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Synthesis, Characterization and Bioactivity Studies of *S*-Allyl-β-*N*-(1-(4-methoxyphenyl)-ethylidene)dithiocarbazate and its *Bis*-chelated Cu(II), Ni(II) and Zn(II) Complexes

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The general formula M(mAp-sadtc)$_2$ type of metal complexes (where M = Cu^{2+}, Ni^{2+}, Zn^{2+}) were synthesized by reaction of *S*-allyl-β-*N*-(1-(4-methoxyphenyl)ethylidene)dithiocarbazate ligand [H-(mAp-sadtc)] with metal(II) acetate salts (M = Ni^{2+}, Cu^{2+} or Zn^{2+}). The *bis*-chelated metal complexes were synthesized by subsequent reaction of metal(II) acetate salts and dithiocarbazate ligand in 1:2 proportion, respectively. The metal complexes and dithiocarbazate Schiff base were characterized by available methods like elemental analysis, ^{1}H NMR, UV-Vis spectroscopy, ^{13}C NMR, FT-IR spectroscopy, molar conductance and magnetic moments. Both nitrogen atoms of azomethine moiety (C=N) and deprotonated thiolate sulfur of dithiocarbazate ligand coordinated to the central metal ion formed five-membered rings on chelation. The synthesized dithiocarbazate ligand [H-(mAp-sadtc)] (**1**) and its *bis*-chelated M(mAp-sadtc)$_2$ complexes (**2-4**) were screened for bioactivity against bacterial strains. The antibacterial results show that the metal(II) complexes exhibited significantly prominent antibacterial activity than dithiocarbazate ligand. Among the synthesized *bis*-chelated metal complexes, Ni-complex exhibited prominent antibacterial and antifungal activity as compared to other metal(II) complexes and ligand.

Keywords: *Bis*-chelated complex, Dithiocarbazate ligand, Metal complex, Schiff base, Biological activity.

INTRODUCTION

In recent years, dithiocarbazate ligand and its metal complexes have become of growing significance in homogenous catalysis, synthetic chemistry and biomedical fields [1]. Further dithiocarbazate ligands also showed interesting characteristics to be used in semiconductor devices [2]. Moreover because of their soft-hard character, metal complexes with dithiocarbazate ligands (containing sulfur and nitrogen donors) are interesting and can demonstrate a structure-activity correlation [1,3]. In addition, due to several oxidation states of metal atoms, the transition metals show an important part in the preparation of many coordination compounds, facilitating their structural, stereochemical, spectroscopic and electrochemical characteristics [4-7]. The current study focuses on Cu^{2+}, Ni^{2+}, Zn^{2+} ions among the different transition metals due to their broad industrial use and shows biological activity such as antibacterial [8-10], antifungal [10,11] and cytotoxic activities [12-14]. A wide range of chemicals has sparked intense attention in the creation of novel complexes with biological assay, which are driven by structural changes produced by complexation with metal ions, to target more efficient and less hazardous modes of action [15,16]. Dithiocarbazates ligands are gaining popularity, owing to their ability to be considerably changed by the insertion of various chemical groups, resulting in a range of donor abilities significant to coordination chemistry. Furthermore, the interaction of these nitrogen-sulphur donors of dithiocarbazate ligand with metallic ions results in complexes with diverse shapes and properties, as well as increased potential biological strengths as compared to a free ligand [11,17-19]. The actions of dithiocarbazate derivates varied dramatically in some situations, despite minor structural differences. These ligands contain both hard nitrogen and soft sulphur donor atoms and they may form coordination molecules with a wide range of metal ions, resulting in coordination molecules with unique physico-chemical characteristics and biological uses [11,20].

Such dithiocarbazate ligand and [M(methoxyacetophenone-*S*-allyldithiocarbazate)$_2$] showed the interesting applications. Nanjundan *et al*. [1] reported synthesis, spectroscopic characterization and bioanalysis investigation of dithiocarbazate ligand (Schiff base, H-Ap-sadtc) and its *bis*-chelated metal complexes [Cu(Ap-sadtc)$_2$ (**1**), Ni(Ap-sadtc)$_2$ (**2**) and Zn(Ap-sadtc)$_2$ (**3**)]. Based on the prominent biological results, we have scope to synthesize the dithiocarbazate ligand of S-allyl dithiocarbazate with substituted acetophenone.

