Synthesis, structural characterization, thermal analysis and antimicrobial assay of Co (II) complexes derived from benzaldehyde N^4-substituted thiosemicarbazone

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Abstract:

Microwave assisted Co (II) complexes of N^4-Substituted thiosemicarbazone were synthesized (TSC-La-f) and characterized by UV-visible spectra, IR spectra, ^1H and ^{13}C NMR spectra, elemental analysis, TGA, magnetic measurements and molar conductance. On the basis of spectral data, magnetic moment and thermal analysis square planar geometry assigned to Co(II) complexes. The electrolytic nature of the complexes was confirmed by their moderately high molar conductance values. All the metal complexes were screened for antimicrobial assay. Among all the complexes (TSC-Le) showed more activity than other Co (II) complexes. From this study it was concluded that complexes are more potent bactericide and fungicide than their corresponding ligands.

Keywords: Thiosemicarbazones, benzaldehyde, Co(II) complexes, antimicrobial activity.

1. Introduction:

Thiosemicarbazones represent a category of organic compounds with biological activity that include antiviral, antibacterial, antifungal, and anticancer effects [1-5]. Thiosemicarbazones are often used as bidentate ligands due to nitrogen and sulfur donor atoms. The inclusion of extra donor groups with thiosemicarbazones moiety enables them to act as tridentate ligands as well [6]. The parent aldehyde or ketone moiety determines the biological activity of thiosemicarbazones [7,8]. Additionally, the structure of thiosemicarbazone consists of N, S donor atoms and a >C=N group with little steric hindrance and good coordination ability, is capable of providing an electron pair needed to form a complex with metal ions [9,10]. The thiosemicarbazide conjugated N-N-S tridentate ligand system appears to be crucial for anticancer action, presumably due to the discovery that structural changes which impair a thiosemicarbazone's capacity to operate as a chelating agent tend to eliminate or limit its medical efficacy [11]. Thiosemicarbazones acquired much attention as prospective therapeutic candidates earlier this decade due to their various pharmacological characteristics [12]. The substantial chelating capacity of these ligands with biologically significant metal ions including Fe, Cu, and Ni, as well as their reductive capabilities, are responsible for these pharmacological effects [13,14]. Because of their varied pharmacological characteristics, thiosemicarbazones received a lot of attention as possible therapeutic candidates earlier this decade.

In acidic media, certain thiosemicarbazones have excellent corrosion inhibition properties. The insertion of groups with delocalized - electron density on the thiosemicarbazone moiety improves the inhibitory activity of thiosemicarbazones against mild steel corrosion [15]. Certain thiosemicarbazone compounds have been claimed to have used as nano precursors [16,17]. It has been shown that adding a benzaldehyde moiety to thiosemicarbazones increases their antibacterial activity [18, 19]. The study of the interaction of thiosemicarbazones with pesticide and drug molecules is now gaining popularity [20]. The introduction of various heterocyclic amino groups or aldehydes with distinct substituents is significant as they exhibit good activity for thiosemicarbazone compounds. As a result, they might be candidates for the development of novel antimicrobial medicines. It has discovered that the biological activity of the thiosemicarbazone moiety is enhanced by the presence of bulky groups at the N^4-position [21,22]. In particular, heterocyclic-N^4-thiosemicarbazones have shown promising anti-breast cancer efficacy [23] additionally, the presence aromatic group at position N^4-of isatin-b thiosemicarbazone derivatives has demonstrated enhanced cytotoxicity against the P-glycoprotein-expressing cell line KB-V1 and the parental KB-3-1 cell lines [24]. As a result, the scientific community has shifted its attention to the discovery of new N-substituted thiosemicarbazone molecules [25-27]. In order to investigate this phenomenon further, we present here the synthesis of N^4-alkyl/aryl substituted thiosemicarbazones derived from unsubstituted benzaldehyde. We have synthesized and investigated coordination behavior of benzaldehyde N^4-substituted thiosemicarbazone ligands with Co(II) metal ions. With a particular interest in microbiological investigations, newly synthesized ligands and their corresponding complexes are being tested for cytotoxic activity against various pathogenic microorganisms. In the current work, the general pathway for the synthesis of ligands and their structures is presented below.

