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Synthesis, characterization, biological and catalytic applications of transition metal complexes derived from Schiff base

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ABSTRACT

A novel series of Cu(II), Ni(II), Zn(II), Co(II), and Cd(II) complexes have been synthesized from the Schiff base. Structural features were determined by analytical and spectral techniques like IR, ^{1}H NMR, UV–vis, elemental analysis, molar electric conductibility, magnetic susceptibility and thermal studies. The complexes are found to be soluble in dimethylformamide and dimethylsulfoxide. Molar conductance values in dimethylformamide indicate the non-electrolytic nature of the complexes. Binding of synthesized complexes with calf thymus DNA (CT DNA) was studied. There is significant binding of DNA in lanes 2, 3, and 5. Lanes 4 and 6 are showing more florescence when compared to the control indicating that these molecules are strongly bound to the DNA by inserting themselves between the two stacked base pairs and exhibiting their original property of fluorescence. Angiogenesis study has revealed that the compounds B-2, B-4 and B-5 have potent antitumor efficacy and activation of antiangiogenesis could be one of the possible underlying mechanisms of tumor inhibition.

A significant rising interest in the design of metal compounds as drugs and diagnostic agents is currently observed in the area of scientific inquiry appropriately termed medicinal inorganic chemistry.[1] Investigations in this area focus mostly on the speciation of metal species in biological media, based on possible interactions of these metal ions with diverse biomolecules, in an effort to contribute to future development of new therapeutics or diagnostic agents.[2–4] A wide range of metal complexes are already in clinical use,[5] and encourage further studies for new metallodrugs, such as metal-mediated antibiotics, antibacterial, antiviral, antiparasitic, radiosensitizing agents, and anticancer compounds.[6]

During recent years coordination compounds of biologically active ligands have received much attention. Chelation causes a drastic change in the biological properties of the ligands and also the metal moiety. It has been reported that chelation is the cause and cure of many diseases including cancer.[7]

Schiff base complexes play an important role in designing metal complexes related to synthetic and natural oxygen carriers. The compounds of this type can be greatly modified by introducing different substituents providing very useful model compounds for investigation of different chemical processes and its effects. It is important to emphasize the structural similarity between Schiff bases possessing different donor atoms (N, O, S, etc.) and biologically active compounds found in natural biological systems.[8] Schiff bases are potential anticancer drugs and, when administered as their metal complexes, the anticancer activity of these complexes is enhanced in comparison to the free ligand.[9]

Schiff bases of o-phenylenediamine and its complexes have a variety of applications including biological,[10] clinical[11] and analytical.[12] Earlier work has shown that some drugs showed increased activity when administered as metal chelates rather than as organic compounds,[13] and that the coordinating possibility of o-phenylenediamine has been improved by condensing with a variety of carbonyl compounds.

Schiff base and their metal complexes have been extensively investigated due to their wide range of applications as catalysts.[14] Several research groups have developed different catalytic methods for oxidation of benzyl alcohol to benzaldehyde. Among the various methods, transition metal Schiff base complex catalyzed oxidation is worth mentioning.[15] Copper(II) complexes have been found to show excellent catalytic activity toward different oxidation reactions.[16]

Angiogenesis is a feature of embryonal development and in several physiological and pathological conditions, including rheumatoid arthritis, psoriasis, tumor growth and metastasis, diabetic

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retinopathy and age-related macular degeneration.[17] It appears to depend on the balance of several stimulating and inhibiting factors,[18] Angiogenesis-dependent diseases are controlled by using chemotherapy, immunotherapy and radiation therapy to inhibit the stimulating or stimulate the inhibiting factors.[19] It is a complex process encompassing endothelial cell migration, proliferation and tube formation. These are well-regulated processes involving a number of stimulators. Inhibition of angiogenesis is considered to be one of the promising strategies in the development of novel antineoplastic therapies.[20]

DNA is an important drug target and it regulates many biochemical processes that occur in the cellular system. The different loci present in the DNA are involved in various regulatory processes such as gene expression, gene transcription, mutageneis, carcinogenesis, etc. Many small molecules exert their anticancer activities by binding with DNA, thereby altering DNA replication and inhibiting the growth of tumor cells. DNA cleavage reaction is also considered of prime importance as it proceeds by targeting various constituents of DNA viz., the nucleic bases, deoxyribose sugar moiety and phosphodiester linkage.[21] Survey of literature demonstrates that interest in the design of novel transition metal complexes capable of binding and cleaving duplex DNA with high sequence and structure selectivity[22,23] increases continuously. Additionally, the metal ion type and different functional groups of ligands, which are responsible for the geometry of complexes, also affect the affinity of metal complexes to DNA. In addition, as small molecules, a great many Schiff-base complexes with transition metals have provoked wide interests because of their diverse biological and pharmaceutical activities.[24]

