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RESEARCH ARTICLE

Synthesis, Characterization, Chemical Nuclease Activity and Antimicrobial Evaluation of Tridentate (NOS Donor) Schiff Base Ligand: 2-(4-(Thiophen-2-yl)but-3-en-2-ylideneamino)phenol and their Metal-Organic Hybrids

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Abstract: Cu(II), Co(II), Ni(II) and Zn(II) metal-organic hybrids of new tridentate (NOS donor) Schiff base ligand derived from 4-(thiophen-2-yl)but-3-en-2-one (TB) and 2-aminophenol (AP) were synthesized, characterized and their pharmacological activities were evaluated. Possible geometry of the hybrid derivatives and the chelating atoms were investigated on the source of elemental analysis, magnetic moment, molar conductivity, infrared, EPR, NMR, electronic and mass spectral studies. The results were consistent with a three coordination environment around the metal ion. Synthesized compounds were screened for *in vitro* antimicrobial activity against bacteria *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumonia, Staphylococcus aureus, Staphylococcus saprophyticus* and fungi *Candida albicans*. Hybrid derivatives showed improved antibacterial and antifungal activity compared with the ligand 2(-4-(thiophen-2-yl)but-3-en-2-ylidene amino)phenol (TBAP). DNA cleavage experiments done by means of gel electrophoresis with corresponding hybrid derivatives in the presence of H_2O_2 showed pronounced discernible DNA cleavage.

Keywords: Antimicrobial, DNA cleavage, Schiff base, Tridentate, Thiophene

Introduction

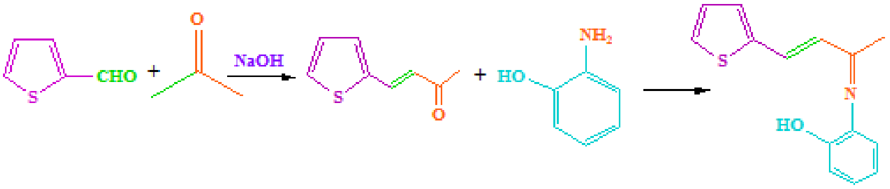
Schiff base ligands containing N, O, S donor atoms show broad biological activity and are of particular interest because of the array of ways in which they are bonded to metal ions[1]. Thiophene and its derivatives are essential heterocyclic compounds. They possess wide variety of biological activities such as antimicrobial, diabetes mellitus[2], cholesterol inhibition activity[3], antitumor and antiallergic activities[4]. On the other hand, 2-aminophenol based Schiff bases have been the subject of extensive exploration because of their wide application. Also hybrid derivatives of Schiff bases with heterocyclic system find applications as potential drugs[5]. Resistance of pathogenic bacteria towards existing antibiotics is swiftly becoming a foremost world-wide problem. Thus invent of new compounds to deal with resistant bacteria has become one of the vital area of antibacterial research today. Although many Schiff bases and their metal complexes had been extensively studied, a perusal of literature revealed that no Schiff base of 2(-4-(thiophen-2-yl)but-3-en-2-ylidene amino)phenol and their hybrid derivatives had been reported. Thus there is a great necessitate to explore their potential and the present study is one in this direction. Motivated by the above observations in the present work we had reported the synthetic as well as characterisation particulars and biological activities (antimicrobial and DNA cleavage activity) of the Schiff base ligand TBAP by the condensation of 4-(thiophen-2-yl)but-3-en-2-one with 2-aminophenol and their metal(II) hybrid derivatives of Cu(II), Co(II), Ni(II) and Zn(II).

