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# Synthesis, spectral characterization, thermal, DNA cleavage and in-vitro antimicrobial activity studies of Co(II), Ni(II) and Cu(II) metal complexes of 1, 2, 4-triazole Schiff bases

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## ABSTRACT

*A new series of Co (II), Ni (II) and Cu (II) metal complexes with biologically active Schiff bases derived from 3-substituted-4-amino-5-mercapto-1,2,4-triazole and 2-Chloro-3-formylquinoline have been synthesized. The synthesized Schiff bases and their metal complexes have been characterized in the light of elemental analyses, spectral data (IR,*$^1$*H-NMR,* $^{13}$*C-NMR, ESR and ESI-Mass) Magnetic and thermal studies. The stoichiometry of all the metal complexes is found to be 1:2 of the type* $ML_2.2H_2O$*. The measured molar conductance values in DMSO indicate that, the complexes are non-electrolytic in nature. It has been concluded that, all the metal complexes possess octahedral geometry in which ligand is coordinated to metal ion through azomethine nitrogen and thione sulfur atoms via deprotonation. The Schiff bases and their metal complexes have been screened for their in vitro antibacterial (Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa) and antifungal activities (Aspergillus niger, Penicillium chrysogenum and Candida albicans) by Minimum Inhibition Concentration(MIC) Method. The DNA Cleavage activity is studied by agarose gel electrophoresis method.*

**Key words:** 1, 2, 4-Triazole, Schiff bases, Spectroscopic, DNA Cleavage, Antimicrobial Activity, Thermal Studies.

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## INTRODUCTION

In modern era, Schiff bases have been used in various fields of science such as medical, biological and catalysis applications; these compounds appear to be important intermediates in a number of enzymatic reactions involving enzyme interaction with an amino or a carbonyl group of a substrate[1]; Moreover, the last decade has seen an upsurge of interest in Chemistry of 1, 2, 4-triazole Schiff bases and their transition metal complexes have attracted wide spread attention due to their diverse biological activities viz; antimicrobial, antitubercular, anti-inflammatory and cytotoxic activities[2]; Very recently, a number of metal complexes of 1,2,4-triazole Schiff bases, which possess very good antimicrobial properties have been reported from our laboratory [3,4].

Quinoline is the backbone for most natural products, which is used for the design of many synthetic compounds having diverse pharmacological applications. Further, 2-chloroquinoline-3-carbaldehydes and their derivatives have Interesting pharmacological properties such as antimicrobial, antimalarial, anti-inflammatory, antitumor and anti-parasitic activities[5-7]. Moreover, Synthetic applications of 2-chloro-3-formyl-quinoline have been reported by

Meth-Cohn et. al. [8]. Literature survey shows that, still there is a scope for synthesis of metal complexes of 1,2,4-triazole Schiff bases. Hence, in view of their wide range of usage, it was thought to synthesize the new Schiff bases of 1,2,4- triazole derivatives would be worthwhile. All these developments in the synthesis of Schiff bases with various metal ions are most fascinating. Keeping the diverse biological activities of 1,2,4-triazole and quinoline derivatives, we, in the present work, reporting the various studies of Co(II), Ni(II) and Cu(II) metal complexes of Schiff bases derived from 3-substituted- 4-amino-5-mercapto-1,2,4-triazole and 2-Chloro-3-formylquinoline.

## MATERIALS AND METHODS

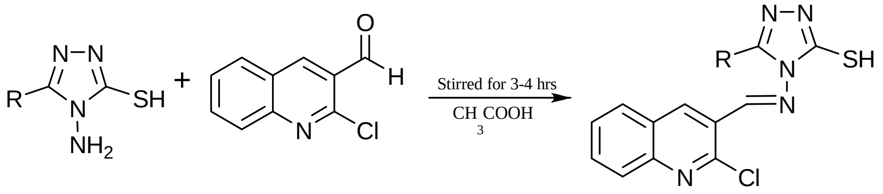
### *Analyses and Physical Measurements*

Carbon, hydrogen and nitrogen were estimated by using Carlo Erba EA1108 Elemental Analyzer. The IR spectra of the Schiff bases and their Co(II), Ni(II) and Cu(II) metal complexes were recorded on a HITACHI-270 IR spectrophotometer in the 4000–400 $cm^{-1}$ region in KBr disc. The electronic spectra of the complexes were recorded in HPLC grade DMSO on a VARIAN CARY 50-BIO UV-spectrophotometer in the region of 200–1100 nm. The $^{1}H$ and $^{13}C$-NMR spectra of the Schiff bases were recorded in DMSO-d6 on a BRUKER 400 MHz spectrometer at room temperature using TMS as an internal reference. The mass of Schiff bases and metal complexes was recorded in GCMS and ESI-Mass. The ESR spectrum was recorded under liquid nitrogen temperature (LNT) on Varian-E-4X-band EPR spectrometer and the field set is 3000 G at modulation frequency of 100 K Hz using TCNE as ‘g’ marker. Thermogravimetric analyses data were measured from room temperature to $1000^{0}C$ at a heating rate of $10^{0}C$/min. The data were obtained by using a PERKIN–ELMER DIAMOND TG/ DTA instrument. Molar conductivity measurements were recorded on ELICO-CM-82 T Conductivity Bridge with a cell having cell constant 0.51 and magnetic moment measurements were carried out by using Faraday balance.

All the chemicals used were of reagent grade. 3-substituted- 4-amino-5-mercapto-1, 2, 4-triazole [9-11] and 2-Chloro-3-formylquinoline [8] were synthesized according to the literature. Metal salts used in the study are $CoCl_2.6H_2O$, $NiCl_2.6H_2O$ and $CuCl_2.2H_2O$ were of BDH make.