In this Letter, we report the synthesis of metal(II) complexes of Schiff base tetradentate ligand (N_2O_2) formed by the condensation of o-phenylenediamine with carbonyl compounds and subjected to biological and catalytic activity.

All the reagents used in the preparation of schiff bases and their metal complexes were of reagent grade(Merck).The solvents used for the synthesis of schiff bases and metal complexes were distilled before use. All other chemicals were of AR grade and used without further purification. The elemental analysis of the compounds was performed on a Perkin Elmer 2400 Elemental Analyser. The FT-IR spectra were recorded using KBr disks on FT-IR Jasco 4100 infrared spectrophotometer. The ^{1}H NMR spectra were recorded using Bruker DRX 400 spectrometer at 400 MHz with TMS as the internal standard and DMSO-d_6 as solvent. The magnetic moments were measured out using Gouy balance. Purity of the compounds was checked by TLC.

The Schiff base was synthesized by the condensation of o-phenylenediamine and *ortho*-toluic acid (1:1 M ratio), dissolved in dichlromethane. The resulting reaction mixture was stirred for half an hour with lutidine. To the above reaction mixture TBTU (*O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyl uronium tetrafluoroborate) is added and stirred for 8 h at 0 °C. The volume of the solution was reduced to one third or till the liquid becomes syrupy and 10 mL of diethyl ether was added with constant stirring. The solid obtained was treated with an equimolar volume of benzaldehyde in ethanol and stirred over night with few drops of glacial acetic acid. The yellow solid precipitate of Schiff base obtained was filtered, washed with distilled water dried, recrystallized from ethanol (Scheme 1).

Aqueous ethanolic solution of metal chloride of Co(II), Ni(II), Cu(II), Cd(II) and Zn(II) was added to the hot ethanolic solution of the ligand in 1:2 M ratios. The mixture was then refluxed with stirring for ca. 5 h, which resulted in the precipitation of metal derivatives in all the cases. The product formed was filtered, washed and dried in vacuum desiccators.

Further the synthesized complexes were subjected for catalytic study. The catalytic activity study toward the oxidation of benzyl alcohol was carried out in a 50 mL two necked RB flask fitted with a water cooled condenser. In a typical reaction, benzyl alcohol (3.11 mL, 30 mmol) and 30% H_2O_2 (4.8 mL, 45 mmol) were mixed and the reaction mixture was heated in an oil bath with continuous stirring. An appropriate amount of catalyst (30 mmol) was added to the hot mixture and the reaction was continued. The progress of the reaction was determined by analyzing the reaction mixture by withdrawing small aliquots of the reaction mixture at specific intervals of time.

To carry out biological activities fertilized eggs were obtained from IVRI, Bangalore, India. CT DNA was purchased from Sigma. All chemicals and solvents were of reagent grade and purchased from Merck, DNA stock solution was prepared by dilution of CT DNA to buffer (containing 150 mM NaCl and 15 mM trisodium citrate at pH 7.0) followed by exhaustive stirring at 4 °C for three days, and kept at 4 °C for no longer than a week. The stock solution of CT DNA gave a ratio of UV absorbance at 260 and 280 nm (A_{260}/A_{280}) of 1.89, indicating that the DNA was sufficiently free of protein contamination. The DNA concentration was determined by the UV absorbance at 260 nm after 1:20 dilution using $\varepsilon = 6600\ M^{-1}\ cm^{-1}$.

Antiangiogenic effect of the Schiff base and their metal complex was studied according to the method of Auerbach et al.,[25] briefly, fertilized hens eggs were surface sterilized using 70% alcohol. The eggs were incubated in fan assisted humidified incubator at 37 °C. On the 4th day, the eggs were cracked out into thin films of hammock within a laminar flow cabinet and were further incubated. On the 5th day when blood vessels were seen proliferating from the center of the eggs within the hammock, filter paper disk loaded with 100 µg of the Schiff base and its metal complexes were placed over the proliferating blood vessels and the eggs were returned to the incubator. Results for antiangiogenic effect of the compound were observed after 24 h.