2. Experimental

2.1. Chemicals and Materials

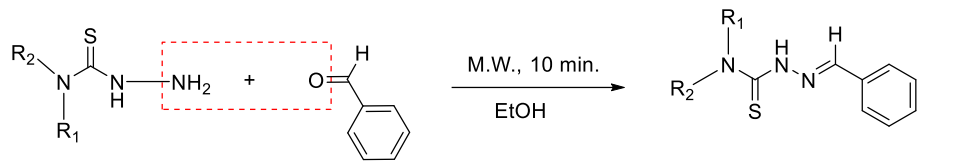
All the chemicals used were of > 98% purity, purchased from Sigma Aldrich and used without further purification.

2.2. Characterization Methods

Microwave-assisted reactions were carried out in a microwave oven labeled "CATALYST SYSTEM." The reaction was monitored using a thin-layer chromatography aluminum TLC plate, silica gel covered with the fluorescent indicator F_{254}, and viewed under UV light (254 nm). The ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded at 300 MHz in deuterated DMSO-d_6 as a solvent and TMS as an internal reference using a Bruker Advance III spectrometer. The values of ^1H NMR spectral data are expressed as δ in ppm relative to residual signals from deuterated solvents, while coupling constants are expressed as J in Hz. The ^{13}C NMR data has been given as position (δ) and atom assignment. The IR spectra have been recorded in wave numbers (cm^{-1}) using a Perkin Elmer FTIR ATR spectrometer. Thermogravimetric analysis was performed at temperatures ranging from ambient temperature to 800 °C using a Perkin Elmer Diamond TG/DTA with a heating rate of 10 °C. Elemental analysis (C, H, N, S) was carried out to ascertain the percentage presence of each element present. Melting points of synthesized ligands were taken using Labcare Cast Iron Melting Point Apparatus, LB-MPS8.

3. General Procedure for the Synthesis of N^4 - substituted benzylidene hydrazine Ligands (TSC-La-f)

A previously described method from the literature, with minor modifications, was employed to synthesize N^4-substituted thiosemicarbazones. For this, equimolar quantities of benzaldehyde (50 mmol) and thiosemicarbazide/s (50 mmol) with absolute ethanol were taken in a 200 mL round bottom flask supported by a funnel placed in microwave oven which is equipped with water condenser **(Scheme 1)**. The reaction mixture was then stirred in microwave oven and irradiated at 340 W (40% power) for 10 minutes in two cycles of 5 minutes each. The extent of reaction was monitored by TLC using n-hexane: ethyl acetate (4:1) ratio. The reaction mixture was allowed to attain room temperature after the completion of reaction and the separated solid was filtered. The resulting solid was purified and dried in an oven at 70 °C.



N^4 - substituted Thiosemicarbazide Benzaldehyde N^4 - substituted Thiosemicarbazone

	TSC-La	TSC-Lb	TSC-Lc	TSC-Ld	TSC-Le	TSC-Lf
R_1	H	H	H	H	Me	H
R_2	H	Me	Et	Ph	Ph	Cy

Scheme 1: General route for the synthesis of N^4-substituted benzylidenehydrazine ligands (TSC-La-f)

3.1. Synthesis of (E)-2-benzylidenehydrazine-1-carbothioamide (TSC-La)

White Solid; yield: 85.4%; m.p. 294-298 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δH (ppm): 11.41 (s, 1H, NH), 8.26 (s, 1H, N=CH), 8.10 (brs, 1H, NH_2), 8.07 (brs, 1H, NH_2), 7.75-7.79 (m, 2H, phenyl-$C_{2,6}$-H), 7.42- 7.45 (m, 3H, phenyl $C_{3,4,5}$-H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ_c (ppm): 178.04 (C=S), 142.5 (HC=N), 134.7 (C_1), 130.5 (C4), 129.3 (C_3,C_5), 127.6 (C_2,C_6); IR (KBr) *ν* (cm-1): 3478.09 (NH_2), 3294.05 (NH), 3150.44 (=CH stretch), 1590.7 , 1610.12 (C=C aromatic), 1335(CN), 1178.52 (C=S stretch); ESI-MS(m/z): calc: 179.05 Found: 180.2

