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Synthesis, Characterization and *in vitro* Antibacterial Activities of Cu(II) and Ni(II) Complexes of N-(benzo[*d*]thiazol-2-ylcarbamothioyl)benzamide

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A chelating ligand, N-(benzo[*d*]thiazol-2-ylcarbamothioyl)benzamide (N-btcb), with sulfur and oxygen donor atoms, was synthesized using 2-aminobenzothiazole and benzoyl isothiocyanate. Cu(II) and Ni(II) complexes of N-btcb were prepared by refluxing chelating ligands with the respective metal acetates in acetone. Structures of both the complexes were established using elemental analysis and spectroscopic methods (IR, ^{1}H NMR, electronic spectra) and physical properties like colour, solubility, melting point, and thermal stability were recorded. Structural analysis suggests that for both the complexes N-btcb is coordinated to the metal ion through the sulfur and oxygen donor atoms, forming a six-membered ring. The coordination geometry of the Cu(II) complex was found to be distorted octahedral, and that of the Ni(II) complex was found to be octahedral. Biological activity (*in vitro*) assessments suggest slightly improved antibacterial activities for both the metal complexes compared to the organic ligand, except against *E. coli.*

Key words: Antibacterial activity; benzamides; benzothiazole ; metal complexes

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Coordination chemistry is one of the most actively researched areas of inorganic chemistry due to the innumerable applications of complexation products in various fields [1-3]. In recent years, a special class of polymeric coordination compounds, namely metal-organic frameworks, have been widely used as efficient materials in many applications due to their structural stability and diversity [4-6]. The structural tuneability achievable by a variety of metal ions and ligands also enables one to build complex compounds that are involved in specific interactions with proteins, nucleic acids, antibiotics, and many other biomolecules [7]. When an organic ligand coordinates with a metal ion, it undergoes numerous structural changes and the complexation can dramatically accelerate its bioactivity [8-10]. In particular, studies on transition metal complexes of polydentate organic ligands have been a popular area of research as these compounds not only possess interesting physical and spectral properties but also exhibit a range of biological activities [11]. Copper exhibits considerable biochemical activity as it is an important trace metal and a constituent of several externally-controlled compounds in the human body. It is known to have interactions with various biomolecules such as albumin, ceruloplasmin, and other proteins. Lately, complexes of copper with organic ligands have been shown to have therapeutic effects through binding interactions with relevant biomolecules, mainly proteins and nucleic acids [12]. Like copper complexes, coordination complexes of nickel are also of great importance in various aspects of chemistry. They draw a lot of interest due to their low environmental toxicity and specific chemotherapeutic properties [13-14].

Heterocyclic compounds containing oxygen and sulfur as donor atoms are extensively used as polydentate ligands in coordination chemistry [15]. Compounds with carbonyl and thiocarbonyl groups also occupy an important position in coordination chemistry as potential donor ligands [16-18]. Thiourea as a ligand can coordinate with several metal ions and form stable complexes as neutral ligands, mono-anions, or di-anions [19-20]. Substituted thioureas form stable, neutral coordination complexes with different transition metal ions [21]. Benzoyl thiourea is also an important chelating agent with -C=O and -C=S donor functional groups. Several studies have been reported on the coordination ability of the thiourea ligand to determine the coordination site and geometry of complexes [22-25]. Due to their ability to combine with various metal ions, thiourea derivatives are extensively studied in coordination chemistry [26-28]. Various ligands containing thiourea and benzoyl thiourea groups as well as their metal complexes exhibit a broad spectrum of biological effects including antibacterial [29], antifungal [30], anti-tubercular [31], anticancer [32], antimalarial [33], anti-oxidant [34] activities. They also show efficient DNA binding ability [35-36].

In this article, the synthesis, characterization and antibacterial activity assessments of a N-substituted benzamide ligand namely, N-(benzo[*d*]thiazol-2-ylcarbamothioyl)benzamide (N-btcb) and its Cu(II) and Ni(II) complexes are reported, with the intention of exploring novel and potent antimicrobial agents.

EXPERIMENTAL

1. Synthesis

1.1. Synthesis of N-btcb Ligand:

In the present work, the target chelating ligand N-btcb was prepared by the reaction of 2-aminobenzothiazole and benzoyl isothiocyanate, as presented in our previous paper [37]. 2-Aminobenzothiazole (0.01 mol, 1.5 g) and benzoyl isothiocyanate (0.01 mol, 1.4 mL) were refluxed in a mixture of dry benzene (25 mL) and 2-propanol (5 mL) for 3 hours. The obtained solid N-(benzo[*d*]thiazol-2-ylcarbamothioyl)benzamide (N-btcb) ligand was filtered, washed with dilute HCl, dried, and recrystallized from benzene.

Colour: yellow; Yield: 83%; M.P.: 189 ºC; Anal. Calcd for $C_{15}H_{11}N_3OS_2$ (%): C, 57.49; H, 3.54; N, 13.41; S, 20.46. Found (%): C, 56.39; H, 3.49; N, 13.52; S, 20.49.

IR (KBr, ν_{max}, cm^{-1}): The infrared spectrum exhibited characteristic bands at 750.7 (C-S, stretching), 1164.15 (C=S, stretching), 1521.10 (Ar C=C, stretching), 1612.11 (C=N, stretching), 1677.17 (C=O, stretching), 3086.18 (Ar C-H, stretching), 3343.17 and 3401.16 (NH, stretching) (see supplementary material, figure: **S1**). ^{1}H NMR (DMSO, δ, ppm): ^{1}H-NMR spectra showed a characteristic singlet near δ 8.84 ppm due to the NHC=O proton, a broad singlet near δ 12.59 ppm for NHC=S and -NH protons, and multiplets around δ 7.29-8.28 ppm were observed for aromatic protons (See supplementary material, figure: **S4**).

1.2. Synthesis of Cu(II) and Ni(II) N-btcb Complexes:

Cu(II) and Ni(II) complexes of N-btcb were synthesized from the respective metal salts as explained below and presented in **Scheme I.**

1.2.1. Synthesis of Cu(II) N-btcb complex [Cu(N-btcb)$_2$(H_2O)$_2$]: Metal and ligand were used in the molar ratio 1:2 [ML_2] for the reaction. A methanolic solution of copper acetate (0.05 mol) was mixed with a hot solution of ligand (0.1 mol) in acetone and refluxed for 30 minutes. The resulting solution was poured into a petri dish and allowed to stand overnight at room temperature. After complete evaporation of the solvent, the obtained solid material was collected and washed with cold methanol and diethyl ether. The product was dried over anhydrous calcium chloride in a desiccator for 24 hours.

Colour: Pear green; Yield: 81%; Anal. Calcd for $C_{30}H_{24}CuN_6O_4S_4$ (%): C, 49.74; H, 3.34; N, 11.60; S, 17.71. Found (%): C, 50.01; H, 3.16; N, 11.09; S, 17.82.