Experimental

All solvents and chemicals used were of analytical reagent grade from Merck and Sigma Aldrich. Melting point of all synthesized compounds was determined using open capillary tube and was reported uncorrected. UV spectra were recorded on Systronic pc based double beam spectrophotometer 2202. IR spectra were recorded by making KBr pellets on Shimadzu Fourier transform IR spectrophotometer, FT/IR-8400S. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer in DMSO-d6 solvent. C, H, N and S data were obtained by using Elementar Vario EL III. Molar conductance was measured on the ELICO (CM-185) conductivity bridge using 10^{-3} M solution in DMSO by dip-type conductivity cell fitted with a platinum electrode. Magnetic susceptibility of complexes was measured by Gouy's method using copper sulphate as calibrant. Thermogram was analysed and recorded using NETZSCH STA 449F3 TG/DTA instrument in the temperature range from 30 °C to 900 °C under nitrogen atmosphere. The mass spectral analysis was carried out using JEOL D-300 (EI) mass spectrometer. EPR measurement of the copper complex of TBAP was recorded at liquid nitrogen temperature using a JEOL Model JES FA200 instrument. Gel electrophoresis experiment was done with CT DNA, with hydrogen peroxide as oxidant. Pharmacological activity of the synthesized compounds against selected bacteria and fungi species was tested using Kirby-Bauer disc diffusion method.

Synthesis of ligand: 2(-4-(Thiophen-2-yl)but-3-en-2-ylideneamino)phenol (TBAP)

To an ethanolic solution of acetone (5 mmol), sodium hydroxide solution (5 mmol) was added gradually with even stirring. To the above mixture ethanolic solution of 2-thiophene-carboxaldehyde (5 mmol) was added drop wise and stirred for 2-3 hours. Then ethanolic solution of 2-aminophenol (5 mmol) was added drop by drop and refluxed for 5-6 hours. After completion of the reaction (monitored by TLC) the yellow precipitate obtained was filtered, washed with ethanol, dried and recrystallized from ethanol yield 89%. Reaction sequence for the synthesis of TBAP is shown in Scheme 1.



Scheme 1. Synthesis of Schiff base ligand: (TBAP)

Synthesis of metal complexes

Hot ethanolic solutions of TBAP (2 mmol) and respective hydrated metal(II) chlorides (*viz*., Cu, Co, Ni and Zn) (2 mmol) were mixed in the ratio 1:1 under constant stirring and refluxed for 5-6 hours. Coloured precipitates of hybrid derivatives obtained in each case was filtered, washed with ethanol followed by diethylether and dried in vacuum over fused $CaCl_2$.

CT DNA cleavage study

Cleavage of CT DNA was examined by means of agarose gel electrophoresis. The gel-electrophoresis experiment was performed by incubation of the samples containing 50 μM of each synthesized compound, 30 μM CT DNA and 40 μM hydrogen peroxide (H_2O_2) for 2 h at 37 ^oC in Tris-HCl/NaCl buffer (pH 7.2). The samples were electrophoresis after incubation at 50 V for 2 h on 1% agarose gel using Tris-acetic acid-EDTA buffer, (pH 8.0). The gel was then stained using 1 μg cm^{-3} ethidium bromide (EB) and photographed under ultraviolet light.

Antimicrobial activity

In vitro antimicrobial activity of synthesized compounds was investigated using Kirby-Bauer disc diffusion method[6]. From the many media available, the current NCCLS: national committee for clinical laboratory standards guidelines has recommend using Sabouraud dextrose agar medium for Candida and Mueller–Hinton agar medium for bacteria. The antibacterial and antifungal activity was done at 1 mg/mL concentration of the synthesized compounds in DMSO solvent. Plates inoculated with bacteria and fungi was incubated at 35-37 ^oC for 24-48 h and at 30 ^oC for 24-48 h respectively and then the diameter of the inhibition zone was measured in millimetres. Standard discs of ciprofloxacin (antibacterial agent) and nystatin (antifungal agent) served as positive control. Blank paper disks were impregnated with 10 μL of the stock solutions. When filter paper disc impregnated with tested chemical is placed on agar, the chemical would diffuse from the disc into the agar and place the chemical in the agar around the disc. The area of chemical infiltration around the disc will be determined by the solubility and molecular size of the chemical. When an organism is positioned on the agar it will not grow in the area around the disc if it is susceptible to the chemical. This area of no growth around the disc is called ‘‘Zone of inhibition’’.