3.2. Synthesis of N-methyl hydrazinecarbothioamide (TSC-Lb)

White Solid; yield: 87.2%; m.p. 142-145 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δH (ppm): 11.51 (s, 1H, N-NH), 9.36 (s, 1H, N=CH), 3.05 (d, N-CH_3), 8.38 (q, 1H, CS-NH), 7.80-7.85 (m, 2H, phenyl-$C_{2,6}$-H), 6.82- 8.25 (m, 3H, phenyl $C_{3,4,5}$-H); ^{13}C NMR (DMSO-d_6, 100 MHz): δc (ppm): 177.44 (C=S), 154.37 (HC=N), 30.05 (N—CH_3), 134.5 (C_1), 130.7 (C_4), 129.9 (C_3,C_5), 126.8 (C_2,C_6); IR (KBr) *ν* (cm-1): 3415 (NH), 3083 (=CH stretch), 1590, 1550 (C=C aromatic), 1625 (C=N), 1271 (C=S stretch); ESI-MS(m/z): calc: 193.07 Found: 193.02

3.3. Synthesis of N-ethyl hydrazinecarbothioamide (TSC-Lc)

White Solid; yield: 84%; m.p. 216-220 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δH (ppm): 11.39 (s, 1H, N-NH), 8.61 (s, 1H, N=CH), 1.15 (t, 2H, CH_2-CH_3), 4.12 (q, 2H, CH_2-CH_3), 8.21 (t, 1H, CS-NH), 7.85-7.90 (m, 2H, phenyl-$C_{2,6}$-H), 6.90- 8.30 (m, 3H, phenyl $C_{3,4,5}$-H); ^{13}C NMR (DMSO-d_6, 100 MHz): δc (ppm): 177.89 (C=S), 139.37 (HC=N), 39.81 (NH—CH_2), 15.03 (CH_2—CH_3), 133.5 (C_1), 129.7 (C_4), 128.9 (C_3,C_5), 128.8 (C_2,C_6); IR (KBr) *ν* (cm-1): 3340 (NH), 3090 (=CH stretch), 1553, 1572 (C=C aromatic), 1683 (C=N), 1370 (C=S stretch); ESI-MS(m/z): calc: 207.08 Found: 208.01

3.4. Synthesis of N-phenyl hydrazinecarbothioamide (TSC-Ld)

White Solid; yield: 85%; m.p. 194-196 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δH (ppm): 10.45 (s, 1H, N-NH), 8.01 (s, 1H, N=CH), 9.21 (s, 1H, phenyl-NH), 7.65-7.70 (m, 4H, phenyl), 7.41-7.47 (m, 5H, phenyl) ; ^{13}C NMR (DMSO-d_6, 100 MHz): δc (ppm): 175.82 (C=S), 142.37 (HC=N), 132.5 (C_1), 131.7 (C_4), 129.1 (C_3,C_5), 129.2 (C_2,C_6); IR (KBr) *ν* (cm-1): 3295 (NH), 3090 (=CH stretch), 1562, 1579 (C=C aromatic), 1545 (C=N), 1267 (C=S stretch); ESI-MS(m/z): calc: 255.07 Found: 256.02