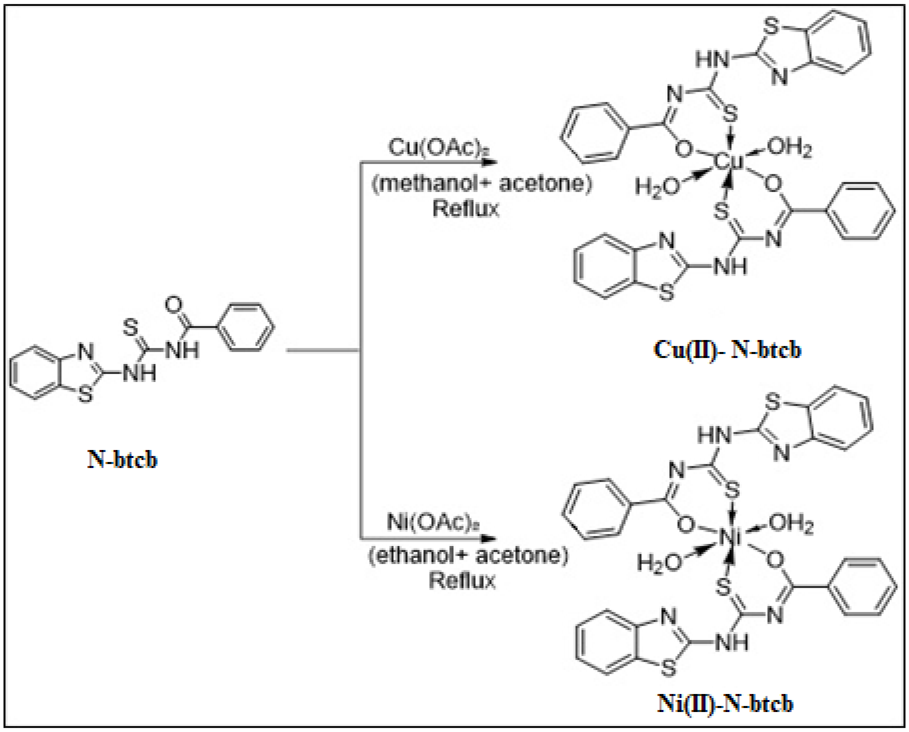
IR (KBr, ν_{max}, cm^{-1}): The infrared spectrum of the product exhibited characteristic bands at 754.20 (C-S, stretching), 1090.30 (C=S, stretching), 1591.19 (Ar C=C, stretching), 1676.60 (C=N, stretching), 1168.47 (C-O, stretching), 3066.50 (Ar C-H, stretching), 3340.56 (NH, stretching) and 453.39 (Cu-O, stretching). (See supplementary material, figure: **S2**).

^{1}H NMR (DMSO, δ, ppm): ^{1}H-NMR spectra showed a characteristic broad singlet near δ 11.91 ppm for NHC=S protons and multiplets around δ 6.52-8.62 ppm were observed for aromatic protons. (See supplementary material, figure: **S5**).

1.2.2. Synthesis of Ni(II) N-btcb complex [Ni(N-btcb)$_2$(H_2O)$_2$·H_2O]: Metal and ligand were used in the molar ratio 1:2 [ML_2] for the reaction. Nickel acetate (0.05 mol) was dissolved in ethanol and the ligand (0.1 mol) was dissolved in a minimum amount of acetone separately. Then both solutions were mixed and warmed in a water bath with stirring. The reaction mixture was refluxed for 30 minutes and then poured into a petri dish which was allowed to stand overnight. After complete evaporation of the solvent, the collected solid complex was washed with hot water and diethyl ether to remove excess nickel acetate and unreacted ligand. The product was dried over anhydrous calcium chloride in a desiccator for 24 hours.

Colour: Pear green; Yield: 76%; Anal. Calcd for $C_{30}H_{26}N_6NiO_5S_4$ (%): C, 48.86; H, 3.55; N, 11.39; S,17.39. Found (%): C, 48.59; H, 3.26; N, 11.28; S, 17.12.

IR (KBr, ν_{max}, cm^{-1}): The infrared spectrum of the product exhibited characteristic bands at 751.19 (C-S, stretching), 1116.27 (C=S, stretching), 1548.4 (Ar C=C,



Scheme I. Synthesis of Cu(II) and Ni(II) complexes of N-btcb

stretching), 1682.17 (C=N, stretching), 1026.25 (C-O, stretching), 3062.27 (Ar C-H, stretching), 3369.18 (NH, stretching) and 462.18 (Ni-O, stretching) (See supplementary material, figure: **S3).**

^{1}H NMR (DMSO, δ, ppm): ^{1}H-NMR spectra showed a characteristic broad singlet near δ 12.87 ppm for NHC=S and multiplets around δ 6.08-8.22 ppm were observed for aromatic protons (See supplementary material, figure: **S6**)

2. Antibacterial Activity

The antibacterial activities of the synthesized ligand (N-btcb) and its respective metal complexes Cu(II)- N-btcb and Ni(II)-N-btcb were screened against various bacterial strains for both gram-positive (*Staphylococcus aureus and Bacillus subtilis*) and gram-negative (*Escherichia coli* and *Proteus aeruginosa*) bacteria. All bacterial strains were obtained from the Department of Biotechnology, Dr. Ambedkar College, Nagpur, India. The agar well diffusion method was used for carrying out antibacterial screening. All glassware was sterilized by dry heat in an oven at a temperature of 160°C for an hour. Muller Hinton agar was used as the culture medium for the growth of the bacterial colony that was prepared by using beef extract (2.00 g), acid hydrolysate of casein (17.50 g), starch (1.50 g), and agar (17.00 g) in 1 L of distilled water. The pH of the agar medium was adjusted to 7.3 at 25 ºC. To sterilize the media, the prepared agar medium was mixed well and autoclaved at 15 lbs pressure for a minimum of 20 minutes. All the plates were labeled with the names of the organisms. 2 mL of the bacterial culture was taken and mixed well with the autoclaved agar media (500 mL) and poured into each Petri dish slowly in a laminar flow environment. These were allowed to solidify and kept at 30°C for 24 hours.

A single well was created in the agar medium with the help of a sterile borer of 6 mm diameter. 0.05 mL of a newly synthesized test sample/standard was introduced into the well. All the plates were kept in a refrigerator at 2 to 8ºC for 2 hours for effective diffusion of test samples and standards, and then incubated at 37ºC for 24 hours. The antibacterial activities of these compounds were evaluated by measuring the zone of inhibition on the Muller Hinton agar plate. The presence of a definite zone of inhibition of any size around the well indicated antibacterial activity. The diameter of the zone of inhibition for each sample was measured and recorded. The tests were repeated thrice, and the results were reported as means of the three determinations. Measurements were also performed on standard drugs with corresponding cultures for direct comparison with the compounds of interest.