In present study, the synthesis, spectroscopic characterization and bioactivity assay of the dithiocarbazate ligand [H-(mAp-sadtc)] (**1**) and Cu(mAp-sadtc)$_2$ (**2**), Ni(mAp-sadtc)$_2$ (**3**) and Zn(mAp-sadtc)$_2$ (**4**) metal complexes is carried out. The dithiocarbazate ligand (H-mAp-sadtc) synthesized by the reaction of *p*-methoxy acetophenone with *S*-allyl dithiocarbazate. Furthermore, the synthesized metal(II) complexes were also examined against antimicrobial activity strains and compared to free ligands for their biological responses.

EXPERIMENTAL

The chemicals were of A.R. grade and used as it without any further purification for the synthesis of dithiocarbazate ligand and complexes. The chemicals such as 80% hydrazine hydrate, potassium hydroxide (Flakes), carbon disulfide (CS_2) were purchased from Merck (India), while *p*-methoxy acetophenone, allyl bromide, zinc acetate, nickel acetate and copper acetate were obtained from SRL Pvt. Ltd. (India).

The IR spectra of dithiocarbazate ligand and its bischelated metal complexes M(mAp-sadtc)$_2$ were performed on Lambada 7600 PC FT-IR spectrophotometer (range 400-4000cm^{-1}). The UV-Visible spectra were performed on a double beam UV-visible spectrophotometer (Shimadzu) in the range of 200-800 nm. The ^{1}H & ^{13}C NMR were recorded on 400 MHz NMR (TMS as an reference compound). Magnetic moments were recorded by using Gouy's method with magnetic susceptibility balance. Conductivity measurements were carried out on a digital conductometer. Further, elemental analysis was executed on a microanalyzer to measure the percentage of particular elements in the ligand and metal complexes.

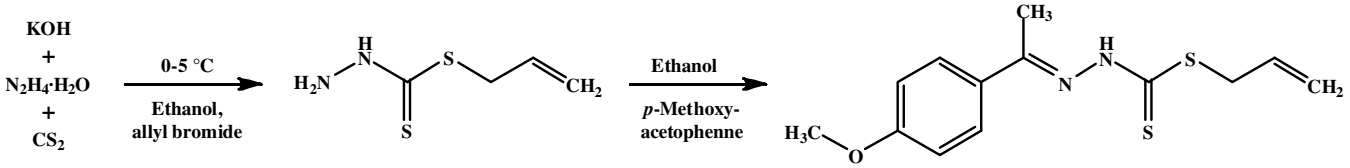
Synthesis of *S*-allyl-β-*N*-(1-(4-methoxyphenyl)ethylidene)dithiocarbazate: Dithiocarbazate Schiff base [H-(mAp-sadtc)] was synthesized as per reported procedure [8,21]. An ethanoic solution of mixture of potassium hydroxide (2.8 g, 50 mmol) and 80 % hydrazine hydrate (2.5 g, 50 mmol) was cooled at 5 ºC, then carbon disulfide (3.8 g, 50 mmol) and allyl bromide (6.05 g, 50 mmol) were added one-by-one with stirring and cooling. To this above solution, an equimolar proportion of *p*-methoxy acetophenone (50 mmol) was added dropwise and the whole mixture of the solution was heated for 30 min. The yellow solid appeared that was remove from mother liquor by filtration, followed by washing with 95 % ethanol and finally desiccated over anhydrous silica gel (**Scheme-I**). Yield 72 %, colour: faint yellow, m.p.: 459 K, Elemental analysis calcd. (found) % of $C_{13}H_{16}N_2OS_2$: C, 55.71 (55.72); H, 5.70 (5.71); N, 9.99 (10.01); S, 22.87 (22.85). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.99 (s, 1H, -NH), 7.81 (d, *J* = 9.4 Hz, 2H, aromatic), 6.94 (d, *J* = 9.4 Hz, 2H, aromatic), 6.05-5.98 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H, allyl, -CH=C), 5.37 (dd, *J* = 17.0, 1.3 Hz, 1H, allyl, -C=CH$_2$), 5.22 (dd, *J* = 10.0, 1.3 Hz, 1H, allyl, -C=CH$_2$), 4.01 (d, *J* = 7.0 Hz, 2H, allyl, -S-CH$_2$-C), 3.86 (s, 3H, methoxy, -OCH$_3$), 2.29 (s, 3H, methyl, -CH$_3$). ^{13}C NMR (101 MHz, $CDCl_3$): δ [199.11, (s), (C=S)], [161.41, (s), aromatic], [149.04, (s), (C=N)], [132.60, (s), allyl -CH], [129.34, (s), aromatic], [128.20, (s), aromatic], [118.74, (s), allyl =CH$_2$], [114.00, (s), aromatic], [55.40, (s), (-OCH$_3$)], [37.55, (s), -S-CH2], [13.00, (s), (-CH$_3$)].