For the gel electrophoresis experiment, the solution of complexes in DMF (1 mg/mL) was prepared and these test samples (1 µg) were added to the CT-DNA samples and incubated for 2 h at 37 °C. Agarose gel was prepared in TAE buffer (4.84 Tris base, pH 8.0, 0.5 M EDTA/1. pH 7.3); the solidified gel attained at approximately 55 °C was placed in electrophoresis chamber flooded with TAE buffer. After that 20 µL of each of the incubated complex-DNA mixtures (mixed with bromophenol blue dye at 1:1 ratio) was loaded on the gel along with standard DNA marker and electrophoresis was carried out under TAE buffer system at 50 V for 2 h. At the end of electrophoresis, the gel was carefully stained with EtBr (Ethidium bromide) solution (10 mg/mL) for 10–15 min and visualized under UV light using a Bio-Rad Trans illuminator. The illuminated gel was photographed by using a Polaroid camera (a red filter and Polaroid film were used). Both the experiments were repeated thrice and obtained results were concordant.

All the metal(II) complexes were obtained upon reaction between metal ions and ligand at 1:2 [M:L] molar ratio. The synthesized complexes are very stable at room temperature. All the metal complexes are colored and insoluble in water and many common organic solvents but soluble in DMF and DMSO, decomposed at higher temperature. The yield, elemental analysis and molar conductance data of metal complexes are presented in Table 1. The analytical data are in a good agreement with the proposed stoichiometry of the complexes. The metal-to-ligand ratio in the metal(II) complexes was found to be 1:2 ratios. Elemental analysis is in good agreement with the proposed formula. The purity of ligand and their metal complexes has been checked by TLC.

The metal complexes discussed herein were dissolved in DMF and the molar conductivities of their 10^{-3} M solutions at room temperature were measured to establish the charge of the metal complexes. The conductance values of each metal complex are listed in Table 1, which indicates that all the metal complexes have

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Table 1
Elemental analysis of Schiff base and its metal(II) complexes and their molar conductance data

Compound	Molecular formula	Color	Yield%	Found (calcd) in %				Molar conductance (Ω^{-1} cm^2 mol^{-1})
				C	H	N	M	
L	$C_{21}H_{18}N_2O$	Pale yellow	80	80.03 (80.23)	5.72 (5.72)	8.78 (8.76)	–	–
$[Co(L)_2]Cl_2\cdot 2H_2O$ (6a)	$C_{42}H_{38}CoN_4O_4$	Light brown	65%	69.50 (69.90)	5.30 (5.31)	7.55 (7.76)	8.01 (8.17)	21.2
$[Ni(L)_2]Cl_2$ (6b)	$C_{42}H_{34}N_4NiO_2$	Dark yellow	75	73.54 (73.60)	4.93 (5.00)	8.12 (8.17)	8.52 (8.56)	15.3
$[Cu(L)_2]Cl_2$ (6c)	$C_{42}H_{34}CuN_4O_2$	brown	60	73.01 (73.08)	4.89 (4.96)	8.09 (8.12)	9.15 (9.21)	17.4
$[Zn(L)_2]Cl_2$ (6d)	$C_{42}H_{34}N_4O_2Zn$	White	70	72.82 (72.88)	4.90 (4.95)	8.03 (8.09)	9.42 (9.45)	18.9
$[Cd(L)_2]Cl_2$ (6e)	$C_{42}H_{34}CdN_4O_2$	Pale yellow	50	68.20 (68.25)	4.61 (4.64)	7.52 (7.58)	15.19 (15.21)	14.7

non-electrolytic nature due to no counter ions in the proposed structures of the Schiff base metal complexes.[26]

The formation of Schiff base ligand was studied by ^{1}H NMR spectra. In ^{1}H NMR spectra the appearance of peak at δ 2.4 indicates —CH_3 attached to the aromatic ring and disappearance of —NH_2, —CHO, —COOH and appearance of NH and N—CH peak at δ 9.7 and δ 8.7, respectively, clearly indicates the formation of Schiff base ligands and further the increase in aromatic protons evidenced the formation of Schiff base.