RESULTS AND DISCUSSION

The current work starts with the synthesis of the target chelating ligand N-btcb from the reaction of 2-aminobenzothiazole and benzoyl isothiocyanate.

Synthesis of copper and nickel coordination complexes have been reported by many researchers [24, 38-41]. We have used a similar general procedure to synthesize complexes as follows. Coordination complexes of ligand with Cu(II) and Ni(II) ions were synthesized by reacting two moles of a ligand with one mol of respective metal salts in the mixed solvent of methanol (for Cu(II))/ethanol (for Ni(II)) and acetone. This synthesis protocol was finalized after performing several trials with different ratios of methanol/ethanol and acetone solvents.

The solubility of complexes was investigated with 0.01 g of a compound in 2 mL of the solvent. Based on visual estimation, the ligand **(**N-btcb**)** was highly soluble in benzene and DMSO while its metal complexes were found to be soluble in DMF and DMSO. In general, both the synthesized complexes were found to be less soluble than the ligand in most of the solvents tested. This seems to correlate well with the thermal stability results of the Cu(II)-N-btcb and Ni(II)-N-btcb complexes (described in section 3.4). Molecular structures of the complexes were established through various characterization techniques as described in the following sections.

1. Elemental Analysis/Composition

From the elemental composition values provided in the experimental section, it can be noted that the results obtained are in close agreement with the calculated ones, indicating the formation of 1:2 complexes as proposed in scheme **1**, with two coordinated water molecules.

2. Spectral Analysis

Spectral assignments were made by comparing the infrared spectra of the complexes with that of the ligand. The IR spectrum of the free ligand shows a strong band for aromatic C-H in the region of 3086.18 cm^{-1} along with corresponding C-H bending and stretching bands. The strong peaks at 3343.17 and 3401.16 cm^{-1} are due to the N–H vibrations. The presence of absorption bands at 750 cm^{-1} and 1612.11 cm^{-1} are attributed to the C-S and C=N groups, respectively. It also shows the bands corresponding to C=O (carbonyl) and C=S (thiocarbonyl) vibrations at 1677.17 cm^{-1} and 1164.15 cm^{-1} respectively. Absorption bands corresponding to the carbonyl and thiocarbonyl groups strongly support the formation of the desired ligand.

The IR spectra of metal complexes exhibit prominent changes compared to the spectra of the ligand. With the formation of metal complexes, a notable change was observed for the N-H vibration: only one band was seen at 3340.56 cm^{-1} for Cu(II)- N-btcb and at 3369.18 cm^{-1} for Ni(II)-N-btcb, where the NH stretching indicated the presence of only one type of N-H group. The disappearance of N-H stretching bands correlates to the deprotonation of the NHC=O proton. Another striking change was observed for the C=O (carbonyl) vibration in the region of 1677.17 cm^{-1} for the ligand which disappeared in the IR spectra of both the complexes. A new band appeared at 1168.47-1026.25 cm^{-1} for C-O stretching, indicating the involvement of the O atom of the (C=O) group in coordination with the metal(II) ions. A strong peak at 1164.15 cm^{-1} assigned for (C=S) in the ligand also shifts to lower energy at 1090.30 cm^{-1} and 1116.27 cm^{-1} in the Cu(II)- N-btcb and Ni(II)-N-btcb metal complexes respectively. This may be because of the coordination of the sulfur atom of the thiocarbonyl group to the metal ions, resulting in the weakening of the C=S bond by donation of electrons from the sulfur atom to the metal. Formation of metal complexes is further supported by the appearance of a new band at 462.18-453.39 cm^{-1} due to the M-O stretching (453.39 cm^{-1} for Cu-O in Cu(II)- N-btcb and 462.18 cm^{-1} for Ni-O in Ni(II)-N-btcb).

NMR spectra of the ligand and its coordination complexes were recorded in DMSO-d_6. Chemical shifts (δ) are expressed in ppm down field from TMS. The prominent resonance signals of these compounds were compared with the reported peaks. The ^{1}H NMR spectra of the ligand displayed a singlet at 8.84 ppm for (NHC=O) and a broad singlet at 12.59 ppm for (NHC=S) exchangeable with D_2O. The aromatic protons, which appeared as multiplets, were observed at 7.29-8.28 ppm. In the coordination compounds Cu(II)- N-btcb and Ni(II)-N-btcb, the absence of the signal at δ8.84 ppm due to the (NHC=O) proton indicates deprotonation and the subsequent involvement of its O atom in coordinating with the respective metal ions.

3. Ultraviolet-Visible Spectrophotometry and Magnetic Properties

3.1. Cu(II)- N-btcb: The electronic spectrum of the Cu(II) complex (**Figure 1**) exhibits two spin-allowed transitions i.e. $^2A_{1g} \leftarrow {}^2B_{1g}$ and $^2E_g \leftarrow {}^2B_{1g}$ which correspond to absorption bands at 690 nm and 610 nm, respectively, while another band is also observed at 440 nm which may be assigned to a charge transfer transition. This suggests a distorted octahedral configuration for the Cu(II) complex [42]. The observed magnetic moment for the complex was in the range of 1.93 B.M., slightly higher than the spin-only value which is also indicative of the distortion from regular octahedral geometry.

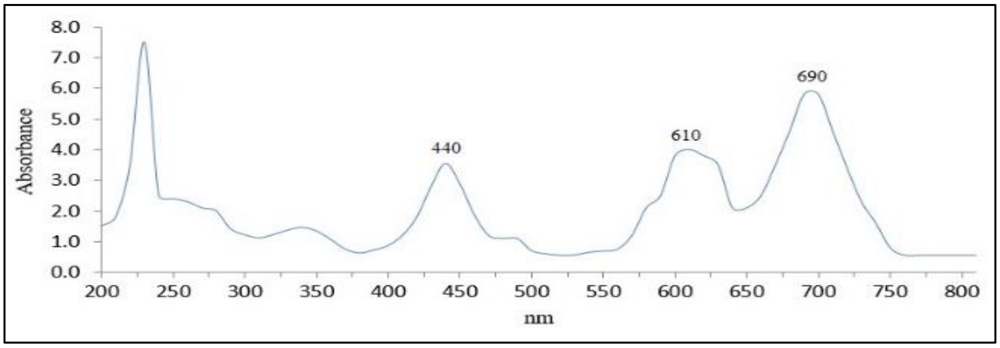


Figure 1. Electronic Spectra of N-(benzo[d]thiazol-2-ylcarbamothioyl)benzamide Cu(II) complex

