm/mole):Clac.%C, 48.37; H, 4.87; N, 33.85; S, 12.91; Found.% C, 48.3; H, 4.8; N, 33.8; S, 12.9.

IR Spectral Features (cm^{-1}) shows at 3385-3230(N-H of NH2 and NH Str.),2874,1480, 1390(C-H Str.),1620,1560(C=N),3032(Aromatic C-H Str.),1600, 1475(Aromatic C-C Str.) and 775-780(C=S). NMR Signals (δ ppm) at 2.05(singlet, 3H, -CH3),7.45-8.00(multiplate,

4H, benzotriazole C-H),4.90-4.95(singlet, 2H, -CH2-),8.56(singlet, 1H, -NH-),3.70(singlet, 2H, -NH2). LC-MS: M/z at 250.6 (M+).



Scheme-1 Reaction scheme

Table-1. Analysis of BTTS Ligand And Its Metal Complex

Ligand and Metal Complex	Elemental analysis (%)							
	mol. wt	color	Yield %	C%	H%	N%	S%	M%
				Cald. Found	Cald. Found	Cald. Found	Cald. Found	Cald. Found
$C_{10}H_{12}N_6S$	248	Pale yellow	72	48.37 48.3	4.87 4.8	33.85 33.8	12.91 12.9	- -
$C_{20}H_{24}N_{12}S_2Cu^{2+}\cdot 2H_2O$	595.54	yellow	70	40.30 40.2	4.70 4.6	28.21 28.1	10.75 10.7	10.67 10.6
$C_{20}H_{24}N_{12}S_2Ni^{2+}\cdot 2H_2O$	590.71	Light green	67	40.63 40.6	4.74 4.7	28.44 28.4	10.83 10.8	9.94 9.9
$C_{20}H_{24}N_{12}S_2Co^{2+}\cdot 2H_2O$	590.94	Reddish brown	65	40.61 40.6	4.74 4.7	28.43 28.4	10.83 10.8	9.97 9.9
$C_{20}H_{24}N_{12}S_2Zn^{2+}\cdot 2H_2O$	597.38	Pale yellow	69	40.18 40.1	4.69 4.6	28.12 28.1	10.71 10.7	10.94 10.9
$C_{20}H_{24}N_{12}S_2Mn^{2+}\cdot 2H_2O$	586.94	Light blue	66	40.89 40.8	4.77 4.7	28.62 28.6	10.90 10.8	9.36 9.3

Synthesis of Metal complex of (2-(1-(1H-benzo[d][1,2,3]triazol-1-yl) propan-2-ylidene)hydrazinecarbo thioamide(BTTS-M)[vii-x]:

The metal chelates of BTTS (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.

RESULTS AND DISCUSSION:

The reaction between thiosemicarbazide and 1-(1H-benzo[d][1,2,3]triazol-1-yl)propan-2-one yielded (2-(1-(1H-benzo[d][1,2,3]triazol-1-yl)propan-2-ylidene) hydrazine carbo thioamide (BTTS). Table-1 represent the elemnetal analysis, which are consistent with the structure predicted(Scheme-1). The IR spectrum of BTTS comprises the important bands due to thiosemicarbazide. The bands were observed at 3385(N-H,NH2),3230(N-H,NH),1620, 1560(C=N),775-780(C=S) cm^{-1}.

The NMR spectrum of BTTS indicates that the singlet of 2 H and 1H at 3.70 and 8.56 for NH of thiosemicarbazide. The methylene proton shows singlet at 2.05 δ. Thus the structure of BTTS is confirmed as shown in Scheme-I.

The metal and C, H, N contents of metal complexes of BTTS(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-Sulphar group of parent BTTS 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-BTTS ligand.

The observed μ_{eff} values in the range 2.39-5.63 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,xiii-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 BTTS- metal chelates

Metal Chelates	**μ_{eff} (BM)**	**Electronic spectral data(cm^{-1})**	**Transition**
BTTS-Cu^{2+}	2.39	14960 24618	CT $^2B_{1g} \rightarrow {}^2A_{1g}$
BTTS-Ni^{2+}	3.45	22308 15718	$^3A_{2g} \rightarrow {}^3T_{1g}$ (P) $^3A_{2g} \rightarrow {}^3T_{1g}$ (F)
BTTS-Co^{2+}	4.50	24936 19890 8417	$^4T_{1g}(F) \rightarrow {}^6T_{2g}(\square_1)$ $^4T_{1g}(F) \rightarrow {}^4A_{2g}(\square_2)$ $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$