Synthesis of metal complexes (2-4): An ethanoic solutions of acetate metal salts (0.5 mmol) such as cupric acetate monohydrate ($C_4H_6CuO_4{\cdot}H_2O$, 0.100 g), nickel acetate tetrahydrate ($C_4H_6NiO_4{\cdot}2H_2O$, 0.124 g), zinc acetate ($C_4H_6ZnO_4{\cdot}4H_2O$, 0.129 g) were added dropwise to an hot ethanoic solution of dithiocarbazate Schiff base (0.280 g, 1 mmol). The final solution was then refluxed for 0.5 h. Synthesized *bis*-chelated metal complexes Cu(mAp-sadtc)$_2$ (**2**), Ni(mAp-sadtc)$_2$ (**3**) and Zn(mAp-sadtc)$_2$ (**4**) were separated by filtration method, then washed with a little amount of methanol and finally dried over silica gel.

Cu(mAp-sadtc)$_2$: Yield 72 %, colour: bluish black; m.p.: 477 K; Elemental analysis calcd. (found) % for $C_{26}H_{30}N_4O_2S_4Cu$: C, 50.19 (50.20); H, 4.82 (4.81); N, 9.00 (9.02); S, 20.61 (20.59). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, 4H, aromatic), 7.06 (d, *J* = 8.7 Hz, 4H, aromatic), 5.96-5.87 (ddt, *J* = 16.9, 9.9, 7.0 Hz, 2H, allyl, -CH=C), 5.07 (dd, *J* = 17.0, 0.7 Hz, 2H, allyl, -C=CH$_a$), 5.01 (dd, *J* = 10.0, 0.7 Hz, 2H, allyl, -C=CH$_b$), 3.83 (s, 6H, -OCH$_3$), 3.65 (d, *J* = 6.9 Hz, 4H, allyl, -S-CH$_2$-C), 2.15 (s, 6H, -CH$_3$).

Ni(mAp-sadtc)$_2$: Yield 68%, colour faint black; m.p.: 491 K; Elemental analysis calcd. (found) % for $C_{26}H_{30}N_4O_2S_4Ni$: C, 50.59 (50.57); H, 4.86 (4.89); N, 9.07 (9.06); S, 20.77 (20.78). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (s, 4H, aromatic), 7.12 (d, *J* = 8.7 Hz, 4H, aromatic), 5.96-5.86 (ddt, *J* = 16.9, 9.9, 7.0 Hz, 2H, allyl, -CH=C), 5.23 (d, *J* = 17 Hz, 2H, allyl, -C=CH$_a$), 5.13 (d, *J* = 10.0 Hz, 2H, allyl, -C=CH$_b$), 3.93 (s, 6H, -OCH$_3$), 3.60 (d, *J* = 6.9 Hz, 4H, allyl, -S-CH$_2$-C), 1.93 (s, 6H, -CH$_3$).