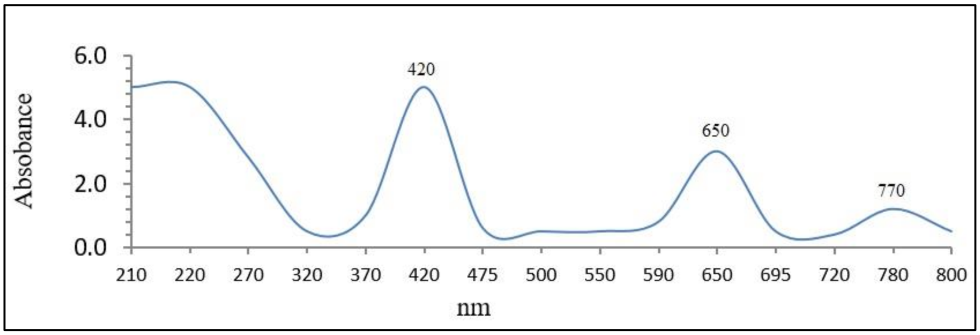


Figure 2. Electronic Spectra of N-(benzo[d]thiazol-2-ylcarbamothioyl)benzamide Ni(II) complex

3.2. Ni(II)-N-btcb : In its complex, the Ni(II) ion is expected to have a d^8 configuration, with the ground term ^3F and a higher ^3P term. In the electronic spectrum of the complex (**Figure 2**), three spin-allowed transitions i.e. $^3A_{2g}\rightarrow{}^3T_{2g}$, $^3A_{2g}$ (F)$\rightarrow{}^3T_{1g}$ (F), $^3A_{2g}$(P)$\rightarrow{}^3T_{1g}$(P), at 770, 650 and 420 nm respectively were observed, indicating an octahedral geometry for the complex [43]. The magnetic moment value of the complex was found to be 3.38 B.M. which falls within the range of 2.8-3.5 B.M. for Ni complexes, suggesting an octahedral geometry.

Table 1 below summarizes the electronic spectral assignments and magnetic data for Cu(II) and Ni(II) complexes with their respective suggested coordination geometries.

Table 1. Electronic spectra assignments and magnetic moment of complexes

Metal Complex	μ_{eff} (B.M.)	Observed energies (nm)	Assignments	Coordination geometry
[Cu(N-btcb)$_2$.(H$_2$O)$_2$]	1.93	690 610 440	$^2B_{1g}\rightarrow{}^2A_{1g}$ $^2B_{1g}\rightarrow{}^2B_{2g}$ CT	Distorted octahedral
[Ni(N-btcb)$_2$.(H$_2$O)$_2$·H$_2$O]	3.38	770 650 420	$^3A_{2g}\rightarrow{}^3T_{2g}$ $^3A_{2g}$(F)$\rightarrow{}^3T_{1g}$(F) $^3A_{2g}$(P) $\rightarrow{}^3T_{1g}$(P)	Octahedral

Key to symbols: $\mu_{eff:}$ effective magnetic moment; B.M: Bohr Magnetons

4. Thermo-Gravimetric Analysis

The thermal stability of the Cu(II)-N-btcb and Ni(II)-N-btcb complexes was investigated using thermogravimetric analysis (TGA) (**Fig. 3** and **4**). The TGA profile of a compound provides clues about changes in its chemical composition with respect to temperature i.e. thermal decomposition or degradation. For the coordination complexes, it also helps in gaining a deeper understanding of the modes of binding of water molecules in the compound, e.g. lattice water vs. coordinated water. The removal of lattice water usually occurs below 140°C whereas coordinated water is stable and generally volatilized only above 140°C. Thus a small weight loss between 50-140°C was assigned to the loss of lattice water [43-44]. Further weight loss at higher temperatures (450-800ºC) corresponds to the complete decomposition of ligand moiety around the metal ion and formation of the corresponding metal oxide.

TGA thermograms of the complexes are provided in Figures **3** and **4** below. According to the observed mass losses, degradation patterns are proposed for the Cu(II)- N-btcb and Ni(II)-N-btcb complexes, which are represented in **Table 2.** Both complexes exhibit multistage decomposition patterns.

4.1. Cu(II)- N-btcb: No significant weight loss was observed up to 140ºC, indicating the absence of lattice water in the compound. The weight loss observed in the 140˚C - 201˚C range corresponds to a loss of two molecules of coordinated water (calc.4.969%, obs. 5.22%). A weight loss observed between 201ºC to 571ºC may be due to the decomposition of the ligand (calc. 83.94%, obs. 82.335%). The weight remaining at the end up to 966ºC corresponds to the CuO residual fraction (calc.11.056%, obs. 12.445%). From the thermogram, the half-decomposition temperature was determined to be 361.04 ºC (**Table 2)**.

4.2. Ni(II)-N-btcb: TGA of the nickel complex showed a weight loss up to 140ºC corresponding to the presence of one lattice water molecule (calc. 2.44%, obs. 2.83%). Also, the loss of two molecules of water coordinated to the metal ion was indicated by the weight loss observed between 140-210ºC (calc. 4.882%, obs. 4.37%). Loss of weight between 215ºC to 631ºC indicated the decomposition of ligand moiety (calc. 82.55%, obs. 82.21%). Finally, the complex was oxidized to NiO as suggested by the % weight remaining till the end of the measurement (calc.10.128%, obs. 10.59%). From the thermogram, the half-decomposition temperature of the nickel complex was found to be 351.03 ºC (**Table 2)**.

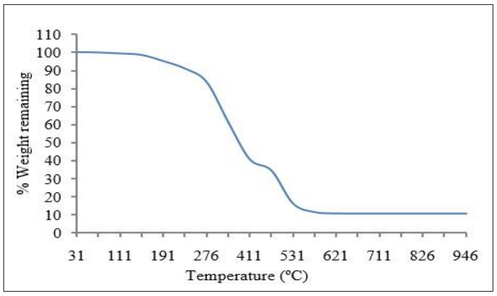


Figure 3. Thermograms of Cu(II) complex

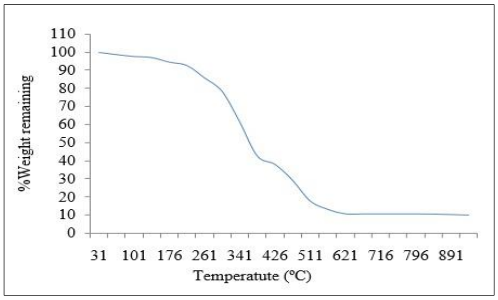


Figure 4. Thermograms of Ni(II) complex

Table 2. Thermal data of complexes

Metal Complex	Lattice water (1 eq.) % Weight loss		Coordinated water (2 eq.) % Weight loss		Half Decomposition Temperature (ºC)	% Weight loss		% Weight CuO/NiO (Residue)	
	Obsd	Cald	Obsd	Cald		Obsd	Cald	Obsd	Cald
[Cu(N-btcb)$_2$(H$_2$O)$_2$]	Nil	Nil	5.22	4.97	361.04	82.34	83.94	12.45	11.06
[Ni(N-btcb)$_2$(H$_2$O)$_2$.H$_2$O]	2.83	2.45	4.37	4.88	351.04	82.21	82.55	10.59	10.13