The functional groups of the Schiff base ligand and their metal complexes have been detected by infrared spectra. The IR spectral bands of metal(II) complexes are listed in Table 2. In the IR spectrum of o-phenylenediamine, a pair of bands corresponding to $\nu(NH_2)$ was present at ≈3210 and ≈3270 cm^{-1} but was absent in the IR spectra of all the complexes.[27] However, a single broad medium band at ≈3360–3450 cm^{-1} was observed in the spectra of all the complexes, which may be assigned to ν (NH).[28,29] A strong peak at ≈1660 cm^{-1} in the IR spectrum of benzamide was assigned to the >C=O group of the CONH moiety. This peak was shifted to a lower frequency (≈1620–1640 cm^{-1})[30,31] in the spectra of all the complexes, suggesting the coordination of the oxygen of the carbonyl group with the metal. Furthermore, no strong absorption band was observed near 1700 cm^{-1} in the IR spectra of all complexes as was observed in spectrum of benzylaldehyde. These facts confirm the condensation of carbonyl groups of benzylaldehyde and the amino groups of Benzamide moiety.[32,33] The IR spectra of the complexes showed a new strong absorption band in the region ≈1595–1610 cm^{-1}, which may be attributed due to ν(C=N).[34,35] These results provide strong evidence for the formation of the macrocyclic frame.[36] The lower value of ν(C=N) indicates coordination of the nitrogens of azomethine to the metal.[37] The bands present at ≈1300–1000 cm^{-1} were assigned to ν(C—N) vibrations. The bands presents at ≈3080 cm^{-1} may be assigned to ν(C–H) vibrations. The far IR spectra showed bands in the region ≈420–450 cm^{-1} corresponding to ν(M—N) vibrations in all the complexes.[38] The presence of these bands supports the fact concerning the coordination of the azomethine nitrogen with the metal.[39] The bands present at ≈510–540 cm^{-1} in all complexes were due to ν(M—O).[38]

The UV–visible spectra are often very useful in the evaluation of results furnished by other methods of structural investigation. The electronic spectral measurements were used for assigning the stereochemistry of metal ions in the complexes based on the positions and number of d–d transition peaks. The electronic absorption spectra of the Schiff base ligand and its Cu(II), Ni(II) Zn(II), Co(II), and Cd(II) complexes were recorded in DMF solution in the range of 200–800 nm region and data are presented in Table 3.

Table 2
Important infrared frequencies of Schiff bases and their metal complexes

Compound	ν (N—H)	ν (C=O)	ν (C=N)	ν (M—N)	ν (M—O)
L	3360	1660	1665	–	–
6a	3450	1635	1610	420	290
6b	3440	1640	1595	450	310
6c	3380	1625	1600	425	320
6d	3415	1620	1605	440	240
6e	3360	1640	1605	435	310

The electronic transitions due to the organic ligand in the metal complexes, showed the absorption bands of the $\pi\rightarrow\pi^*$ and $n\rightarrow\pi^*$ transitions results from the C=N and C=O groups and appeared at 315–278 and 409–375 nm regions, respectively. These values are lower than the corresponding absorption bands for the ligand, which were observed at 317–285 and 413–409 nm, respectively for C=N and C=O groups. This may be due to the coordination of the nitrogen and oxygen atoms of the ligand to the metal ions.

The effective magnetic moment (μ_{eff}) of copper(II) complex is 1.72 BM which is consistent with the presence of one unpaired electron.[40] The lower value of magnetic moment at room temperature is consistent with square planar geometry around the metal ions. For a square planar copper(II) complex with $d_{x}{}^{2}{}_{-y}{}^{2}$ ground state, three transitions are possible viz, $d_{x}{}^{2}{}_{-y}{}^{2} \rightarrow d_{z}{}^{2}$, $d_{x}{}^{2}{}_{-y}{}^{2} \rightarrow d_{xy}$, and $d_{x}{}^{2}{}_{-y}{}^{2} \rightarrow d_{xy}, d_{yz}$ ($^2B_{1g} \rightarrow {}^2A_{1g}$ $^2B_{1g} \rightarrow {}^2B_{2g}$ $^2B_{1g} \rightarrow {}^2E_g$) Since the four *d* orbitals lie very close together, each transition cannot be distinguished by their energy and hence it is very difficult to resolve the bands into separate components. The broad band observed at 500–550 nm in the electronic spectrum of the complex is assigned to $^2E_g \rightarrow {}^2T_{2g}$ transition.[41,42]