Zn(mAp-sadtc)$_2$: Yield 71 %, colour: faint yellow; m.p.: 479 K; Elemental analysis calcd. (found) % for $C_{26}H_{30}N_4O_2S_4Zn$: C, 50.05 (50.07); H, 4.80 (4.82); N, 8.97 (8.95); S, 20.55 (20.56). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.8 Hz, 4H, arom.), 6.95 (d, *J* = 8.8 Hz, 4H, aromatic), 5.98-5.88 (ddt, *J* = 16.9,



Scheme-I: Synthetic route of dithiocarbazate ligand [H-(mAp-sadtc)]

10.0, 6.9 Hz, 2H, allyl, -CH=C), 5.24 (dd, *J* = 17.0, 1.3 Hz, 2H, allyl, -C=CH_a), 5.13 (d, 10.0, 1.3 Hz, 2H, allyl, -C=CH_b), 3.90 (s, 6H, -OCH_3), 3.65 (d, *J* = 7.0 Hz, 4H, allyl, -S-CH_2-C), 2.23 (s, 6H, -CH_3).

Antimicrobial activity: Three pathogenic bacteria *E. coli*, *S. aureus*, *B. cereus* and one fungus *C. albicans* were used to investigate the biological assay of the proposed dithiocarbazate ligand H-(mAp-sadtc) and its chelated metal complexes were cultured at Department of Biotechnology, Shivaji University, Kolhapur, India. Test compounds [H-(mAp-sadtc) and its metal complex (**2-4**)] of stock solutions were achieved by dissolving compounds in DMSO solvent (2 mg/mL). The antimicrobic potential of the newly synthesized compounds was examined employing the well-diffusion technique on routinely used medium *i.e*. nutrient agar [22,23]. Microorganisms was cultured freshly one night before the experiment at 37 ºC on nutrient agar plates and 100 µL of microbial suspension was dispersed on the surface of nutrient agar plates using sterile glass spreader. Similarly, for antifungal activity, fungal suspension was spread on a potato dextrose agar plate with the help of a sterile glass spreader to achieve lawn growth. Wells (6 mm diameters) were derived and filled with 25 µL (50 µg/well) of each compound stock solution. Kanamycin and nystatin (Sigma-Aldrich) (1.0 mg mL^{-1}) and DMSO were used as control. The prepared plates for biological assay were incubated for 24 h at 30 ºC for bacteria and for 4 days 37 ºC for fungi. The investigation of antimicrobial potential depends on the extent of zone of inhibition on the surface of the nutrient agar medium around the well. The zones of inhibition (in mm) produced by metal complexes and ligands were compared to conventional antibiotics (kanamycin 30 µg/disc and amoxycillin).

RESULTS AND DISCUSSION

The dithiocarbazate ligand undergoes thione-thiol tautomerism as shown in Fig. 1. The dithiocarbazate ligand on further reaction with metal(II) salts in 2:1 proportions respectively, yielded the corresponding metal complexes (Fig. 2). The spectroscopic and physico-chemical measurements are in good agreement with the synthesized compounds. Molar conductivity data suggested the non-electrolytic nature of proposed compounds.

IR spectra: The selected IR bands of ligand and its chelated metal complexes are shown in Table-1. Dithiocarbazate (SADTC) ligands showed the thione-thiol tautomerism [NH-C(=S)-, N=C(-SH)-], respectively, Additionally, ligand may be complexed either in thione or in thiol or both as evident from previous literature reported by Yazdanbaksh *et al*. [24]. Fig. 3 shows dithiocarbazate ligand band at 3189 cm^{-1}, which is assigned for N-H stretching frequency in FTIR spectrum indicating that ligand predominantly exists in thione form [25,26]. Further, the N-H stretching peak become vanished in FT-IR spectra of complexes showed that dithiocarbazate ligand undergoes thione to thiol tautomerism and then deprotonation of thiol moiety before complexation with metal ions which leads to increase conjugation in the structure of metal complexes. Moreover, the dithiocarbazate ligand shows another band at 1609 cm^{-1} which is predicted for azomethine moiety (CH=N) stretching frequency in the FTIR spectrum. Further, the (C=N) band of azomethine moiety was shifted towards the lower absorption frequency in metal complexes (1599-1598 cm^{-1}) indicating that azomethine nitrogen complexed with metal ions [8,27]. The dithiocarbazate ligand [H-(mAp-sadtc)] absorbs at 1095 cm^{-1} is assigned to (C=S) absorption of dithiocarbazate ligand, which were absent after metal(II) complex formation indicating a complexation of thionyl sulfur of dithiocarbazate ligand to the central metal ion [1]. The complexation through azomethine nitrogen moiety (C=N) and thionyl sulfur [C(-S)S] of dithiocarbazate ligand to a metal ion is further affirmed by the existence of absorption band at 488-468 cm^{-1} due to (M-N) and 425-418 cm^{-1} due to (M-S) in FT-IR spectra of complexes (**2-4**).