Key to symbols: Obsd: Observed; Cald: Calculated

From analytical and spectral studies, it has been observed that the N-substituted benzamide coordinates to the central metal ion as a bidentate ligand through O and S donor yielding [ML_2] complexes. Similar complexes showing the involvement of the C=O and C=S groups have been reported in recent studies as having square planar geometry [23], [40]. From the electronic assignments and magnetic moment data, it is noted that the Cu(II) and Ni(II) metal ions are coordinating with the ligand in a distorted octahedral and octahedral fashion respectively. These observations are further supported by thermal analysis, where two coordinated water molecules are found in both complexes. It also provides evidence for the presence of one lattice water in the Ni(II) complex. Obtained data supports the coordination number, geometry, and general molecular formula for the metal complexes. The general molecular formulae for Cu(II) and Ni(II) complexes are proposed as [$Cu(N\text{-}btcb)_2(H_2O)_2$] and [$Ni(N\text{-}btcb)_2(H_2O)_2 \cdot H_2O$] respectively based on the overall findings. In support of the present study, similar structures were found reported for Cu(II) and Ni(II) complexes in the literature [45-47].

5. Antibacterial Activity

The newly synthesized metal complexes were screened for antibacterial activity using a well diffusion method. Measurements were also performed on the ligand for comparison and to confirm improvements with the use of metal complexes, if any. The in-vitro antibacterial activities of the compounds N-btcb, Cu(II)- N-btcb and Ni(II)-N-btcb were studied against different bacterial strains, namely *S. aureus* (Gram-positive), *B. subtilis* (Gram-positive), *E. coli* (Gram-negative) and *P. aeruginosa* (Gram-negative). The compounds under evaluation and a standard drug, ampicillin, were dissolved in DMF to prepare stock solutions.

The antibacterial activities were evaluated by measuring the zone of inhibition on Muller Hilton agar plates using the well diffusion method. The reported results are means of three determinations and are listed in **Table 3**. From the obtained values it can be observed that the ligand and the metal complexes possessed good to moderate antimicrobial activity compared with the standard drug**.** The ligand was highly active only towards *E. coli*. The copper complex was moderately active towards all strains of bacteria tested. Compared to other compounds tested, the nickel complex showed better antibacterial activity for the gram-positive bacteria. A detailed study [48] carried out on different metal complexes' antibacterial activities also states that there are no nickel-based drugs available. Nickel is the main trace element in many bacteria [49]. Gram-positive bacteria have only one cell membrane whereas gram-negative bacteria have a minimum of two membranes [50] and disintegrating one membrane for antimicrobial action is easier [51]. The presence of certain enzymes which are susceptible to Ni and other properties like dipole moment, solubility, or conductivity [52] may also be reasons for the improved biological activity of Ni toward gram-positive bacteria. As the electron microscopy and crystal structure studies of the complexes have not been carried out, a detailed hypothesis is difficult to state precisely.

A comparison of antibacterial activity between ligand and metal complexes indicated that the metal complexes showed slightly improved antibacterial activity over the ligand except with *E. coli*. This may be explained in terms of Overtone's concept of cell permeability [53] and Tweedy's chelation theory [54-55]**.**

Table 3. Antibacterial activity

Compound	Gram-positive		Gram-negative	
	A	B	C	D
(N-btcb)	+ +	+	+ + +	+ +
[$Cu(N\text{-}btcb)_2(H_2O)_2$]	+ +	+ +	+ +	+ +
[$Ni(N\text{-}btcb)_2(H_2O)_2.H_2O$]	+ + +	+ + +	+ +	+ +
AMP	+ + +	+ +	+ +	+ + +

Key to symbols: AMP: Ampicillin; A: *S. aureus*; B: B. subtilis; C: *E. coli*; D: *P. aeruginosa*. Highly active = + + + (inhibition zone >15 mm); moderately active = + + (inhibition zone 10-15 mm); slightly active= + (inhibition zone 5-10 mm).

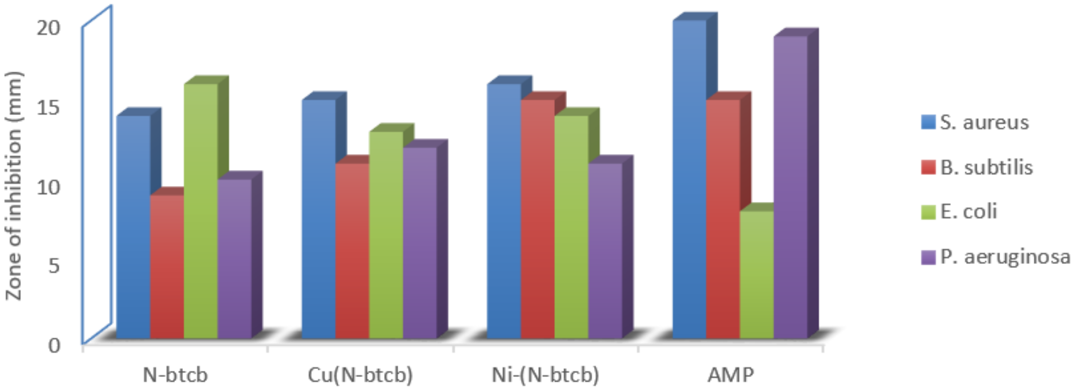


Figure 5. Antibacterial activity of compounds N-btcb, Cu(II)- N-btcb and Ni(II)-N-btcb

CONCLUSION

The synthesis of Cu(II) and Ni(II) complexes of N-(benzo[*d*]thiazol-2-ylcarbamothioyl)benzamide has been reported. Based on elemental and spectral analyses, it was shown that the ligand coordinated to the central metal ion through oxygen and sulfur atoms. The number and nature of coordinated water molecules were confirmed by thermal analysis (TGA). While two water molecules were found to be coordinated suggesting a coordination number of six for both the complexes, the Ni(II) complex also showed the existence of one lattice water per molecule of the complex. Based on the overall analysis, the molecular formulae $[Cu(N\text{-}btcb)_2(H_2O)_2]$ and $[Ni(N\text{-}btcb)_2(H_2O)_2{\cdot}H_2O]$ were proposed for the Cu(II) and Ni(II) complexes. Based on electronic spectra and magnetic susceptibility measurements, a distorted octahedral geometry for the Cu(II) complex and an octahedral geometry for the Ni(II) complex have been proposed. The synthesized products were screened for their antibacterial activity and it was observed that the coordination of organic moiety with metal showed enhanced antibacterial activities for certain bacterial species. It was also noted that the nickel complex showed high activity towards Gram-positive bacteria compared to the corresponding copper complex.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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Supplementary Data