At room temperature these complexes show the diamagnetic behavior, indicating the square planar environment around the Ni(II) ion.[43] The electronic spectrum of Ni(II) complex shows absorption bands at 769, 600 and 425 corresponding to square planar geometry. These bands may be assigned to $^1A_{1g} \rightarrow {}^1A_{2g}$ ($d_{xy} \rightarrow d_{x}{}^{2}{}_{-y}{}^{2}$), $^1A_{1g} \rightarrow {}^1B_{2g}$ ($d_{z}{}^{2} \rightarrow d_{x}{}^{2}{}_{-y}{}^{2}$) and $^1A_{1g} \rightarrow {}^1E_{1g}$ ($d_{xy}, d_{yz} \rightarrow d_{x}{}^{2}{}_{-y}{}^{2}$) transitions, respectively.

The effective magnetic moments (μ_{eff}) of cobalt(II) complex are found in the range 4.49–4.37 BM. These values are in accordance with high spin d^7 complexes[44] which are higher than the spin only value (3.87) due to the orbital angular momentum contribution in d^7 system and close to the value required for an octahedral structure.[45] The electronic spectrum of cobalt complex displays absorption bands at 730, 590 and 360 nm corresponding to $^4T_{1g} \rightarrow {}^4A_{2g}$ (F), $^4T_{1g}$ (F) $\rightarrow$ $^4T_{1g}$ (P), and $^4T_{1g}$ (F) $\rightarrow$ $^4T_{2g}$ (F), transition, respectively for an octahedral geometry.[46]

Zn and Cd(II) ion with d^{10} electronic configuration permits a wide range of symmetries and coordination numbers. Since d^{10} configuration affords no crystal field stabilization, the stereochemistry of a particular compound depends on the size and polarizing power of the M(II) cation and the steric requirement of the ligands. Zn and Cd(II) have no d–d transition.

Mass spectrometry is an important tool widely applied to the characterization of coordination compounds.[47] The mass spectra of all the M(II) complexes have been recorded. All the spectra exhibit parent peaks due to molecular ions (M^+). The proposed molecular formula of these complexes was confirmed by comparing their molecular formula weights with *m*/*z* values. In addition to the peaks due to the molecular ions, the spectra exhibit peaks assignable to various fragments arising from the thermal cleavage of the complexes. The peak intensity gives an idea of the stability of the fragments.

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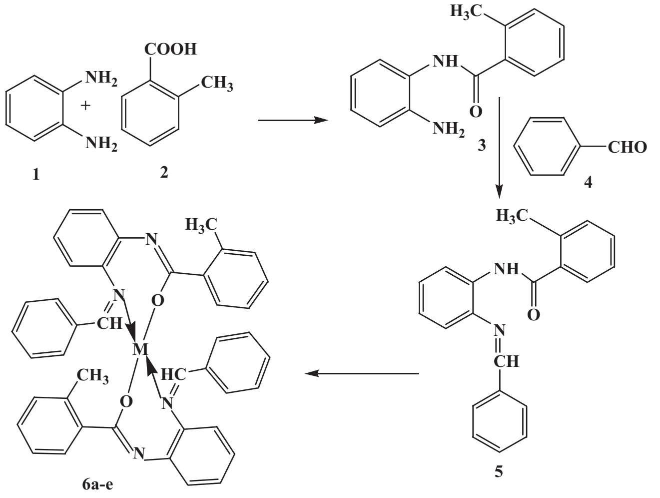
Table 3
Electronic absorption bands and magnetic values of ligand and their metal(II) complexes

Complexes	Electronic absorption bands and their assignments (nm)				Magnetic moment μ_{eff} BM
	π–π*	n–π*	Charge-transfer transition	d–d transition	
Ligand	317	410	—	—	—
6a	315	409	542	730, 590, 360 nm	4.49–4.37
6b	298	402	375	769, 600, 425	2.54
6c	284	396	430	450	1.72–2.47
6d	294	406	—	—	—
6e	295	403	—	—	—



Scheme 1.