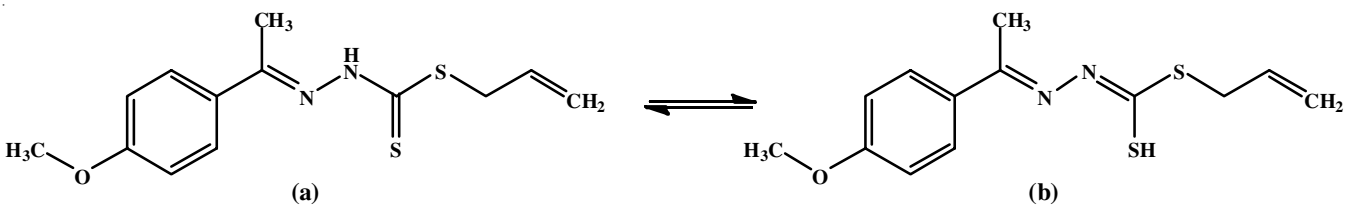


Fig. 1. Tautomeric forms of Schiff base [H-(mAp-sadtc)] (a) thione form (b) thiol form

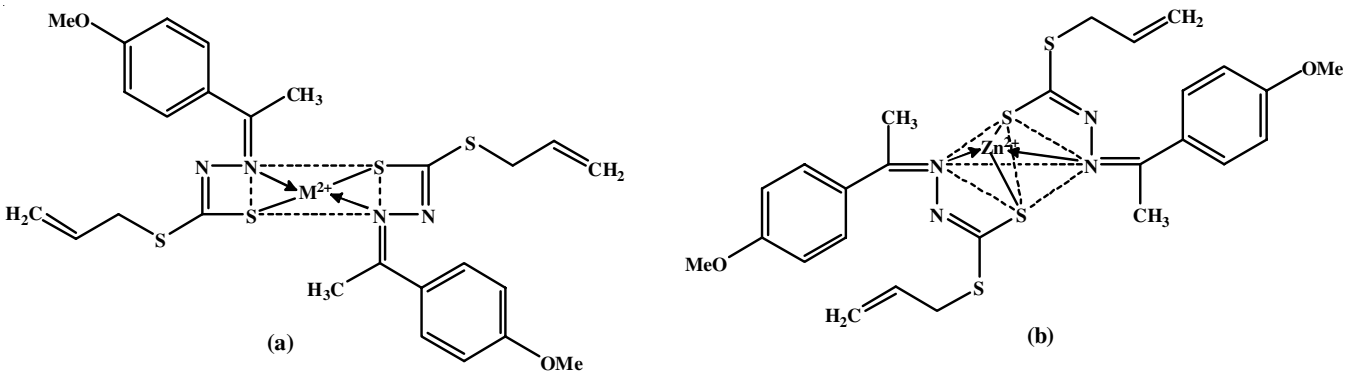


Fig. 2. Proposed structure of metal [(a) Cu^{2+} and Ni^{2+}, (b) Zn^{2+}] complexes

TABLE-1
KEY IR BAND (cm^{-1}) OF LIGAND AND M(mAp-sadtc)$_2$ COMPLEXES

Compounds	ν(N-H)	ν(C=S)	ν(C=N)	ν(C-S)	ν(M-N)	ν(M-S)
H-(mAp-sadtc)	3189	1095	1609	835	–	–
Cu(mAp-sadtc)$_2$	–	–	1598	818	488	418
Ni(mAp-sadtc)$_2$	–	–	1598	821	468	425
Zn(mAp-sadtc)$_2$	–	–	1599	827	469	418