1. General Information (Materials and measurements)

All reactions were performed in oven-dried glassware. All chemicals and solvents were obtained from E-Merck, India (AR grade) and were used without further purification. Melting points of compounds were measured in an open capillary tube by the Toshniwal melting point apparatus in the Celsius scale and are uncorrected. IR spectra were recorded using KBr pellets on the FTIR spectrophotometer (Perkin Elmer - Spectrum RX-IFTIR). ^{1}H-NMR spectra were recorded on a multinuclear FT NMR Spectrometer model Avance II (Bruker) with ^{1}H frequency of 400 MHz. Chemical shifts (δ) are expressed in ppm relative to tetramethylsilane (TMS) as an internal standard. Mass spectra (FAB-MS) were recorded on a Waters Micromass Q-TOF Microspectrophotometer and elemental analysis was carried out using the Elementar Vario EL III CHN analyzer. Thermogravimetric studies were carried out on a Perkin Elmer SII, Diamond TG/DTA thermogravimetric analyzer. The samples were heated in the range of 30ºC to 1000ºC under a N_2 atmosphere, and the rate of heating was 50ºC per minute. UV-Visible spectra were recorded on a UV-VIS-NIR Spectrophotometer, Model Lambda 750, Perkin Elmer in the range of 200-100 nm. Magnetic Susceptibility of the metal complexes was determined by Gouy's method[4,5] at room temperature, and recorded on a Sherwood Scientific Balance (Auto model).

2. FTIR, ^{1}H, ^{13}C NMR and mass spectra data

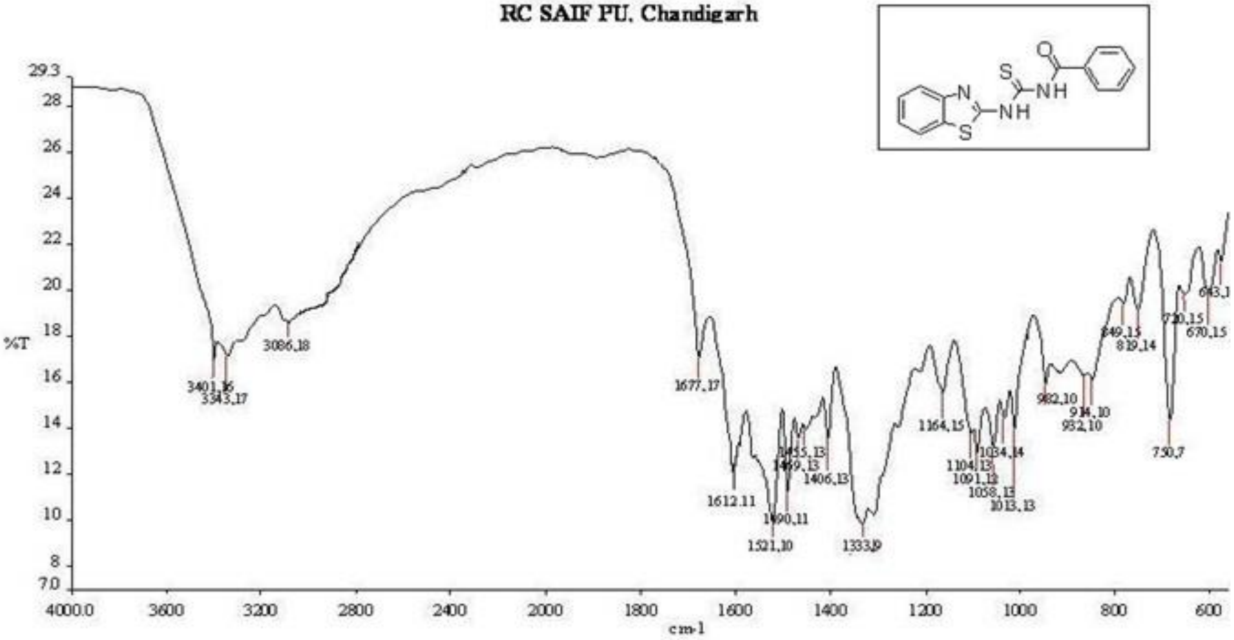

Figure S1. FTIR Spectra of ligand (N-btcb)