### *Synthesis of Schiff Bases (I & II)*

The synthesis of Schiff bases is schematically represented in the **Scheme 1**. The Schiff bases have been synthesized by stirring the solution (30 ml, methanol) of 3-substituted- 4-amino-5-mercapto-1, 2, 4-triazole and 2-Chloro-3-formylquinoline (30 ml, methanol) for 3-4 hours with addition of catalytic amount of acetic acid. The product separated was filtered and washed with water followed by cold methanol and recrystallized from hot methanol. Yield of the Schiff base-I (SB-I) and Schiff base-II (SB-II) was noted to be 76% and 78% and, their corresponding melting points were observed to be 145±2 and 162±2 $^{O}C$ respectively.



| Schiff Base | R | Emperical Formula |
|---|---|---|
| I | H | C12H8N5ClS |
| II | C2H5 | C14H13N5ClS |

**Scheme 1 Synthesis of Schiff bases I and II**

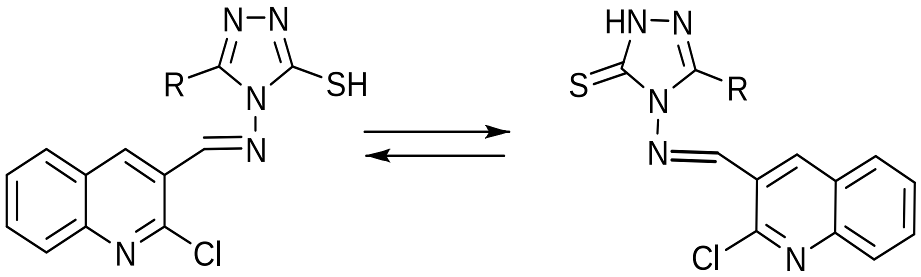


**Fig. 1 Structure of Schiff bases of I and II: thiol –thione tautomerism**

**SB-I 4-((2-chloroquinolin-3-yl)methyleneamino)-4H-1,2,4-triazole-3-thiol**
Yield: 76%; M.P 145-147 $^{O}$C; IR (KBr): 2350 (-SH), 1622 (-CH=N), 1053 (-C=S)cm$^{-1}$; $^{1}$H NMR (DMSO-d6; 400 MHz, δppm): 14.11 (s,1H), 10.42 (s,1H), 9.11 (s,1H), 9.01 (s,1H), 8.27 (d,1H), 8.035 (d,1H), 7.95 (t,1H), 7.75 (t,1H); $^{13}$CNMR(DMSO-d6;400MHz,δppm): 162.95, 155.20, 149.31, 148.53, 140.12, 138.20, 133.44, 129.93, 128.67, 128.25, 126.95, 124.95; Elemental analyses calculated for $C_{12}H_8N_5ClS$ (Mol. Wt. m/z = 289): C-49.74%, H-2.78% and N-24.17% found: C-49.65%, H-2.63% and N-24.01%.

**SB-II 4-((2-chloroquinolin-3-yl)methyleneamino)-5-ethyl-4H-1,2,4-triazole-3-thiol**
Yield: 78%; M.P 162-164 $^{O}$C; IR (KBr): 2280 (-SH), 1620 (-CH=N), 1050 (-C=S)cm$^{-1}$; $^{1}$H NMR (DMSO-d6; 400 MHz, δ ppm): 13.91 (s,1H), 11.03 (s1H), 9.16 (s,1H), 8.25 (d,1H), 8.01 (d,1H), 7.93 (t,1H), 7.74 (t,1H), 2.88 (q,2H, $CH_2$), 1.29 (t, 3H, $CH_3$); $^{13}$C NMR (DMSO-d6;400 MHz, ppm):161.85, 155.12, 153.32, 149.41, 148.47, 137.83, 133.23, 129.45, 128.71, 128.51, 127.86, 125.08, 18.67, 10.50; Elemental analyses calculated for $C_{14}H_{13}N_5ClS$ (Mol. Wt. m/z = 317): C-52.91%, H-3.81% and N-22.04% found: C-52.85%, H-3.61% and N-21.96%.

**Synthesis of Co(II), Ni(II), and Cu(II) complexes [1–6]**
An alcoholic solution (30 ml) of Schiff base (2 mmol) was mixed with alcoholic solution (15 ml) of $CoCl_2.6H_2O$/ $NiCl_2.6H_2O/CuCl_2.2H_2O$ (1 mmol) and refluxed on water bath for 2 h. Then, to the reaction mixture sodium acetate (2 mmol) was added and reflux was continued for further 2 h. The separated metal complexes were filtered, washed thoroughly with water and alcohol, finally dried over fused CaCl2. Melting point of all the metal complexes are > 300°C and Yield were found to be in the range of 63–71%.

## RESULTS AND DISCUSSION

The Schiff bases (I and II) form octahedral complexes (1–6) with $CoCl_2.6H_2O/NiCl_2.6H_2O/CuCl_2.2H_2O$ in ethanol (**Scheme 2**). All the Co(II), Ni(II), and Cu(II) metal complexes are stable and non-hygroscopic in nature. The complexes are insoluble in common organic solvents but soluble in DMF and DMSO. The elemental analyses showed that, the Co(II), Ni(II) and Cu(II) metal complexes have 1:2 stoichiometry of the type $ML_2.2H_2O$; where, 'L' stands for a singly deprotonated ligand, which exhibits thiol–thione tautomerism (**Fig.1**). The molar conductance values are too low to account for any dissociation of the complexes (in DMSO) indicating the non-electrolytic nature of the metal complexes (**Table 1**). Several attempts were made to develop the single crystal of the metal complexes. However, those attempts failed due to insolubility of the metal complexes in common organic solvents.