Characterization data

2(-4-(Thiophen-2-yl)but-3-en-2-ylideneamino)phenol (TBAP)

Yellow. Yield: 89%. M.p.: 103 ^oC. Anal. Calc. ($C_{14}H_{13}NOS$). M.wt: 243.32. Elem. Anal. Calc: C, 69.11; H, 5.39; N, 5.76, S, 13.18; found: C, 68.97; H, 5.42; N, 5.64, S, 13.02; % EI-MS: (*m/z*) 243 (RI 17%), (*m/z*) 228 (RI 100%), (*m/z*) 109 (RI 16%), (*m/z*) 84 (RI 11%), (*m/z*) 58 (RI 4%); UV/Vis λ_{max}(nm): 256, 372. IR ν_{max}(cm^{-1}): 3203 (OH), 1696 (C=N), 1606 (olefinic C=C), 1366 (CH_3), 1251 (C-O), 766 (C-S (thiophene)). ^1H NMR (DMSO-d6 ppm): 2.03 (s, 3H, CH_3), 6.58, 6.92 (d, 1H, CH=CH), 6.72-7.89 (m, aromatic-H), 11.71 (s, 1H, OH). ^{13}C NMR (DMSO-d6 ppm): 156.27 (carbonyl), 162.34 (azomethine), 136.21, 147.68 (olefinic C=C), 115-140 (aromatic), 24.27 (CH_3).

Copper complex of 2(-4-(thiophen-2-yl)but-3-en-2-ylideneamino)phenol (CuTBAP)

Dark green, Yield: 87%. M.p.: 128 ^oC. Anal. Calc. ($C_{14}H_{14}CuNO_2S$). M.wt: 323.88. Elem. Anal. Calc: C, 51.92; H, 4.36; N, 4.32; Cu, 19.62; S, 9.90; found: C, 51.96; H, 4.25; N, 4.21; S, 9.74; Cu, 19.51; Molar conductance Λm ($\Omega^{-1}cm^2mol^{-1}$): 84.92; μ_{eff} (magnetic moment

(BM): 1.92; UV/Vis λ_{max} (nm): 241, 353, 574. IR ν_{max} (cm^{-1}): 3439 (coordinated water), 1677 (C=N), 1603 (olefinic C=C), 1366 (CH_3), 1223 (C-O), 778 (C-S (thiophene)), 577 (M-O), 463 (M-N). ^{1}H NMR (DMSO-d6 ppm): 2.07 (s, 3H, CH_3), 6.63, 6.89 (d, 1H, CH= CH), 6.83-7.63 (m, aromatic-H), 4.16 (br, 2H, H_2O). TGA wt. Loss: % found/calc. (temp.): 5.53/5.56 (155-215°C); 38.13/38.12 (215-420 °C); 35.64/35.67 (420-615 °C).

Cobalt complex of 2(-4-(thiophen-2-yl)but-3-en-2-ylideneamino)phenol (CoTBAP)

Reddish brown, Yield: 84%. m.p.: 149 °C. Anal. calc. ($C_{14}H_{14}Cl_2CoNO_2S$). M.wt: 390.17. Elem. Anal. Calc: C, 43.10; H, 3.62; N, 3.59; Co, 15.10; S, 8.22; found: C, 43.15; H, 3.58; N, 3.63; S, 8.17; Co, 14.98; Molar conductance Λm ($\Omega^{-1}cm^2mol^{-1}$): 4.75; μ_{eff} (magnetic moment (BM)): 4.87; UV/Vis λ_{max} (nm): 247, 364, 427, 614, 741. IR ν_{max} (cm^{-1}): 3419 (coordinated water), 1680 (C=N), 1609 (olefinic C=C), 1366 (CH_3), 1227 (C-O), 736 (C-S (thiophene)), 568 (M-O), 468 (M-N), 418 (M-Cl). ^{1}H NMR (DMSO-d6 ppm): 2.08 (s, 3H, CH_3), 6.77, 6.99 (d, 1H, CH=CH), 6.86-7.71 (m, aromatic-H), 4.13 (br, 2H, H_2O). TGA wt. Loss: % found/calc. (temp.): 4.59/4.61 (150-210°C); 18.18/18.20 (210-365 °C); 36.66/36.65 (365-560 °C); 21.25/21.28 (560-725 °C).