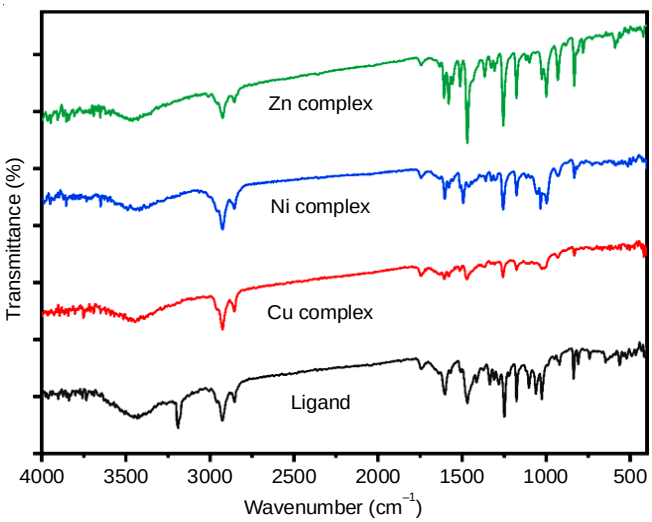


Fig. 3. FTIR spectra of ligand and its metal(II) complexes

^{1}H NMR studies: The ^{1}H NMR spectra of dithiocarbazate ligand in $CDCl_3$ solvent shows the occurrence of an unshielded signal peak at 9.99 ppm, attributed to thioamide (N-H) moiety of dithiocarbazate Schiff base ligand [8,11]. The methylene protons (-CH_2-S-) dithiocarbazate ligand present as a doublet (d, J = 7.0 Hz, 2H) at 4.01 ppm. The allyl group moiety exhibits multiple signals corresponds to -CH and -CH_2 protons at 6.01 ppm (ddt) (^3J = 7 Hz, $^3J_{cis}$ = 17.0 and $^3J_{trans}$ = 10.0 Hz, 1H) and 5.37 ppm (dd) ($^3J_{trans}$= 17.0, $^2J_{geM}$ = 1.3 Hz, 1H) and 5.22 ppm (dd), $^3J_{cis}$ = 10.0 Hz, $^2J_{geM}$ = 1.3 Hz, 1H) corresponds to CH protons and CH_2 protons respectively. A signal for methoxy group of *p*-methoxy acetophenone appears as a singlet at 3.86 ppm (s, 3H) while methyl group of acetophenone moiety exhibit singlet peak in the most deshielded region at 2.29 ppm (s, 3H). The aromatic protons of *p*-acetophenone moiety show two different peaks at 7.81 ppm (d, J = 9.4 Hz, 2H) and 6.94 ppm (d, J = 9.4 Hz, 2H).

The N-H proton peak at 9.99 ppm in ^{1}H NMR spectrum of ligand disappeared in metal complexes indicates that dithiocarbazate ligand undergoes thione-thiol tautomerism then undergo deprotonation of thiol moiety before complexation with metal ions, which confirms that sulfur atom participated in metal complex formation. Again, methylene proton (S-CH_2) of dithiocarbazate ligand and complex (**2-4**) observed at 4.01 and 3.88 ppm respectively, suggests that allyl sulfur [C(=S)S-CH_2] atom does not take part in the complexation of the ligand with metal ions. The aromatic protons of *p*-methoxy acetophenone moiety in Ni(mAp-sadtc)$_2$ and Zn(mAp-sadtc)$_2$ metal complexes spectra appeared at ppm, 8.74 (d, 4H), 7.12 (d, 4H) and δ 7.48 (d, 4H), 6.95 (d, 4H), respectively. Moreover, other proton peaks of -CH, -CH_2,-OCH_3,-CH_3 of dithiocarbazate ligand appear nearly the same δ value in the metal complexes spectra. However, the disappearance of 9.99 ppm peak of ligand in metal complexes spectra indicates the forma-tion of metal complexes (**2-4**).