3.5. Synthesis of N-methyl N-phenyl hydrazine carbothioamide (TSC-Le)

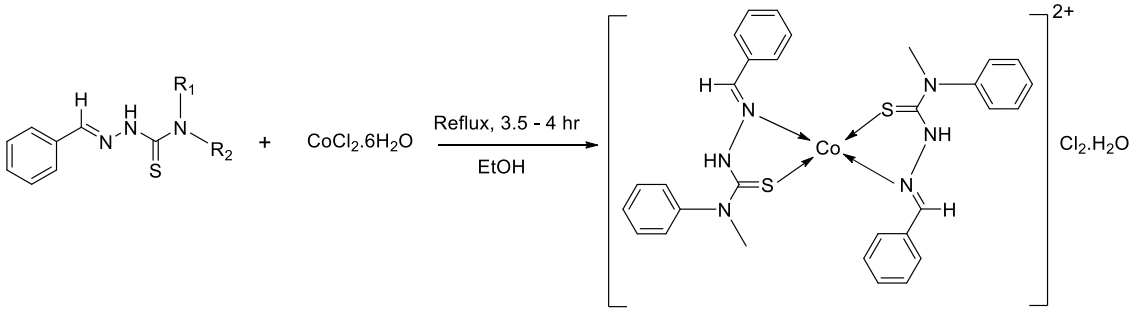
Pale yellow Solid; yield: 80%; m.p. 170-173 °C; ^{1}H NMR (DMSO-d_6, 300 MHz) δH (ppm): 11.65 (s, 1H, N-NH), 8.4 (s, 1H, N=CH), 3.52 (s, 3H, N-CH_3), 7.90-7.85 (m, 2H, phenyl-$C_{2,6}$-H), 7.25- 7.28 (m, 3H, phenyl $C_{3,4,5}$-H), 7.49-7.28 (m, 5H, phenyl) ; ^{13}C NMR (DMSO-d_6, 100 MHz): δc (ppm): 189.2 (C=S), 144.7 (HC=N), 40.2 (N-CH_3), 142.0 (HC-N), 131.2 (C_1), 130.5 (C_4), 130.1 (C_3, C_5), 131.2 (C_2, C_6); IR (KBr) *ν* (cm-1): 3328 (NH), 3114 (=CH stretch), 1041 (N – N), 1560, 1589 (C=C aromatic), 1595-1612 (C=N), 824 (C=S stretch); ESI-MS(m/z): calc: 269.10 Found: 270

3.6. Synthesis of N^4-cyclohexyl hydrazine carbothioamide (TSC-Lf)

Cream colored Solid; yield: 78%; m.p. 182-186 ℃; ^{1}H NMR (DMSO-d_6, 300 MHz) δH (ppm): 10.02 (s, 1H, N-NH), 8.28 (s, 1H, N=CH), 6.36 (d, 1H, C-NH), 4.14 (m, 1H, N-CH), 7.89-7.86 (m, 2H, phenyl-$C_{2,6}$-H), 7.68- 7.51 (m, 3H, phenyl $C_{3,4,5}$-H), 1.89-1.28 (m, 10H, cyclohexyl) ; ^{13}C NMR (DMSO-d_6, 100 MHz): δc (ppm): 179.1 (C=S), 145.3 (HC=N), 58.1 (N-$C_{Cyclohexyl}$), 56.4 (HC-N), 132.4 (C_1), 131.5 (C_4), 129.5 (C_3, C_5), 130.2 (C_2, C_6), 56.4 ($C_{1cyclohexyl}$), 31.2 (C_2, C_6), 24.5 (C_3, C_5), 25.3 (C_4); IR (KBr) *ν* (cm-1): 3124 (NH), 2970, 2924, 2818 ($CH_{aliphatic}$ stretch), 1041 (N – N), 1555, 1579 (C=C aromatic), 1590-1620 (C=N), 828 (C=S stretch); ESI-MS(m/z): calc: 261.13 Found: 262

4. General Synthesis of Co (II) complexes of the ligands (TSC-La-f)

An ethanolic solution of $CoCl_2.6H_2O$ (25 mmol in 30 ml) was dropped into an ethanolic solution of ligand (50 mmol in 30 ml) and refluxed for 3.5-4.0 hours **(Scheme 2)**. Upon cooling the contents after reflux, the colored complexes were separated out in each case. After cautiously evaporating the product, the precipitate was filtered, washed with ethanol several times, and dried over anhydrous $CaCl_2$. TLC was used to confirm the purity of the complexes.