Nickel complex of 2(-4-(thiophen-2-yl)but-3-en-2-ylideneamino)phenol (NiTBAP)

Grassy green, Yield: 86%. m.p.: 144 °C. Anal. calc. ($C_{14}H_{14}Cl_2NiNO_2S$). M.wt: 389.93. Elem. Anal. Calc: C, 43.12; H, 3.62; N, 3.59; Ni, 15.05; S, 8.22; found: C, 43.04; H, 3.64; N, 3.51; S, 8.14; Ni, 14.94; Molar conductance Λm ($\Omega^{-1}cm^2mol^{-1}$): 5.12; μ_{eff} (magnetic moment (BM)): 2.97; UV/Vis λ_{max} (nm): 251, 340, 410, 602, 727. IR ν_{max} (cm^{-1}): 3350 (coordinated water), 1681 (C=N), 1608 (olefinic C=C), 1365 (CH_3), 1229 (C-O), 739 (C-S (thiophene)), 568 (M-O), 465 (M-N), 419 (M-Cl). ^{1}H NMR (DMSO-d6 ppm): 2.09 (s, 3H, CH_3), 6.63, 6.88 (d, 1H, CH= CH), 6.74-7.63 (m, aromatic-H), 4.19 (br, 2H, H_2O).

Zinc complex of 2(-4-(thiophen-2-yl)but-3-en-2-ylideneamino)phenol (ZnTBAP)

Dirty white, Yield: 84%. m.p.: 136 °C. Anal. calc. ($C_{14}H_{14}ZnNO_2S$). M.wt: 325.72. Elem. Anal. Calc: C, 51.62; H, 4.33; N, 4.30; Zn, 20.08; S, 9.84; found: C, 51.53; H, 4.26; N, 4.27; S, 9.80; Zn, 19.93; Molar conductance Λm ($\Omega^{-1}cm^2mol^{-1}$): 98.42; IR ν_{max} (cm^{-1}): 3303 (coordinated water), 1680 (C=N), 1601 (olefinic C=C), 1363 (CH_3), 1226 (C-O), 787 (C-S (thiophene)), 579 (M-O), 468 (M-N). ^{1}H NMR (DMSO-d6 ppm): 2.07 (s, 3H, CH_3), 6.64, 6.95 (d, 1H, CH= CH), 6.86-7.7 (m, aromatic-H), 4.16 (br, 2H, H_2O).

Results and Discussion

The structure of complexes was confirmed by their physiochemical analysis such as elemental and conductivity measurement. Precise information about their structure is obtained from IR, NMR and EPR spectral measurements. The complexes formulated from the analytical data and molar conductance data supported the suggested formulae [MLH_2O] where M = Cu(II), Zn(II) and [MLH_2OCl_2] where M = Co(II), Ni(II) and L= ($C_{14}H_{13}NOS$). The complexes were highly coloured, insoluble in water as well as in common organic solvents but soluble in highly coordinating solvents such as DMSO and DMF. Synthesized compounds were non hygroscopic, highly stable under normal conditions.

Molar conductance

The molar conductance of 10^{-3} M solutions of the complexes in DMSO was carried out at room temperature. CuTBAP and ZnTBAP showed values, 84.92, 98.42 S cm^2 mol^{-1} respectively, which indicated the electrolytic nature of the above complexes. This was further confirmed by the positive silver nitrate test which lead to the formation of white precipitate. On the other hand CoTBAP and NiTBAP showed the values 4.75 and 5.12 S cm^2 mol^{-1} respectively. The obtained values were taken as good indication for the existence of a non-electrolyte nature[7] of the CoTBAP and NiTBAP complexes.