**Table-1: Elemental analyses of Schiff Bases and their Co(II), Ni(II), and Cu(II) Metal Complexes along with their Molar Conductance and Magnetic Moment Data**

| Comp. No. | Empirical Formula | Color/Yield % | M% | | C% | | H% | | N% | | Molar Cond. (Ohm$^{-1}$ cm$^2$ mol$^{-1}$) | Magnetic Moments $\mu_{eff}$ (BM) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Obsd. | Cald. | Obsd. | Cald. | Obsd. | Cald. | Obsd. | Cald. | | |
| SB-I | $C_{12}H_8N_5ClS$ | Pale Yellow/76 | --- | --- | 49.65 | 49.74 | 2.63 | 2.78 | 24.01 | 24.17 | --- | --- |
| SB-II | $C_{14}H_{13}N_5ClS$ | Pale Yellow/78 | --- | --- | 52.85 | 52.91 | 3.61 | 3.81 | 21.96 | 22.04 | --- | --- |
| 1 | $Co(C_{12}H_8N_5ClS)_2.2H_2O$ | Brown/ 66 | 8.63 | 8.65 | 43.96 | 44.05 | 2.38 | 2.46 | 21.28 | 21.40 | 9.2 | 4.89 |
| 2 | $Co(C_{14}H_{13}N_5ClS)_2.2H_2O$ | Brown/69 | 7.95 | 7.98 | 45.62 | 45.76 | 2.79 | 2.95 | 20.48 | 20.52 | 7.6 | 4.95 |
| 3 | $Ni(C_{12}H_8N_5ClS)_2.2H_2O$ | Yellowish Green/63 | 8.50 | 8.52 | 43.98 | 44.06 | 2.36 | 2.47 | 21.29 | 21.41 | 11.02 | 3.31 |
| 4 | $Ni(C_{14}H_{13}N_5ClS)_2.2H_2O$ | Yellowish Green/65 | 7.83 | 7.86 | 45.66 | 45.77 | 2.81 | 2.95 | 20.47 | 20.53 | 10.62 | 3.39 |
| 5 | $Cu(C_{12}H_8N_5ClS)_2.2H_2O$ | Dark Green/71 | 9.31 | 9.33 | 43.68 | 43.74 | 2.37 | 2.45 | 21.09 | 21.25 | 13.02 | 1.79 |
| 6 | $Cu(C_{14}H_{13}N_5ClS)_2.2H_2O$ | Dark Green/68 | 8.59 | 8.61 | 45.33 | 45.45 | 2.86 | 2.93 | 20.21 | 20.39 | 14.32 | 1.77 |

## IR Spectral Studies

The prominent infrared spectral data of Schiff bases and their Co(II), Ni(II), and Cu(II) metal complexes are systematized in **Table 2**. The representative IR spectra of the Schiff base-I (**Fig. 2**) exhibited a characteristic high intensity band at 1622 cm$^{-1}$ assigned to υ(HC=N). A sharp band at 2350 cm$^{-1}$ was assigned to υ(-SH). Other intense peak at 1053 cm$^{-1}$ was ascribed to υ(-C=S) [12]. Appearance of sharp band at 743 cm$^{-1}$ is assigned to υ(C-S). In comparison with the spectra of the Schiff bases, all the Co(II), Ni(II) and Cu(II) metal complexes exhibited the band of υ(HC=N) in the region of 1608–1615 cm$^{-1}$ showing the shift of band to lower wave numbers indicating that, the azomethine nitrogen atom is coordinated to the metal ions [13]. The absence of bands around 2350 and 2280 cm$^{-1}$ in all the metal complexes indicating that, the metal ions are coordinated through the sulfur atom via deprotonation. The representative Cu(II) (5) complex is shown in **Fig. 3.** This IR spectral studies strongly support the formation of metal complexes.