^{13}C NMR studies: ^{13}C NMR spectrum of dithiocarbazate ligand shown signals at 199.11 and 149.04 ppm, which are predicted to the thione (C=S) and azomethine (C=N) fragments respectively. Najundan *et al.* [1] reported that upon coordination of dithiocarbazate ligand of acetophenone with metal ions, C=S group peak position shifted in the downfield region and C=N peak position shifted in the up-field region. The peaks due to thione sulfur of methylene group (S-CH_2), methoxy group and methyl moiety of dithiocarbazate ligand appear at 37.5, 55.40, 13.00 ppm, respectively, while aromatic carbons show peaks at 114.0,128.20,129.34 and 161.14 ppm. In addition, allyl carbon (CH=CH_2) appeared at 132.60 ppm (CH, allyl) and 118.74 ppm (CH_2, allyl) in ligand spectra.

Electronic spectra: The electronic spectra of ligand and its *bis*-chelated metal(II) complexes are shown in Fig. 4. The UV-visible analysis data (Table-2) suggests that synthesized dithiocarbazate ligand and *bis*-chelated metal(II) complexes exhibited π→π* and n→π* transitions bands related to the dithiocarbazate groups. In addition, π→π* transitions represent characteristics of azomethine chromophore, further metal(II) complexes display hypochromic displacement about the complexation of metals to the azomethine nitrogen [19,28,29]. The UV absorption bands in the region of 300-400 nm are generally related to ligand–metal charge transition. The significant band at 256 nm, 295 nm corresponds to π→π* and n→π* transitions of the azomethane group of dithiocarbazate ligand, while

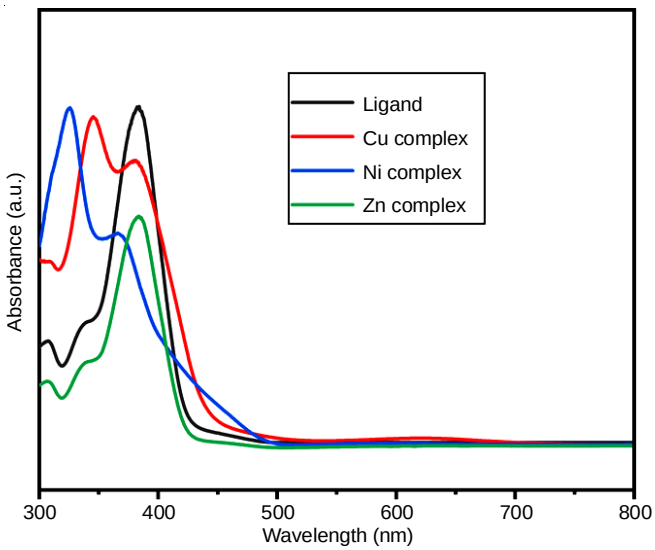


Fig. 4. UV spectra of ligand and complexes

TABLE-2
MAGNETIC AND MOLAR CONDUCTANCE DATA OF LIGAND AND M(mAp-sadtc)$_2$ COMPLEXES

Compounds	Molar conductance (Ω^{-1} cm^2 mol^{-1})	$\mu_{eff.}$ (B.M.)
H-(mAp-sadtc)	6.47	–
Cu(mAp-sadtc)$_2$	3.37	1.97
Ni(mAp-sadtc)$_2$	3.80	Dia
Zn(mAp-sadtc)$_2$	4.25	Dia

another strong band at 340, 441 nm is tentatively considered due to the presence of $\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ transition attributed to the dithiocarbazate group itself respectively [30]. In metal complexes, the UV-Vis absorption band of mentioned transitions become shifted to frequency region (295-310 nm), somewhat due to the strong nitrogen absorption of the azomethine group [11,19]. In addition, the absorption bands in the lower UV region (441 nm) are predicted for the ligand to metal (L-M) charge transfer transition (LMCT) according to one of evidence reported by Ravoof *et al.* [31]. Furthermore, while S→M charge transfer shifts were familiar in dithiocarbazate based transition metal complexes most of the time, this band of transition was not visible in the current spectra due to the smoothness of the UV-vis band inside the area of 340-450 nm, which continued up to the visible area in metal complex spectra [10].