Mass spectra

Mass spectra of the ligand TBAP showed a molecular ion peak at *m/z* 243 (RI 17%), which coincide with molecular weight of TBAP corresponding to $[C_{14}H_{13}NOS]^+$ ion. The spectrum also showed fragments at *m/z* 228 (RI 100%), 109 (RI 16%), 84 (RI 11%) and 58 (RI 4%) corresponding to $[C_{13}H_{10}NOS]^+$, $[C_6H_5S]^+$ and $[C_4H_3S]^+$ respectively. This data was in good agreement with the proposed molecular formula of the ligand TBAP.

Infrared spectra

IR spectra of TBAP and its metal organic hybrids were carried out in the range of 4000-400 cm^{-1}. In TBAP appearance of an intense band at 1696 cm^{-1} was attributed to the formation of C=N (azomethine). In hybrid derivatives this band was found to be shifted. This suggested the coordination of azomethine nitrogen to metal atom in complexation[8] due to the donation of electron density from nitrogen to metal.

FT-IR of the ligand showed a broad band around 3200 cm^{-1} due to OH stretching frequency of phenolic group. Disappearance of this band in all the hybrid derivatives indicated deprotonation of the phenolic OH and involvement of the oxygen atom in bonding. Presence of coordinated water molecules in the metal organic hybrids was indicated by a band around 3502-3303 cm^{-1} and also by the bands in the range 850-873 cm^{-1} which indicated binding of water molecules to the metal ions[9]. Phenolic C-O stretching frequency[10] of TBAP was observed at 1251 cm^{-1}. Upon chelation this band was shifted to lower frequency (1223-1229) cm^{-1} which indicated the participation of the oxygen atom of phenolic group in coordination to the metal ion. This was further supported by the formation of new bands of medium intensity at 568-579 cm^{-1} assigned to (M-O) vibration[11]. The band at 766 cm^{-1} in TBAP due to υ(C-S) stretching of thiophene was shifted in the hybrid derivatives (736-787) cm^{-1}, which suggested coordination of sulphur atom with the metal ion[12]. Appearance of band in the region1606 cm^{-1} and in the region 1601-1609 cm^{-1} was attributed to C=C stretching frequency in TBAP and its complexes respectively. A band at 1366 cm^{-1} in the ligand was due (CH_3) stretching frequency. Upon complexation this band remained unaffected[13]. Further the formation of medium intensity non-ligand bands around 463-468 cm^{-1} and 418-419 cm^{-1} provided compelling evidence for the formation of (M-N) and (M-Cl) bond[11]. From the IR data it was apparent that the ligand TBAP was coordinated to the metal ions *via* azomethine-N, thiophene-S and phenolic–OH. Other coordination sites in the complexes were satisfied by chloride ions.

^1H and ^{13}C NMR spectra

^1H NMR spectra of TBAP in DMSO-d6 and its metal organic hybrids showed the following signals. Ligand (TBAP): 2.03 ppm (s, 3H, CH_3), 6.58 ppm, 6.92 ppm (d, 1H, CH=CH), 6.72-7.89 ppm (m, aromatic-H), 11.71 ppm (s, 1H, OH)[14].

Hybrid derivatives of TBAP: 2.07-2.09 ppm (s, 3H, CH_3), 6.63-6.77 ppm and 6.88-6.99 ppm (d, 1H, CH=CH), 6.74-7.71 ppm (m, aromatic-H). Involvement of phenolic hydrogen (OH) in chelation through the deprotonation of OH was indicated by the disappearance of the OH signal in the ^1H NMR spectrum of the hybrid derivatives. Signal around 4.13-4.19 ppm with integration analogous to two protons was assigned to coordinated water molecule in the hybrid derivatives[15].

^{13}C Nuclear magnetic resonance spectra of TBAP showed signal at 156.27 ppm due to carbonyl carbon, signal at 162.34 ppm due to azomethine carbon, signal at 115-140 ppm due to aromatic carbon and signal at 24.27 ppm due to CH_3 carbon, signal at 147.68 and 136.21 ppm due to CH=CH carbons.