BTTS-Mn^{2+}	5.63	23782 18412 16722	$^6A_{1g} \rightarrow {}^6A_{1g}(^4E_g)$ $^6A_{1g} \rightarrow {}^4T_{2g}(^4G)$ $^6A_{1g} \rightarrow {}^4T_{1g}(^4G)$
BTTS-Zn^{2+}	D	-	-

D*=Diamagnetic

The screening of antibacterial and antifungal activity of BTTS ligand and its all complexes (Table-3 and 4) 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:-3 Antibacterial Activity of BTTS Ligand and Its Metal Chelates

Compound	**Zone of Inhibition (in mm)**			
	Gram positive		**Gram negative**	
	Bacillus subtilis	***Staphylococcs aureus***	***Klebsiella promioe***	***E.coli***
BTTS	9	9	11	12
BTTS-Cu^{2+}	16	17	15	16
BTTS-Ni^{2+}	16	14	13	14
BTTS-Co^{2+}	14	12	11	15
BTTS-Zn^{2+}	11	10	12	13
BTTS-Mn^{2+}	10	12	13	14
Amoxillin control	22	22	23	22

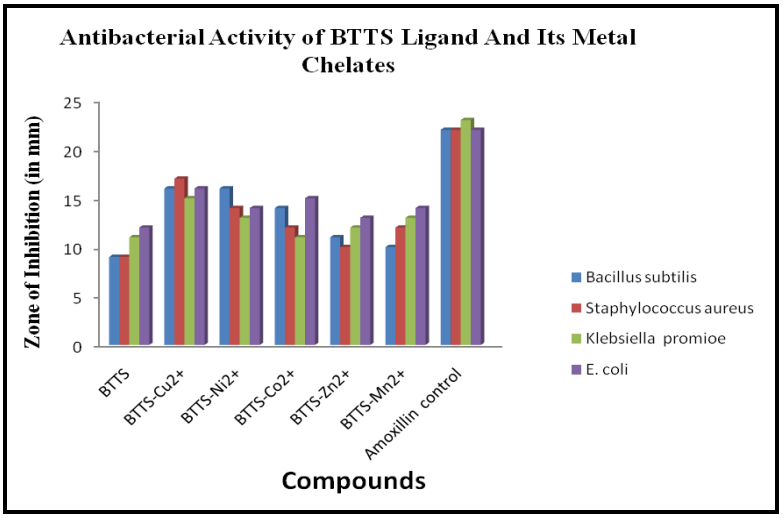


Fig. 1. Antibacterial Activity of BTTS Ligand and Its Metal Chelates

Table :– 4 Antifungal actvity of BTTS ligand and its metal chelates

Sample	**Zone of Inhibition of Fungal at 1000 ppm(%)**			
	Aspergillus niger	***Botrydepladia Thiobromine***	***Nigrospora Sp.***	***Fusarium oxyporium***
BTTS	45	43	55	57

BTTS-Cu^{2+}	77	80	75	82
BTTS-Ni^{2+}	76	67	70	77
BTTS-Co^{2+}	62	60	71	65
BTTS-Zn^{2+}	64	59	68	63
BTTS-Mn^{2+}	67	63	69	65

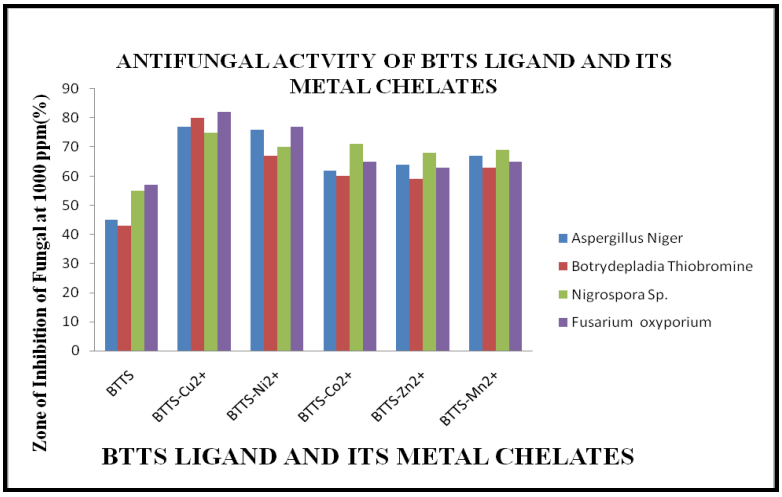


Fig. 2. Antifungal Activity of BTTS Ligand and Its Metal Chelates

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