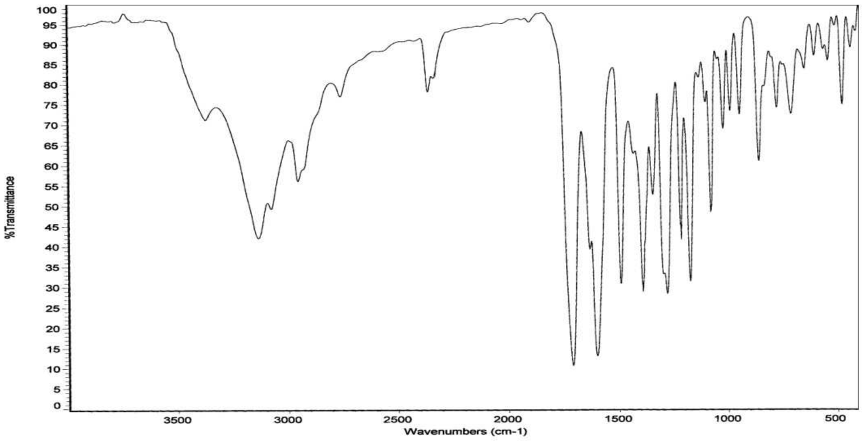


**Fig. 2 IR Spectrum of the Schiff Base-I**

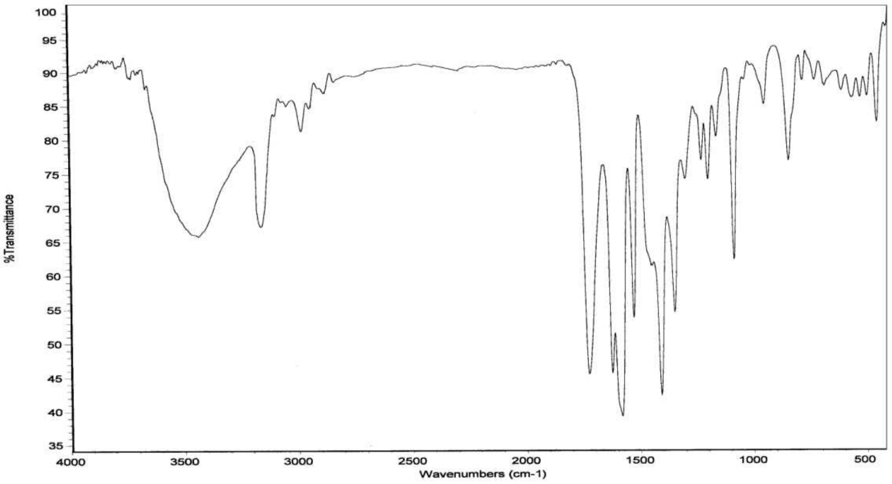


**Fig. 3 IR Spectrum of the $Cu(C_{12}H_8N_5ClS)_2.2H_2O$ complex**

**Table 2 Prominent IR Frequencies ($cm^{-1}$) of Schiff Bases and their Metal Complexes**

| **Compound** | **υ(-OH)** | **υ(HC=N)** | **υ(-SH)** | **υ(C=S)** | **υ(C-S)** | **υ(M-N)** | **υ(M-S)** |
|---|---|---|---|---|---|---|---|
| SB-I | - | 1622 | 2350 | 1053 | - | - | - |
| SB-II | - | 1620 | 2280 | 1050 | - | - | - |
| $Co(C_{12}H_8N_5ClS)_2.2H_2O$ | 3450 | 1614 | - | - | 746 | 480 | 381 |
| $Co(C_{14}H_{13}N_5ClS)_2.2H_2O$ | 3420 | 1608 | - | - | 744 | 466 | 408 |
| $Ni(C_{12}H_8N_5ClS)_2.2H_2O$ | 3465 | 1615 | - | - | 758 | 490 | 416 |
| $Ni(C_{14}H_{13}N_5ClS)_2.2H_2O$ | 3430 | 1609 | - | - | 744 | 468 | 411 |
| $Cu(C_{12}H_8N_5ClS)_2.2H_2O$ | 3485 | 1612 | - | - | 753 | 485 | 419 |
| $Cu(C_{14}H_{13}N_5ClS)_2.2H_2O$ | 3440 | 1610 | - | - | 743 | 466 | 416 |

### $^1$H and $^{13}$C NMR Study of Schiff bases I and II

In $^1$H-NMR spectrum of the Schiff base I, the NH proton of triazole ring resonates at 14.11ppm. A characteristic proton signal at 10.42ppm and a signal at 9.11ppm are assigned to -SH and -CH=N respectively. In addition, the signals in the region 9.01-7.7ppm are ascribed to aromatic protons(**Fig. 4**). In case of Schiff base II, the signal observed at 13.91ppm is attributed to the NH proton of the triazole ring. The strong signal at 11.03ppm and 9.16ppm are assigned to -SH and CH=N respectively. The signals observed at 8.2-7.7, 2.8 and 1.3ppm are due to aromatic, -$CH_2$ and -$CH_3$ protons respectively.

In $^{13}$C-NMR spectrum of Schiff base I, signal at 162ppm is assigned to -CH=N carbon. A characteristic signal at 149ppm is attributed to -C-S carbon of triazole ring. The signals appeared in the region 155-125ppm are ascribed to aromatic carbons(**Fig. 5**). In case of Schiff base II, the signal at 161ppm is attributed to -CH=N carbon. The signal at 149ppm is assigned to -C-S carbon of triazole ring. The signals in the region 155-125ppm, 18.67ppm and 10.50ppm are ascribed to aromatic, -$CH_3$ and -$CH_2$ carbons respectively.

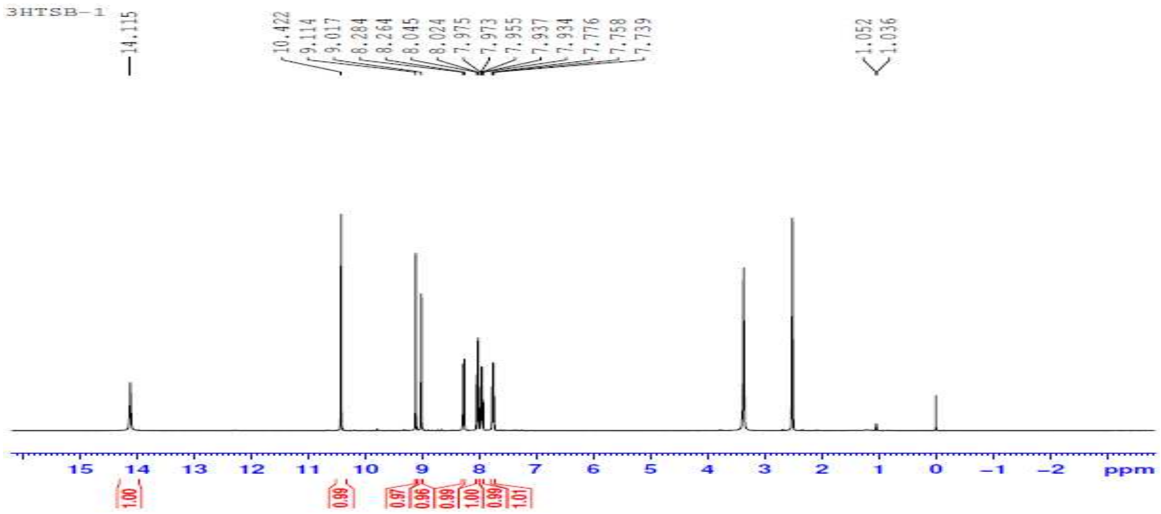


**Fig. 4 $^1$H-NMR Spectrum of SB-I**

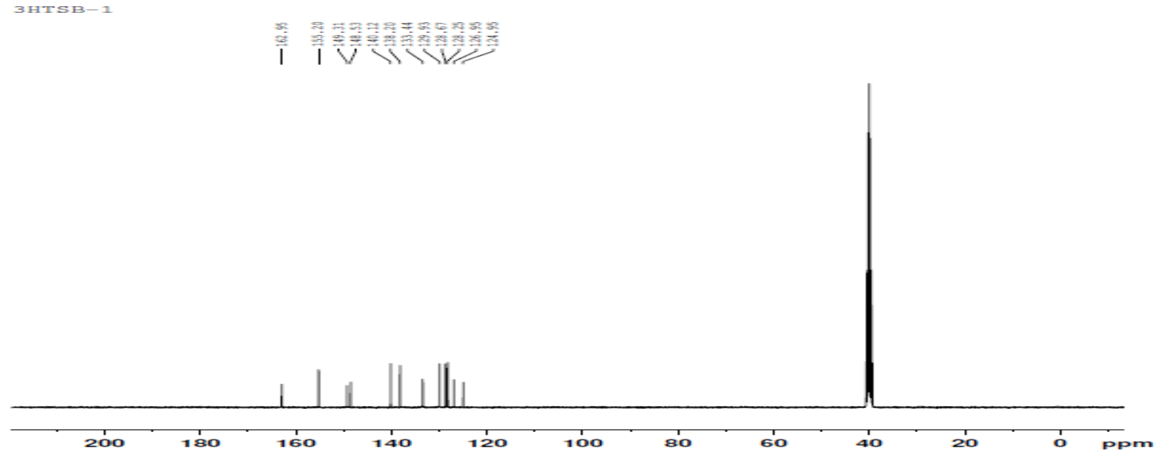


**Fig. 5 $^{13}$C-NMR Spectrum of SB-I**

## Electronic Spectral and Magnetic Studies

The electronic spectra of the metal complexes were recorded in HPLC grade DMSO by using UV-Spectrophotometer in the region 200-1100nm, and magnetic moment measurements were carried out by using Faraday balance.