Electronic spectra and magnetic moment measurements

UV-Vis spectra of TBAP and its hybrid derivatives (Figure 1a) were recorded at room temperature using DMSO as solvent. Electronic spectra of TBAP showed absorptions at 256 nm and 372 nm which were attributed to the intra-ligand charge transfer transitions, assigned to π-π^* and n-π^* transitions. In hybrid derivatives, the intra-ligand transitions were found to be slightly shifted in the region 241-364 nm as a result of coordination. Copper(II) derivative of TBAP displayed band in the region 574 nm due to $^2B_1g \rightarrow {}^2A_1g$ transition typical of square planar geometry[16]. Further confirmation of above geometry was done by magnetic moment value 1.92 BM. Absorption spectrum of nickel(II) complex displayed three d-d bands at 410 nm, 602 nm and 727 nm. These correspond to $^3A_2g(F) \rightarrow {}^3T_1g(P)$, $^3A_2g(F) \rightarrow {}^3T_1g(F)$, $^3A_2g(F) \rightarrow {}^3T_2g(F)$ transitions respectively, being typical of an octahedral geometry[17]. This geometry was further supported by its magnetic susceptibility value (2.97 BM), where that of usual octahedral nickel(II) complexes are 2.9-3.3 BM[18]. Cobalt(II) complex displayed d-d bands in the region 427, 614 and 741 nm, which were assigned to $^4T_1g(F) \rightarrow {}^4T_1g(P)$, $^4T_1g(F) \rightarrow {}^4A_2g(F)$, $^4T_1g(F) \rightarrow {}^4T_2g(F)$ transitions, respectively. These transitions correspond to the octahedral geometry of cobalt(II) complex[17]. This geometry of cobalt (II) complex was also supported by its magnetic susceptibility value (4.87 BM), where that of usual octahedral cobalt(II) complexes are 4.8-5.2 BM[19]. Zn(II) TBAP is diamagnetic and its geometry was most possibly similar to Cu(II) TBAP derivative. Thus tetrahedral geometry was proposed for this complex.

EPR spectra

The x-band EPR was spectra recorded in DMSO at liquid nitrogen temperature (77 K). The observed $g_{\shortparallel}$ and $g_{\perp}$ values for CuTBAP were 2.28 and 2.06 respectively. The trend of $g_{\shortparallel} > g_{\perp}$ indicated the presence of unpaired electron in the $d_{x^2-y^2}$ orbital. This is in agreement with the electronic absorption spectroscopic assignments. Square-planar geometry is thus confirmed for the complex. Furthermore[20], for covalent environment $g_{\shortparallel} < 2.3$ and for ionic environment $g_{\shortparallel} \geq 2.3$. The reported CuTBAP complex with $g_{\shortparallel} < 2.3$, confirmed the covalent character of the Cu(II) ligand bond. The G factor, defined as $G = (g_{\shortparallel} - 2.0023) / (g_{\perp} - 2.0023)$ greater than 4, suggested that the exchange interaction between the copper centres is negligible. On the basis of above observations, tentative structures for the complexes were assigned in Figure 1b,c.

Thermal analyses of copper and cobalt complexes of the Schiff base ligand TBAP

The TG curve of the CuTBAP showed three decomposition stages at 155-215 °C, 215-420 °C and 420-615 °C corresponding to the loss of coordinated water molecule, loss of phenolic part of the ligand moiety and loss of remaining part of the ligand containing thiophene part with a mass loss of 5.53% (calc. 5.56%), 38.13% (calc. 38.12%) and 35.64% (calc. 35.67%) respectively. CoTBAP showed four decomposition stages in the range 150-210 °C, 210-365 °C, 365-560 °C and 560-725 °C, with a weight loss of 4.59% (calculated 4.61%), 18.18% (calculated 18.2%), 36.66% (calculated 36.65%) and 21.25% (calculated 21.28%) corresponding to the loss of, coordinated water molecule, chlorine, phenolic part of the ligand and loss of remaining part of the ligand moiety respectively. Above 615 °C and 725 °C a horizontal curve was observed due to the formation of metal oxide (CuO and CoO respectively) as the final residue (Figure 1d).