Magnetic moments and molar conductance: The magnetic moment and molar conductance data of ligands and M(mAp-sadtc)$_2$ complexes are listed in Table-3. The conductance data suggest that both ligand and M(mAp-sadtc)$_2$ complexes are non-electrolyte [32]. The magnetic susceptibility data showed that Cu(mAp-sadtc)$_2$ complex was paramagnetic (magnetic moment, 1.97 B.M.), while Ni(mAp-sadtc)$_2$ complex (**3**) and Zn(mAp-sadtc)$_2$ complex (**4**) both were diamagnetic in nature. The magnetic susceptibility indicated that the Cu(mAp-sadtc)$_2$ and Ni(mAp-sadtc)$_2$ complexes have square planar geometry with two dithiocarbazate ligands present at four stereochemical sites in the structure. Additionally, Zn(mAp-sadtc)$_2$ complexes has tetrahedral geometry.

TABLE-3
UV-VISIBLE DATA OF LIGAND AND M(mAp-sadtc)$_2$ TYPE COMPLEXES

Compounds	λ_{max} (nm)			
	Band-I	Band-II	Band-III	Band-IV
H-(mAp-sadtc)	256	295	340	414
Cu(mAp-sadtc)$_2$	260	300	339	–
Ni(mAp-sadtc)$_2$	279	310	323	–
Zn(mAp-sadtc)$_2$	257	295	342	–

Antifungal and antibacterial activity: The biological investigation of dithiocarbazate ligand and its *bis*-chelated metal(II) complexes were investigated against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus cereus* and *Candida albicans.* The ligands and its *bis*-chelated metal complexes manifested the significant antibacterial activity to *E. coli* (13 mm and 17-19 mm inhibition zone respectively), *S. aureus* (12 mm and 14-18 mm inhibition zone respectively) and *B. cereus* (11 mm and 11-14 mm inhibition zone respectively) (Table-4). Further, the antifungal test shows complexes exhibited considerable activity against *Candida albicans* (07-09 mm inhibition zone respectively). The ligand and its metal complexes display less activity against *B. cereus*, while Ni(mAp-sadtc)$_2$ complex showed prominent bioactivity against tested microorganisms. Moreover, the biological activity (antimicrobial and antifungal) of metal ions become enhanced when complexation to the dithiocarbazate ligands. The coordination of dithiocarbazates ligand with metal ions lessens their polarity by incompletely sharing the positive charge with the nitrogen-sulfur donor atoms and π-electron delocalization, which might cause a change in the metallic atom's lipophilic behaviour [1,11]. Additionally, due to metal complexation, complexes (**2-4**) exhibited significant activity for all evaluated analyses, which contributes to antimicrobial and antifungal activities.

TABLE-4
BIOLOGICAL ACTIVITY OF LIGAND AND M(mAp-sadtc)$_2$ TYPE COMPLEXES

Compounds	Inhibition zone (diameter in mm)			
	Gram –ve	Gram +ve		Fungi
	E. coli	*S. aureus*	*B. cereus*	*C. albicans*
H-(mAp-sadtc)	13	12	11	–
Cu(mAp-sadtc)$_2$	18	16	11	07
Ni(mAp-sadtc)$_2$	19	18	14	09
Zn(mAp-sadtc)$_2$	17	14	12	–
Standard drug	25	23	24	23

Standard drug = Kanamycin, nystatin and amoxycillin

Conclusion

The synthesis, characterization and bioactivity analysis of dithiocarbazate ligand (**1**) and its *bis*-chelated metal(II) complexes [M(mAp-sadtc)$_2$] was carried out. The spectroscopic characterization and magnetic susceptibility data of Cu(mAp-sadtc)$_2$ (**2**) and Ni(mAp-sadtc)$_2$ (**3**) complexes showed square planar geometry, while Zn(mAp-sadtc)$_2$ complex exhibited tetrahedral geometry. In case of *bis*-chelated metal(II) complexes [M(mAp-sadtc)$_2$] (**2-4**), dithiocarbazate ligand fragments were in the deprotonated form, which behave as bidentate (NS donor) uni-negative agents. Furthermore, *bis*-chelated metal(II) complexes [M(mAp-sadtc)$_2$] complexes show the superior bioactivity responses when compared to the dithiocarbazate ligand.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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