### *Cobalt(II) Complexes*

The electronic spectra of cobalt complexes **(1)** and **(2)** exhibit absorption bands in the region ~ 8000-10000 and ~ 18000-20000 cm$^{-1}$ corresponding to $^4T_{1g}$ (F) → $^4T_{2g}$ (F) ($\nu_1$) and $^4T_{1g}$ (F) → $^4T_{1g}$ (P) ($\nu_3$) transitions respectively. In present study electronic spectra of cobalt(II) complexes exhibit two distinct bands in the region 8950-9790 and 19047-20195 cm$^{-1}$ which may be assigned to $^4T_{1g}$ (F) → $^4T_{2g}$(F) ($\nu_1$) and $^4T_{1g}$ (F)→ $^4T_{1g}$ (P) ($\nu_3$) [14-15]. These bands are characteristic of high spin octahedral cobalt(II) complexes. However, $\nu_2$ band is not observed because of its proximity to strong $\nu_3$ transition. The magnetic measurement for Co(II) complexes exhibit the values of 4.89 and 4.95 BM. These values are within the expected range of 4.7 -5.2 [18-19] for octahedral nature of the complexes.

### *Nickel(II) Complexes*

The octahedral nickel(II) complexes display a simple spectra consisting of three transitions viz., $^3A_{2g} \rightarrow {}^3T_{2g}$; $^3A_{2g} \rightarrow {}^3T_{1g}$ (F) and $^3A_{2g} \rightarrow {}^3T_{1g}$ (P). These are reported to occur in the following regions 7000-13000, 11000-20000 and 19000-27000 cm$^{-1}$ respectively. These bands show shifts to the higher wavelength in the weaker field. In the light of these assignments, the observed bands for these complexes in the region 9570-10000, 15597-15845 and 20492-

27248 cm$^{-1}$. These are assigned to the transitions $^3A_{2g}(F) \rightarrow ^3T_{2g}(F)$ ($\nu_1$); $^3A_{2g}(F) \rightarrow ^3T_{1g}(F)$ ($\nu_2$) and $^3A_{2g}(F) \rightarrow ^3T_{1g}(P)$ ($\nu_3$) respectively and these consistent with their well defined octahedral configuration [16]. The Ni(II) complexes show the magnetic moment values 3.31 and 3.39 BM and it is reported that, the octahedral Ni(II) complexes exhibits magnetic moment values in the range of 2.5-3.5 BM[19].

*Copper (II) Complexes*

The recent studies show that, the absorption spectra of octahedral Cu(II) complexes exhibit three transitions. *viz*., $^2B_{1g} \rightarrow ^2A_{1g}(\nu_1)$, $^2B_{2g}(\nu_2)$, and $^2E_g(\nu_3)$, are of similar energy and often give rise to a single broad absorption band. Because of low intensity of $^2B_{1g} \rightarrow ^2B_{2g}(\nu_2)$ which is usually not observed as spectral band in tetragonal Cu(II) complexes [17]. Hence, the main broad band is assigned to $\nu_3$ as the $\nu_2$ merges with the $\nu_3$ (~ 10 Dq). These observations suggest that, the present copper(II) complexes are tetragonally distorted octahedral species. The copper(II) complexes under investigation exhibit a single broad absorption band in the region 14540-14780 cm$^{-1}$ in the visible region assigned to $^2E_g \rightarrow ^2T_{2g}$. The broadness of the band due to Jahn-Teller effect, which is characteristic of distorted octahedral environment. This data suggests that, no gross deviation in stereochemistry of these complexes occurs in solid and solution phases. The Cu(II) metal complexes show the magnetic moment values 1.79 and 1.77BM, are slightly higher than the spin only value 1.73BM expected for one unpaired electron, which offers possibility of an octahedral geometry[20]. The magnetic moment studies suggest the octahedral geometry around the metal ions.

**Mass Spectral Studies of Schiff bases and their metal complexes**

The representative GCMS spectrum of Schiff base I is depicted in **Fig. 6**. The spectrum showed molecular ion peak at m/z 289 which is equivalent to its molecular weight. In addition to this the fragment ion peaks observed at m/z 254 and 113 are due to the cleavage of chloride ions and $C_2HNS^{\cdot\cdot\cdot}$ respectively. In case of Schiff base II, the molecular ion peak is observed at m/z 317 which is assigned to $C_{14}H_{13}N_5ClS$.

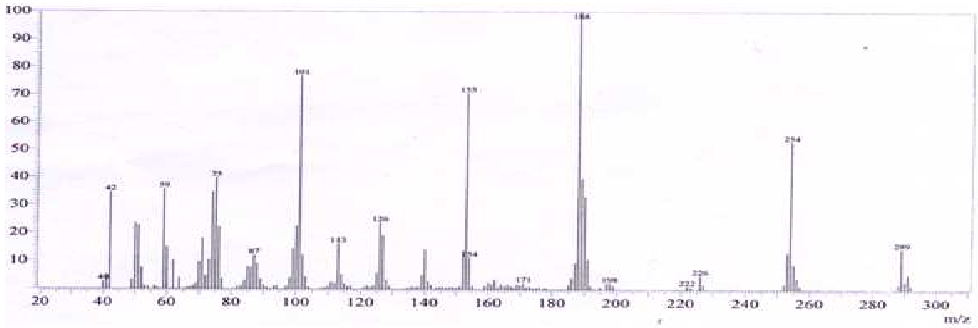


**Fig. 6 GC- Mass Spectrum of SB-I**

The ESI-MS results of Schiff base-I metal complexes showed [M+1] peak at m/z 670, 671 and 675 equivalent to their molecular weights respectively. In case of Co (II), Ni(II) and Cu(II) complexes of Schiff base-II**,** ESI-MS spectra showed [M+1] at m/z 726, 727 and 732 respectively are equivalent to their molecular weight.