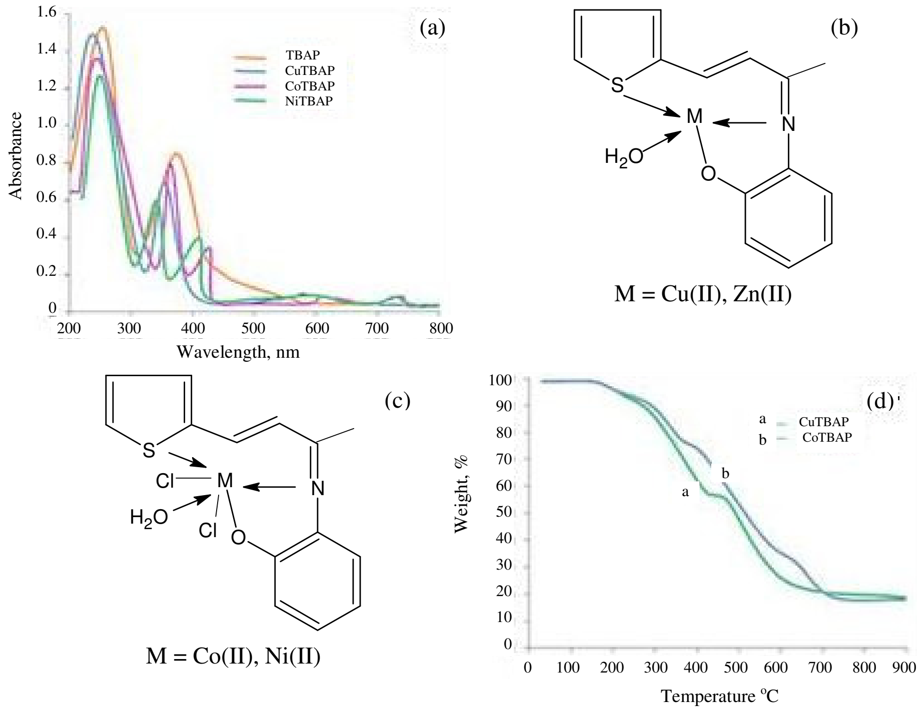


Figure 1. (a) UV of TBAP and its complexes, (b,c) Tentative structure of complexes and (d) TGA of copper and cobalt complexes of the Schiff base ligand TBAP

Chemical nuclease activity

Considerable interest is shown in the DNA cleavage reactions that are activated by transition metal complex[21]. Certain metal organic hybrids when interacted with DNA bring about the breakage of DNA strands as revealed by gel electrophoresis technique. Thus, in the case of cancer genes, after the cleavage of a DNA strand, the DNA double strands breaks. The replication ability of cancer gene is destroyed thereby. To gauge the DNA cleavage ability of TBAP and its transition metal organic hybrids by gel electrophoresis, CT DNA (30 µM) was incubated with TBAP and its hybrid derivatives (50 µM) in the presence of H_2O_2 (40 µM) as an oxidant. Cu(II) and Co(II) derivatives of TBAP afforded complete DNA cleavage, while ZnTBAP showed partial cleavage and NiTBAP did not show any cleavage. Control experiments performed using DNA+H_2O_2 and DNA+H_2O_2+TBAP on separate lanes revealed no cleavage of DNA even on longer exposure of time (Figure 2).