Proposed structure of the Co(II) complex of (TSC-Le) ligand

Scheme 2: synthetic pathway of the Co(II) complexes

5. Antibacterial Assay

The agar well diffusion technique was utilized to ascertain the antibacterial activity of the ligands that were synthesized. Nutrient broth was utilized as the medium in the antibacterial test. The test bacterial strains were cultured for 24 hours at 37 ℃ after being injected in nutrient broth. With the use of a swab, a fresh 0.1 mL bacterial culture containing 108 CFU was spread out over the nutrient agar plate. Each bacterial culture was then inoculated by sweeping the swab across the whole agar surface with a swab stick. Using a sterile cork borer, wells measuring 6 mm in diameter were punched through of the medium. 50 µL of the sample was then aseptically added to each well using a micropipette, and a standard antibiotic was added as a control. The antibacterial activity of the plates was assessed by measuring the zone of inhibition after they were incubated for 24 hours at 37 ℃ in an incubator. Every plate was examined for the existence of bacterial growth inhibition, and the inhibition zone was measured to the closest millimeter (mm). DMSO was used as a negative control or blank, while the standard antibiotics *streptomycin* (50 µg) and *clotrimazole* (50 µg) were used as the positive control and the results are presented in table 3.

To make fungal inoculums, the spores of fungus were suspended in saline water after they had been previously cultivated, properly mixed, and the turbidity level was checked. Using sterile cotton swabs, a suspension of new fungal inoculums was applied to dextrose agar plates. After air drying, 6 mm diameter wells were punched into the medium with a sterile cork borer and filled with 50 µL with test material using an aseptic micropipette. The plates were incubated at 28–37 ℃ for three to four days after being placed in the refrigerator to allow the extract to pre-diffusion for thirty minutes. The zone of inhibition was measured in order to assess the activity.

6. Results and discussion

6.1. Electronic Spectra, Physical Properties and Elemental Analysis

In order to establish the geometry of the metal complexes, the electronic spectral data and magnetic susceptibility measurements provided sufficient evidence. The magnetic moments of the complexes were determined at room temperature and the values of magnetic moments along with molar conductivity are shown in table no.1. The electronic spectra of ligand and metal complexes were recorded in DMSO solvent at 298 K between 200 and 800 nm. All cobalt complexes were found to be paramagnetic, indicating a 2+ oxidation state for cobalt [28]. The TSC-La-f thiosemicarbazone ligand has two prominent bands one at ~260 and another at ~300 nm. The bands are caused by $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of the >C=N group in the ligand field structure. This band was observed to be moved to a lower wavelength region after complexation, indicating that the ligand was coordinated to the metal ion. The Co (II) complexes exhibited a wide band at 690 nm which can be attributed to the Ligand to Metal CT transition (LMCT). The stereochemistry of Co(II) complexes may be distinguished by the magnetic properties because square planar complexes have one unpaired electron and T_d complexes have three [29]. In the present study the cobalt TSC-La-f complexes have magnetic values ranging from 1.71 to 1.93 BM, and light pink color of the complexes indicating a single unpaired electron and a square planar shape around Co(II) [30]. It is evident from the solid-state magnetic susceptibility investigations that the current complexes are paramagnetic at room temperature [31].

For all complexes, the molar conductance (Λ_M) values were measured at a concentration of 10^{-3}M using DMF as the solvent and the values vary from 32–98 $\Omega^{-1}cm^2\ mol^{-1}$. The relatively high molar conductance values suggest that all of the complexes are electrolytic in nature [32]. Elemental analysis results were in good agreement with the isolated metal chelate formula. For all electrolytes, Cl^- anions are outside the metal coordination sphere [33]. Hence, the conductivity observations of Co(II)-chelates support their speculated general formulas based on elemental and spectral analysis.

Table 1.

Magnetic moments and molar conductivity and elemental analysis data of Co(II)-TSC-La-f metal complexes.