The representative ESI-Mass spectrum of Cu(II) complex(6) has been shown in **Fig. 7** and it is discussed in the present context. The molecular ion peak $M^+$ at m/z at 732 which corresponds to the equivalent weight of the metal complex $[ML_2.2H_2O]^+$.

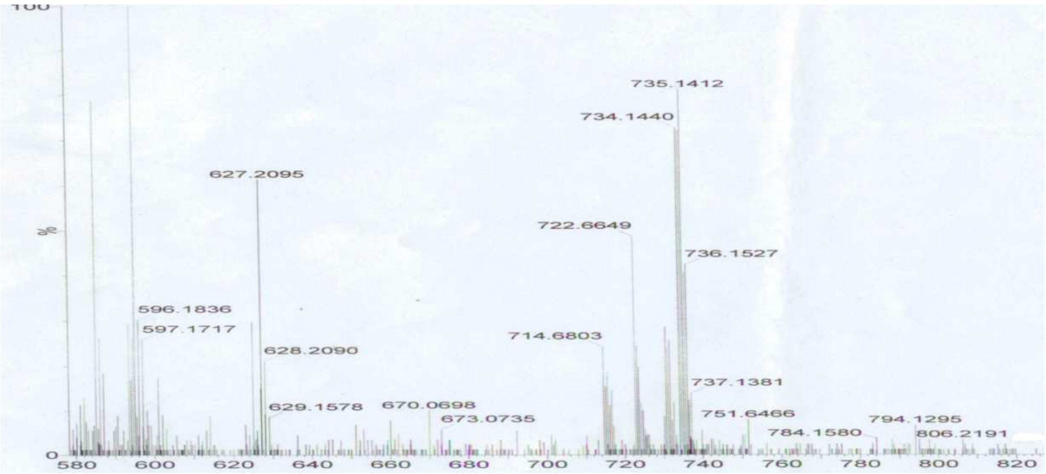


**Fig.7 ESI-Mass Spectrum of Cu(II) complex(6)**

## ESR Spectral Studies

The ESR spectral studies of Cu(II) complexes provide information of the metal ion environment. The ESR spectra of the Cu(II) complexes were recorded in DMSO at liquid nitrogen temperature(LNT) and at room temperature. The ESR spectrum of one representative copper (II) complex (6) has been discussed here, the $g_{\|}$ and $g_{\perp}$ values have been found to be 2.0958 and 2.02792 respectively. The $g_{av}$ was calculated to be 2.0494. The trend $g_{\|} > g_{\perp} > g_e$ observed for the present complex indicates that, the unpaired electron is localised in the orbital $d_{x^2-y^2}$. The slight variation in the $g_{av}$ value is due to the covalence property[21] of the Cu (II) ion. However, this is supported by Kivelson and Neiman, where $g_{\|}$ of less than 2.3 indicates covalent environment. The parameter 'G', determined as $G = (g_{\|}-2) / (g_{\perp}-2)$ is found to be 3.3368 which is less than 4 suggesting the considerable interaction in the solid state. The ESR spectral data clearly suggests that, the Cu(II) complex has distorted octahedral geometry around it. The spectrum is shown in Fig.8

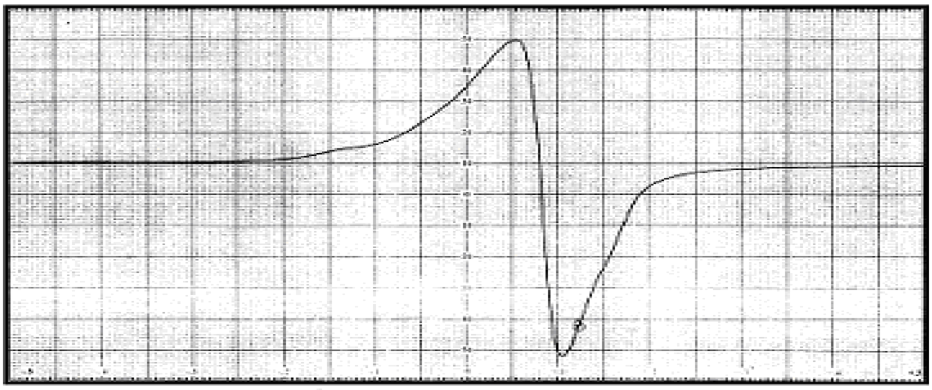


**Fig. 8 ESR Spectrum of the Cu (II) Complex**

## Thermal Study

The thermal behavior of the all the complexes have been studied as a function of temperature. The thermal behavior of synthesized metal complexes is almost same. Hence, only the representative TG/DTA of Co(II)(2), Ni(II)(4) and Cu(II)(6) complexes have been discussed here and their stepwise thermal degradation data are given in **Table 3**.