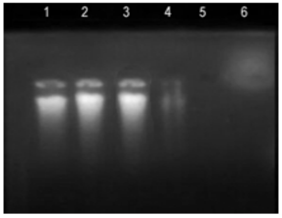


Figure 2. H_2O_2 induced CT DNA cleavage of TBAP and its complexes, Lane 1: DNA+ H_2O_2, Lane 2: DNA+ ligand+H_2O_2, Lane 3: DNA+ NiTBAP + H_2O_2, Lane 4: DNA+ ZnTBAP + H_2O_2, Lane 5: DNA+ CoTBAP + H_2O_2, Lane 6: DNA+ CuTBAP + H_2O_2

General oxidative mechanisms projected, report for DNA cleavage by hydroxyl radicals *via.* Abstraction of a hydrogen atom from sugar units and envisage the release of specific residues arising from transformed sugars, depending on the site from which the hydrogen atom is removed. The reaction is modulated by hybrid derivatives bound hydroxyl radical or a peroxo species generated from the co-reactant H_2O_2. The effectual cleavage efficiency of TBAP derivatives compared to that of the control is due to their proficient DNA binding ability.

Antimicrobial activity

In vitro antimicrobial activity (Table 1, Figure 3) against bacteria *Escherichia coli* (plate a), *Pseudomonas aeruginosa* (plate b), *Klebsiella pneumonia* (plate c), *Staphylococcus aureus* (plate d) and *Staphylococcus saprophyticus* (plate e) and fungi *Candida albicans* (plate f) was carried out with the synthesized compounds by Kirby-Bauer disc diffusion method. Mueller-Hinton agar and Sabouraud dextrose agar were used as medium for bacteria and Candida respectively. The activity was compared with standard antibacterial agent (Ciprofloxacin) and antifungal agent (Nystatin). The results tabulated in Table 1 suggest that the compounds exhibit good inhibitory effect against most of the tested microbes. From the antimicrobial activity data it was found that the zone of inhibition is much larger for metal organic hybrids than TBAP (Figure 3). A probable method of enhancing toxicity of complexes could be speculated by Overtone's concept and chelation theory.

Table 1. Antibacterial activity of TBAP and its metal complexes (mm)

Compounds	Gram (-ve) bacteria			Gram (+ve) bacteria		Fungi
	E. coli	*P. aeruginosa*	*K. pneumonia*	*S. aureus*	*S. saprophyticus*	*C. albicans*
TBAP	10.0	-	-	9.0	10.0	-
CuTBAP	23.0	19.0	21.0	23.0	20.0	15.0
CoTBAP	17.0	15.0	18.0	19.0	23.0	15.0
NiTBAP	12.0	13.0	13.0	12.0	17.0	-
ZnTBAP	16.0	16.0	17.0	15.0	15.0	-
Ciprofloxacin	25	23	23	26	24	
Nystatin						26

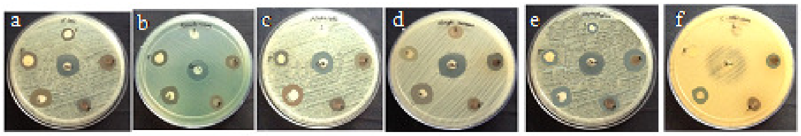


Figure 3. Antimicrobial activity of TBAP and its hybrid derivatives

CuTBAP displayed greater antimicrobial activity than other hybrid derivatives of TBAP. The difference in the enormity of antimicrobial activities of metal hybrids comes from various factors such as, nature of the counter ions that neutralize the complex, solubility, nature of metal ions, charge and geometrical structure of the complexes[22].

Conclusion

In this report, coordination chemistry of the Schiff base ligand TBAP, obtained from the reaction of 4-(thiophen-2-yl)but-3-en-2-one with 2-aminophenol, had been described. Cu(II), Ni(II), Co(II) and Zn(II) complexes of TBAP were synthesized and characterized by spectral and analytical data. Based on these data, square–planar geometry was assigned to CuTBAP, octahedral geometry for CoTBAP and NiTBAP and a tetrahedral geometry for

ZnTBAP. Metal complexes showed higher antimicrobial activity than TBAP. Interaction of the complexes with CT-DNA was investigated by gel electrophoresis in the presence of H_2O_2. Cu, Co and Zn complexes of TBAP were found to cleave DNA effectively. As these complexes were found to cleave the DNA, it can be concluded that the compounds would hamper the growth of the pathogenic organism by cleaving the genome.

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