Complex	Mol. Wt.	Color	Yield (%)	Molar Conductance ($\Omega^{-1}cm^2\ mol^{-1}$)	μ_{eff} (B.M.)	Elemental Analysis found (clcd.) %			
						Co	C	H	N
$[Co(TSC\text{-}La)_2]Cl_2$ $CoC_{16}H_{18}N_6S_2Cl_2$	489	Light Pink	64	98	1.71	12.15 (12.05)	39.50 (39.26)	3.72 (3.68)	17.20 (17.17)
$[Co(TSC\text{-}Lb)_2]Cl_2$ $CoC_{18}H_{22}N_6S_2Cl_2$	517	Light Pink	69	72	1.80	11.42 (10.39)	41.80 (41.77)	4.18 (4.25)	16.20 (16.24)
$[Co(TSC\text{-}Lc)_2]Cl_2$ $CoC_{20}H_{26}N_6S_2Cl_2$	544	Light Pink	61	54	1.93	10.56 (10.83)	44.07 (44.11)	4.90 (4.77)	15.48 (15.44)
$[Co(TSC\text{-}Ld)_2]Cl_2$ $CoC_{28}H_{26}N_6S_2Cl_2$	641	Pink	71	46	1.86	9.21 (9.19)	52.50 (52.41)	4.86 (4.77)	13.14 (13.10)
$[Co(TSC\text{-}Le)_2]Cl_2$ $CoC_{30}H_{30}N_6S_2Cl_2$	669	Pink	68	32	1.90	8.91 (8.80)	53.61 (53.81)	4.52 (4.48)	12.61 (12.55)
$[Co(TSC\text{-}Lf)_2]Cl_2$ $CoC_{28}H_{38}N_6S_2Cl_2$	652	Light Pink	59	41	1.89	9.17 (9.03)	52.48 (52.41)	5.79 (5.82)	12.93 (12.88)

6.2. Thermogravimetric Analysis

Thermogravimetric analyses of the metal complexes give information on their thermal stabilities, the existence and coordination status of water molecules [34]. Thermo gravimetric data of the Co(II) complexes are given in table 2. The Co(II) complexes of TSC-La-f decomposed in two stages. It reported the initial step of breakdown at 65-86 °C, which might be the result of one lattice water molecule being lost [35]. The second stage of breakdown occurred between 239 and 302 °C, which might be related to the subsequent decomposition of the ligand. The mass of the residue that remains in the temperature range 473 - 516 °C, maybe as a result of CoS formation [36].

Table 2
Thermogravimetric analysis data of Co(II)-TSC-La-f metal complexes

Compounds	Temp. range (°C)	Stages	DTG_{max} (°C)	Residual Species	Decomposition Species	Total Loss (%)	
$[Co(TSC\text{-}La)_2]Cl_2.H_2O$	50-800	1^{st}, 2^{nd}, 3^{rd}	69, 239, 483	CoS	$8C_2H_2 + Cl_2 + 3N_2 + H_2S$	82.60	82.65
$[Co(TSC\text{-}Lb)_2]Cl_2.H_2O$			72, 261, 496		$9C_2H_2 + Cl_2 + 3N_2 + H_2S$	86.02	86.11
$[Co(TSC\text{-}Lc)_2]Cl_2.H_2O$			65, 247, 503		$10C_2H_2 + Cl_2 + 3N_2 + H_2S$	81.26	81.30
$[Co(TSC\text{-}Ld)_2]Cl_2.H_2O$			86, 274, 498		$14C_2H_2 + Cl_2 + 3N_2 + H_2S$	83.11	83.16
$[Co(TSC\text{-}Le)_2]Cl_2.H_2O$			82, 302, 516		$15C_2H_2 + Cl_2 + 3N_2 + H_2S$	79.78	79.81
$[Co(TSC\text{-}Lf)_2]Cl_2.H_2O$			77, 281, 473		$14C_2H_2 + Cl_2 + 3N_2 + H_2S$	83.37	83.40