**Table 3 Thermogravimetric Data of Co(II), Ni(II) and Cu(II) Complexes of SB-II**

| Complex No. | Decomposition temperature $^{o}$C | %Weight loss | | Inference |
|---|---|---|---|---|
| | | Obsd. | Cald. | |
| 2 | 115-230 | 14.52 | 14.60 | Loss of two coordinated water molecules and Chloride ions of ligand. |
| | 250-305 | 86.96 | 87.05 | Loss of ligand moiety |
| | Above 600 | 7.88 | 7.98 | Formation of metal oxide |
| 4 | 110-210 | 14.49 | 14.58 | Loss of two coordinated water molecules and Chloride ions of ligand. |
| | 252-450 | 86.89 | 86.93 | Loss of ligand moiety |
| | Above 750 | 8.09 | 8.11 | Formation of metal oxide |
| 6 | 167-257 | 14.45 | 14.48 | Loss of two coordinated water molecules and Chloride ions of ligand. |
| | 260-347 | 86.29 | 86.33 | Loss of ligand moiety |
| | Above 650 | 8.57 | 8.60 | Formation of metal oxide |

The TG and DTG curves of Co(II)(2) complex is shown in **Fig. 9**. The TGA curve for this complex shows three stages; the first step of decomposition within the temperature range of 167-257$^{0}$C with two centres viz first one at 181$^{0}$C corresponds to loss of two coordinated water molecules and other at 245$^{0}$C loss of chloride ions. The second step of decomposition lies within the range of 260-347$^{0}$C which corresponds to loss of ligand moieties. Finally, in the third step above 650$^{0}$C there is a gradual formation of metal oxide. In case of Cu(II) (6) and Ni(II) (4) the similar three step thermal behavior is observed. In step one, loss of coordinated water molecules and chloride ions lies within the range of 115-230$^{0}$C and 110-210$^{0}$C respectively. The second step decomposition starts in the range 250-305$^{0}$C and 252-450$^{0}$C which are assigned to the loss of ligand moieties. The third step is formation of metal oxides which starts above 600$^{0}$C and 750$^{0}$C respectively.

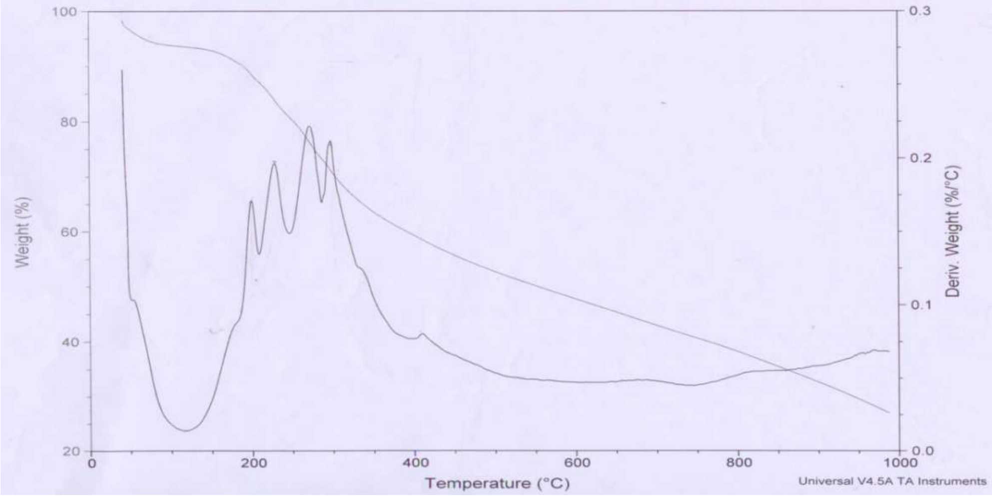


**Fig. 9 Thermogram of Co(II)(2) Complex of SB-II**

## Pharmacological Results

### *DNA Cleavage Activity*

The Co(II), Ni(II) and Cu(II) complexes were studied for their DNA cleavage activities by agarose gel electrophoresis method.

The experimental results of oxidative DNA cleavage are shown in **Fig. 10**. Control experiments clearly revealed that, untreated DNA does not show any cleavage (Figure. 10; Lane C1 and C2) whereas, all the tested metal complexes have exhibited cleavage activity on DNA. The difference in the migration was observed in the Lanes 1 and 2 of Co(II)(1) and Cu(II)(5) metal complexes respectively compared to the control DNA, Lane C1 of *S.aureus*. Similarly in case of Lane 3, 4 and 5 of Co(II)(2), Ni(II)(4) and Cu(II)(6) metal complexes respectively the migration was observed; where, as the untreated control DNA, Lane C2 of *A.niger* has not shown migration. This shows that, the untreated control DNA alone does not show any apparent cleavage; whereas, Co(II), Ni(II) and Cu(II) complexes show. However, the nature of reactive intermediates involved in the DNA cleavage by the complexes has not been clear. The results indicated the important role of metal ions in these isolated DNA cleavage reactions. From these results, we can infer that the Co(II), Ni(II) and Cu(II) metal complexes act as a potent nuclease agents. As the compound was observed to cleave the DNA, it can be concluded that, the compound inhibits the growth of the pathogenic organism by cleaving the genome.

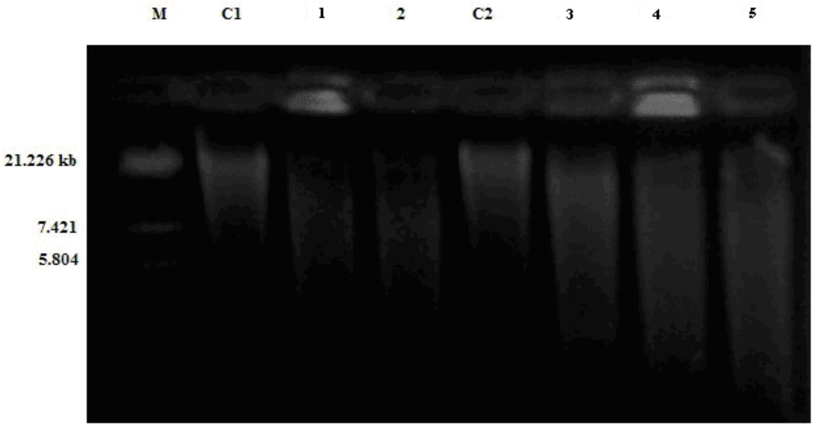


**Fig. 10:M: Standard Molecular Weight Marker; C1- Control DNA of *S. aureus*; Lane 1: *S.aureus* DNA treated with Co(II) Complex (1); Lane 2: *S. aureus* DNA treated with Cu(II) Complex (5); C2: Control DNA of *A. niger*; Lane 3: *A. niger* DNA treated with Co(II) Metal Complex (2); Lane 4: *A. niger* DNA treated with Ni(II) Metal Complex (4); Lane 5: *A. niger* DNA treated with Cu(II) Metal Complex (6)**