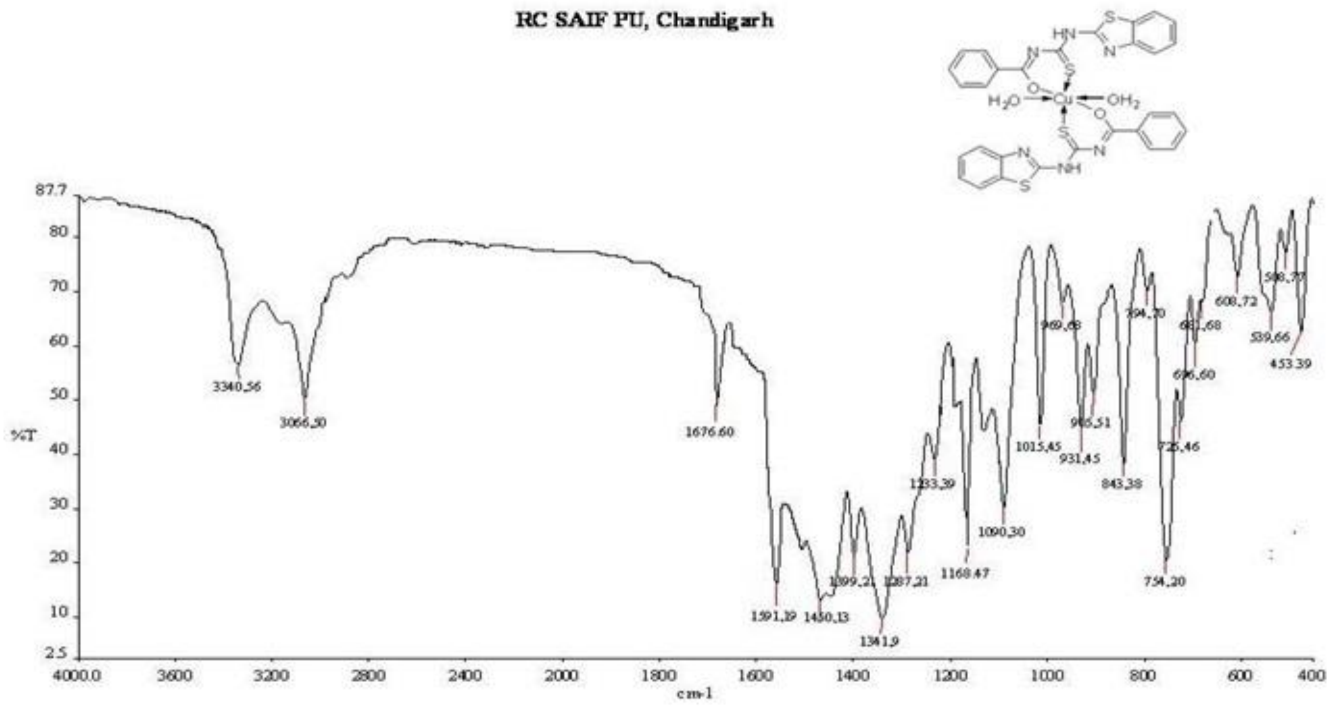

Figure S2. FTIR Spectra of Cu(II) N-btcb complex

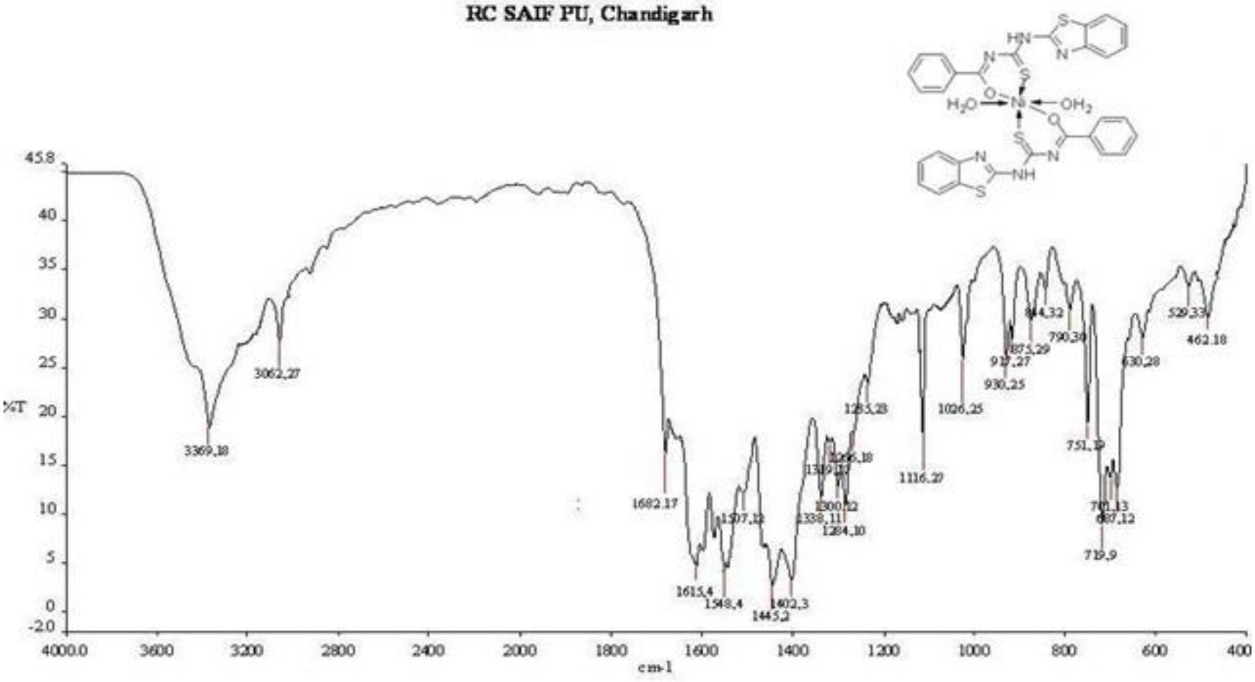

Figure S3. FTIR Spectra of Ni(II) N-btcb complex

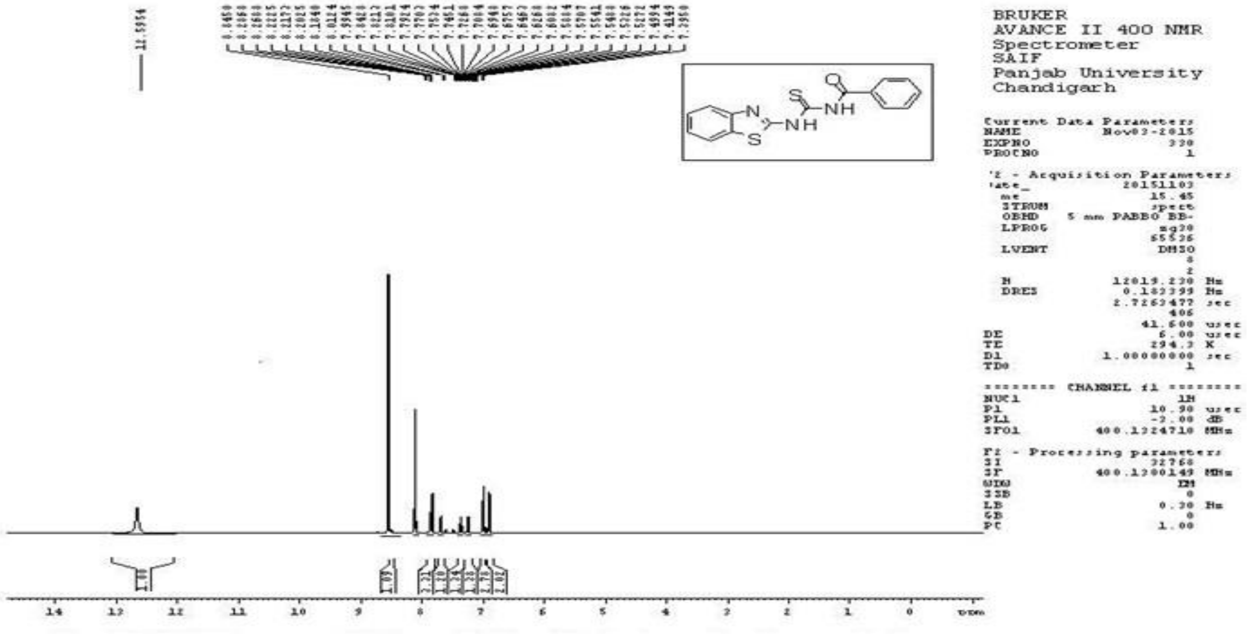

Figure S4. ^{1}H NMR Spectra of ligand (N-btcb)