6.3. In Vitro Antimicrobial Activity Study ligands and its complexes

The antibacterial activity of the synthesized ligands and their complexes has been assessed using the agar well diffusion technique [37]. In our current investigation, we tested activity against two Gram-positive bacteria, *S. aureus* and *B. cereus*, two Gram-negative bacteria, *E. coli* and *K. pneu.*, and two fungal pathogens, *A. niger and Penicillium sp.* Table-2 lists the antibacterial activity that the ligands and complexes have demonstrated. The only modifications made to the ligands are the replacement of alkyl and aryl groups on the thioamide nitrogen. This alteration might only be responsible for demonstrating altered activity on harmful microorganisms.

Table 3
Antimicrobial activity studies of ligand and its complexes.

Compound	Diameter of inhibition zone (mm)					
	B. cereus	*S. aureus*	*E. coli*	*K. pneumonia*	*A. niger*	*Penicillium sp.*
TSC-La	-	-	2	-	-	-
TSC-Lb	3	1	4	4	2	2
TSC-Lc	3	1	4	4	-	3
TSC-Ld	4	3	8	8	5	6
TSC-Le	6	5	12	9	8	10
TSC-Lf	2	2	5	3	4	3

$[Co(TSC\text{-}La)_2]Cl_2.H_2O$	2	-	2	2	-	-
$[Co(TSC\text{-}Lb)_2]Cl_2.H_2O$	4	3	5	5	2	4
$[Co(TSC\text{-}Lc)_2]Cl_2.H_2O$	3	2	6	7	2	3
$[Co(TSC\text{-}Ld)_2]Cl_2.H_2O$	8	4	12	10	6	5
$[Co(TSC\text{-}Le)_2]Cl_2.H_2O$	10	7	18	12	12	15
$[Co(TSC\text{-}Lf)_2]Cl_2.H_2O$	5	2	7	6	3	6
Streptomycin (+ ve)	14	10	24	15	-	-
Clotrimazole	-	-	-	-	20	22
DMSO (-ve)	-	-	-	-	-	-

Antibacterial activity: less than 12 mm-weak activity and more than 16 high activity
Antibacterial activity: less than 07 mm-weak activity and more than 10 high activity

Every complex has demonstrated greater potency compared to the ligand, according to data on the antibacterial activity of thiosemicarbazone and its complexes [38]. The complexes exhibited greater antibacterial activity in comparison to their antifungal activity [39]. The order of activity for the complexes against standard drug is given as $[Co(TSC\text{-}La)_2]Cl_2 < [Co(TSC\text{-}Lb)_2]Cl_2 > [Co(TSC\text{-}Lc)_2]Cl_2 < [Co(TSC\text{-}Ld)_2]Cl_2 <$ **$[Co(TSC\text{-}Le)_2]Cl_2$** $> [Co(TSC\text{-}Lf)_2]Cl_2$. Among all the compounds, $[Co(TSC\text{-}Le)_2]Cl_2.H_2O$ showed more activity followed by $[Co(TSC\text{-}Ld)_2]Cl_2$ than the other complexes.