**Table 4 Antimicrobial Results of Metal Complexes:**

| Compound | Conc. (μg ml$^{-1}$) | Growth Inhibition Against Bacteria (mm) | | | Growth Inhibition Against Fungi (mm) | | |
|---|---|---|---|---|---|---|---|
| | | *S. aureus* | *E. Coli* | *P. auregenosa* | *A. Niger* | *P. Chrysogenum* | *C. albicans* |
| **SB-I** | 100 | 10 | 08 | 09 | 09 | 08 | 09 |
| | 200 | 11 | 09 | 12 | 10 | 09 | 10 |
| | 500 | 16 | 11 | 17 | 11 | 11 | 11 |
| **SB-II** | 100 | 11 | 09 | 08 | 08 | 09 | 08 |
| | 200 | 12 | 10 | 13 | 10 | 10 | 10 |
| | 500 | 17 | 11 | 17 | 12 | 12 | 11 |
| **1** | 100 | 12 | 08 | 10 | 10 | 08 | 12 |
| | 200 | 14 | 10 | 14 | 12 | 12 | 11 |
| | 500 | 19 | 12 | 19 | 12 | 12 | 13 |
| **2** | 100 | 13 | 10 | 10 | 10 | 08 | 08 |
| | 200 | 15 | 11 | 15 | 12 | 08 | 12 |
| | 500 | 20 | 12 | 19 | 13 | 10 | 15 |
| **3** | 100 | 11 | 08 | 11 | 08 | 08 | 11 |
| | 200 | 15 | 10 | 15 | 10 | 08 | 14 |
| | 500 | 21 | 12 | 20 | 10 | 09 | 16 |
| **4** | 100 | 14 | 08 | 10 | 08 | 08 | 10 |
| | 200 | 16 | 10 | 12 | 10 | 10 | 12 |
| | 500 | 20 | 12 | 21 | 12 | 10 | 15 |
| **5** | 100 | 15 | 08 | 12 | 10 | 08 | 16 |
| | 200 | 18 | 10 | 15 | 12 | 13 | 19 |
| | 500 | 22 | 13 | 18 | 15 | 17 | 21 |
| 6 | 100 | 16 | 09 | 10 | 12 | 09 | 14 |
| | 200 | 18 | 11 | 15 | 12 | 10 | 17 |
| | 500 | 24 | 16 | 22 | 14 | 15 | 20 |
| *Gentamycine Std.* | 500 | 28 | 25 | 35 | -- | -- | -- |
| *Flucanoazole Std.* | 500 | -- | -- | -- | 26 | 25 | 26 |

*Note: Less than 12mm - inactive; 12–16mm - moderately active; above 16mm - highly active.*

## *In vitro* antibacterial and anti fungal activity study

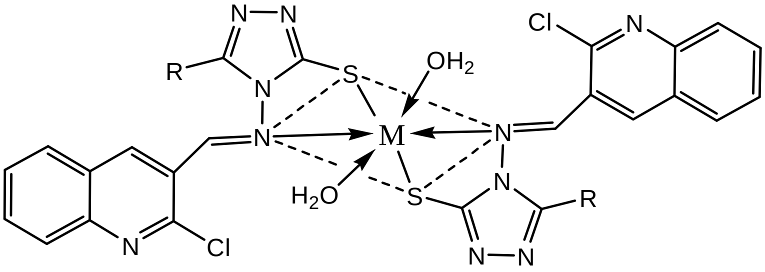
The results of the microbial activity study are presented in Table-4. This antibacterial and antifungal study suggested that, the Schiff bases are found to be biologically active, and some of the metal complexes showed significantly enhanced activity against bacterial and fungal strains. It is, however, known [22] that, the chelating tends to make the Schiff bases act as more powerful and potent bactereostatic agents, thus metal complexes inhibiting the growth of bacteria and fungi more than the parent Schiff bases. It is assumed that factors, such as solubility, conductivity, dipole moment, and cell permeability mechanism (influenced by the presence of metal ions) may contribute to the increase in the activities of the metal complexes relative to Schiff bases.

The Co(II), Ni(II) and Cu(II) metal complexes of these Schiff bases were exhibited good antibacterial activities[23]. In the present case, all the Co(II), Ni(II) and Cu(II) complexes shown high antibacterial activity against *S. aureus*, *E.Coli* and *P. auregenosa* (Table-4). In particular, complexes 5 and 6 showed higher activity than other complexes. Thus, Co(II), Ni(II) and Cu(II) complexes show good selectivity over Schiff bases. The higher activities of the metal complexes compared to their corresponding Schiff bases are may be due to the change in structure due to coordination of transition metal ions, which make the metal complexes act as more powerful and potent bactereostatic agents, thus inhibiting the growth of the microorganisms [24,25]. From the antifungal studies, it is clear that, the Co(II), Ni(II), and Cu(II) complexes are found to possess higher antifungal activities than the respective Schiff bases. However, these metal complexes were found to be moderately active. Thus the results revealed that, the newly synthesized compounds possess high antibacterial activities than the antifungal nature.

## CONCLUSION

The newly synthesized Schiff bases act as a bidentate ligands and coordinated to metal ions through azomethine nitrogen and sulfur atoms via deprotonation. The bonding of the ligand to metal ions were confirmed in the light of elemental analyses, spectroscopic data(IR, Mass, $^1$H& $^{13}$C NMR, UV-Vis, ESR, ESI-Mass etc;) and physico-Chemical Studies (Conductivity, Thermal and Magnetic studies). The synthesized metal complexes screened for their in-vitro antimicrobial activity study, the results revealed that, the newly synthesized compounds possess high antibacterial activities than the antifungal nature. Further, DNA cleavage activity study reveal that, the metal complexes inhibit the growth of the pathogenic organism by cleaving its genome.

Finally, all these observations lead us to propose the following tentative structure for the synthesized metal complexes of the type [$ML_2.2H_2O$]; Where 'L' stands for a singly deprotonated ligand and M= Co, Ni and Cu.



**M= Co, Ni and Cu; R= H, $C_2H_5$**

**Proposed structure of Metal Complexes**

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