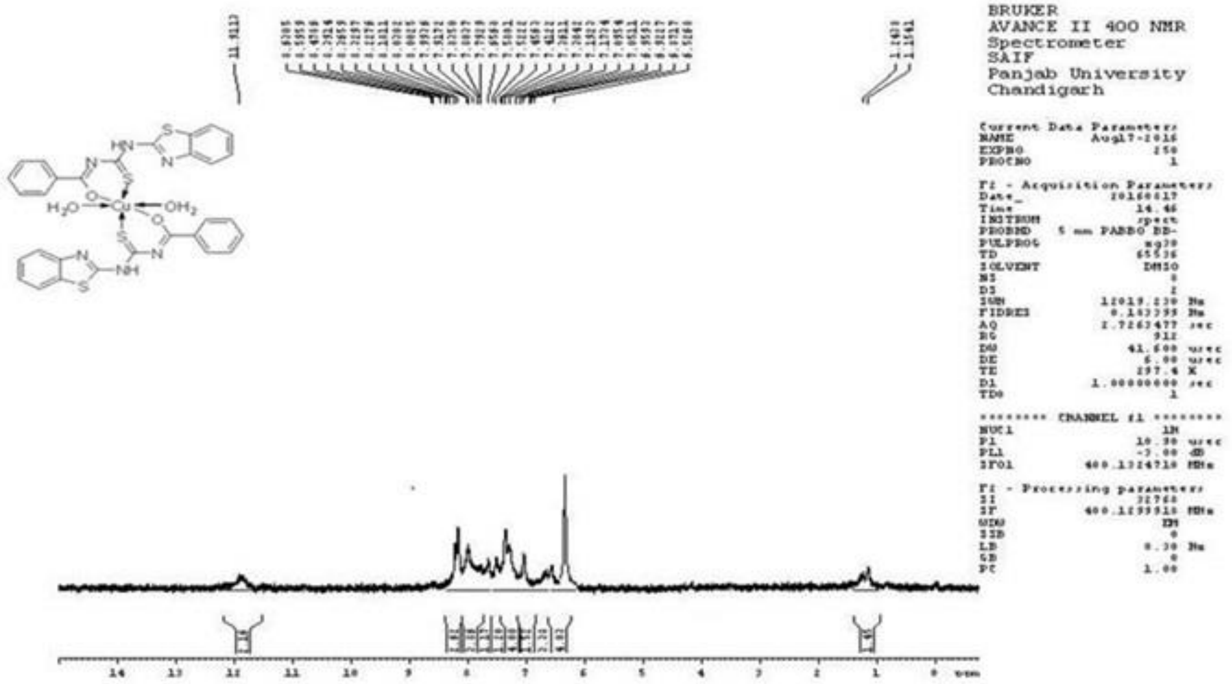

Figure S5. ^{1}H NMR Spectra of Cu(II) N-btcb complex

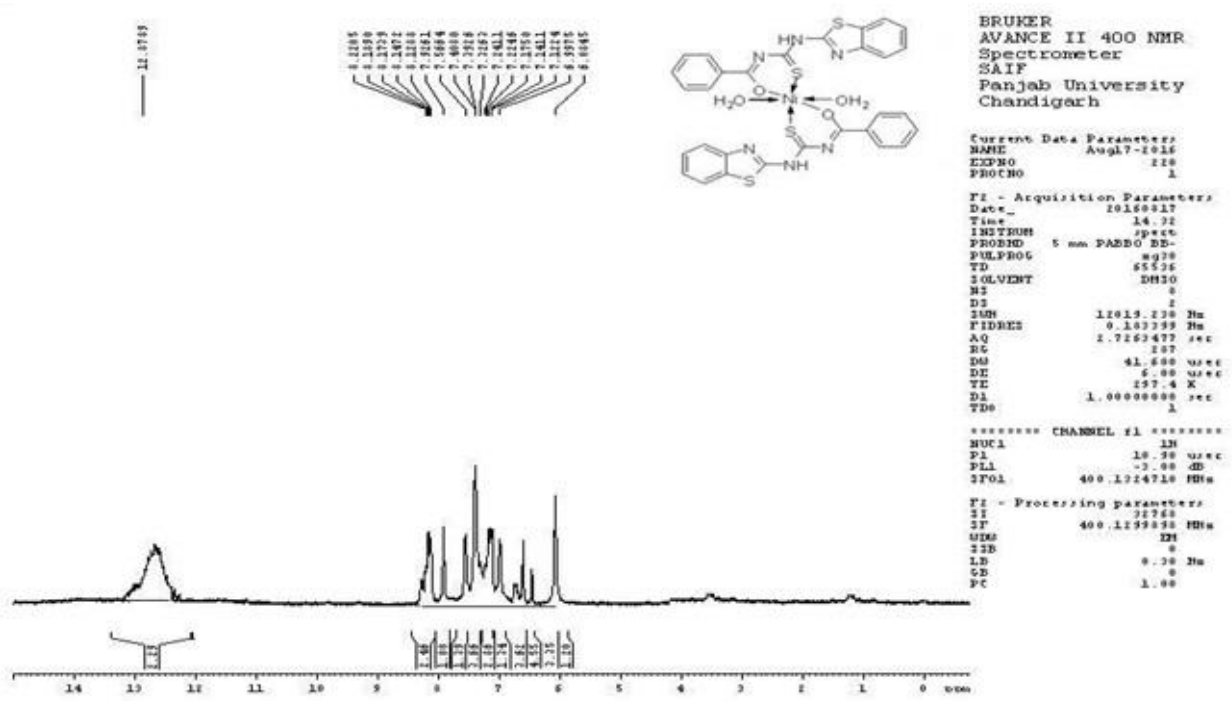

Figure S6. ^{1}H NMR Spectra of Ni(II) N-btcb complex

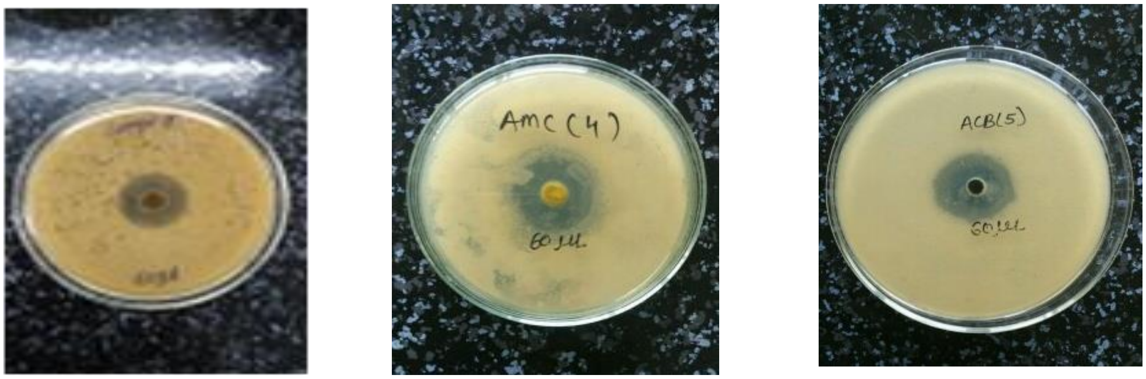

Figure S7: Inhibition zones of N-btcb, Cu(II)- N-btcb and Ni(II)-N-btcb against Gram positive bacteria

Figure S8. Inhibition zones of N-btcb, Cu(II)- N-btcb, and Ni(II)-N-btcb against Gram negative bacteria