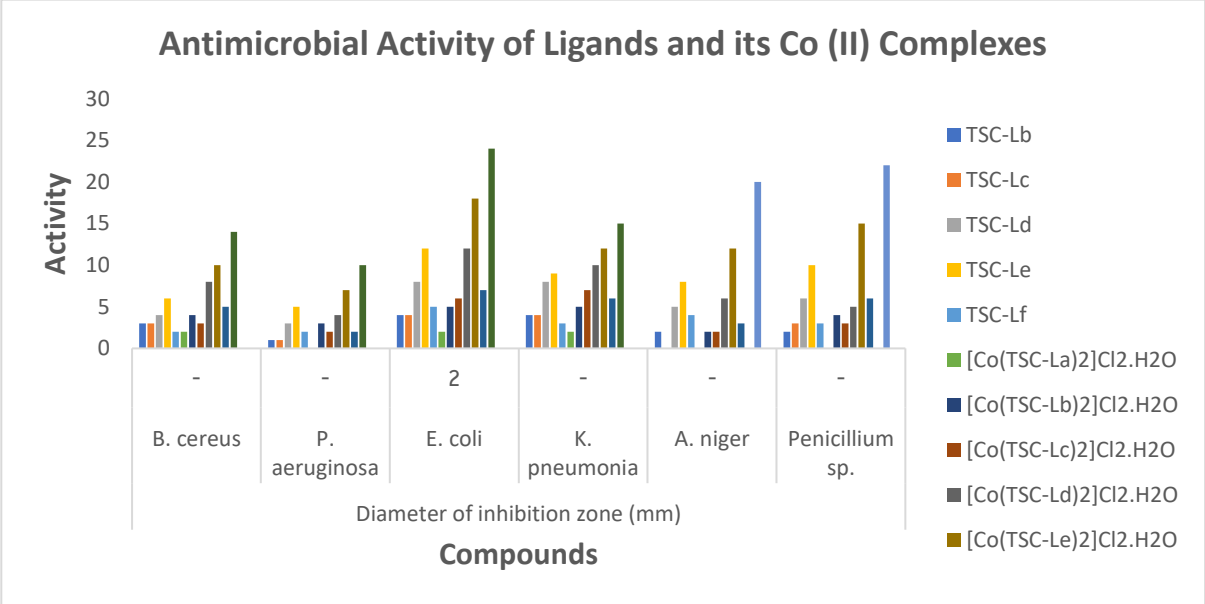


Fig.1. Antimicrobial activity of Co (II) thiosemicarbazone complexes

On the basis of Tweedy's chelation theory the enhanced activity of the complexes is explained. Chelation of the ligands lowers the polarity of the metal ion significantly due to the partial distribution of its positive charge with the donor groups and probable π-electron delocalization over the chelate ring [40]. This enhances lipid solubility, which facilitates lipid absorption into normal microorganism cells. An increase in the lipophilic nature of the central metal atom by chelation may facilitate its penetration through the lipid layer of the cell wall. As a result, lipophilicity is important in determining a compound's antimicrobial efficacy. The microbe's cell's permeability determines how differently the complexes behave against various organisms. The azomethine group in the complexes may form a hydrogen bond with the active centers of the component cells, interfering with normal cell function as a possible mechanism of action [41]. Some of the complexes studied here may have moderate activity due to their poor

lipophilicity. This may prevent them from passing through the lipid membrane and, as a result, they cannot effectively hinder or oppose the development of microbes.

7. Conclusion

In the present study, the N^4 - substituted thiosemicarbazone derivatives of benzaldehyde and their Co(II) complexes have been described. Electron spectra, infrared spectra, ^1H, ^{13}C NMR spectra, elemental analysis, molar conductivity, magnetic moment, and thermogravimetric analysis were used to analyze the synthesized compounds. The ligands coordinate as bidentate using the azomethine nitrogen and sulfur atoms. The spectral data and low magnetic moment values suggests that the cobalt (II) complexes have a square planar shape and the moderately high values of molar conductivity indicates the complexes are electrolytic nature. Thermogravimetric analysis of the complexes indicates that the presence of lattice water. The antimicrobial properties of the Co(II) complexes were assessed using the agar well diffusion method against two gram-positive bacteria (*S. aureus* and *B. cereus*), two gram-negative bacteria (*E. coli* and *K. pneu.*), and two fungal pathogens (*A. niger* and *Penicillium sp.*) using *Streptomycin* and *Clotrimazole* as standard drugs. In-vitro antibacterial investigations revealed that Co(II) complexes are more active than their ligands. $[Co(TSC\text{-}Le)_2]Cl_2$ had more activity than other complexes against the standard drugs streptomycin and clotrimazole. Results showed that the substitution at N^4-position in the thiosemicarbazone moiety enhanced the activity of the compounds. Hence, modifications at N^4-positions in thiosemicarbazones and study their modes of action is the topic of further investigation.

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