Further the stability of complexes was studied by thermal analyses Thermogravimetric analyses of the Schiff base ligand, and their chelates are used to: (i) get information about the thermal stability of these new complexes, (ii) decide whether the water molecules (if present) are inside or outside the inner coordination sphere of the central metal ion, and (iii) suggest a general scheme for thermal decomposition of these chelates. In the present investigation, heating rates were suitably controlled at 10 °C min^{-1} under nitrogen atmosphere, and the weight loss was measured from the ambient temperature up to 800 °C. The data are provided in Table 4. The TGA and DTG curves of complexes **6a** and **6c** are presented in Figure 1. The weight loss for each chelate was calculated within the corresponding temperature ranges.

The TGA indicated that complex **6a** lose 06.10% (calcd 4.99%) of the total weight in the 98–171 °C temperature range. This weight loss corresponds to the release of lattice, as well as coordinated water molecules. When the temperature increases, complex **6a** results in a mass loss of 86.02% (calcd 86.83%) corresponding to a loss of organic moiety in the 175–395 °C temperature range, and finally results in the formation of the metal oxide above 400 °C. The thermogravimetric curves show complexes **6**(**b**–**e**) start to decompose at 300 °C and stop around 500 °C in a single or two successive steps, corresponding to the loss of two Schiff base moieties, thereby leading to the formation of metal oxides. This sequence specifies the absence of water molecules in **6**(**b**–**e**) complexes.

Schiff base transition metal complexes have been extensively studied because of their potential as catalysts in a wide range of reactions. However, not all complexes are catalytically active. The formation of octahedral complexes with no vacant coordination sites or absence of labile ligands could be a possible reason. In this study, of the five metal(II) complexes synthesized from the Schiff base ligands, four were found to have square planar geometry while one had an octahedral geometry with two coordinated water molecules. This favorable geometry could render the complexes catalytically active and hence we have made an attempt to study the efficiency of these mononuclear metal(II) complexes toward the oxidation of benzyl alcohol to benzaldehyde with H_2O_2 as an oxidant. Benzyl alcohol on oxidation gives benzaldehyde with little benzoic acid.

The catalytic activity depends on various reaction conditions like temperature, amount of catalyst, time, oxidant to substrate ratio etc. Initially we have tried only one complex with different amount of catalyst and different temperature range. The percentage of conversion was found to increase with increase in amount of catalyst and only little change with increase in temperature, so that a temperature of 343 K was considered to be optimum.

The amount of catalyst has a significant effect on the oxidation of benzyl alcohol. Four different amounts of catalyst viz., 10, 20, 30 and 40 mmol were used, keeping all the other parameters fixed: namely benzyl alcohol, H_2O_2, temperature and reaction time. The results obtained are given in Table 5 indicating conversion corresponding to the amount of catalyst used, respectively.

Tumor growth and metastasis are dependent on angiogenesis as demonstrated in many in vivo experiments.[48] Increased neovasculature may allow not only an increase in tumor growth but also enhances haematogenous tumor remobilization. Thus inhibiting tumor angiogenesis may arrest the tumor growth and decrease the metastatic potential of tumors. The current study has revealed that the compounds B-2(Zn complex), B-4(Cu complex) and B-5(Cd complex) have potent antitumor efficacy and activation of antiangiogenesis could be one of the possible underlying mechanisms of tumor inhibition. Angioprevention effect was assessed by the CAM assay which is a reliable model for angiogenesis studies.[49] A clear avascular zone around the implanted disk with compounds B-2, B-4 and B-5 indicates the inhibition of angiogenesis in CAM (Fig. 2). This angioprevention effect of the compounds B-2, B-4 and B-5 may be due to the presence of different central metal atoms like zinc, copper and cadmium, respectively.

Further this potentiality of the compounds was further reconfirmed by DNA fragmentation assay (Fig. 3). After binding to DNA, synthetic molecule can induce several changes in DNA

Table 4
Stepwise thermal degradation data obtained from TGA curves and their composition

Complex	Process	Temp. range (°C)	Degradation products	% Weight loss		No. of moles	% Residue		Nature
				Calcd	Expt		Calcd	Expt	
6a	I	98–171	H_2O	4.99	4.50	2	10.38	09.44	CoO
	II	175–375	ligand	86.83	84.45	2			
6b	I	370–480	Ligand	91.36	89.60	2	10.89	09.78	NiO
6c	I	380–490	Ligand	90.72	88.20	2	11.50	10.35	CuO
6d	I	300–410	Ligand	90.48	87.25	2	11.75	11.22	ZnO
6e	I	320–450	Ligand	84.72	83.98	2	17.37	15.35	CdO

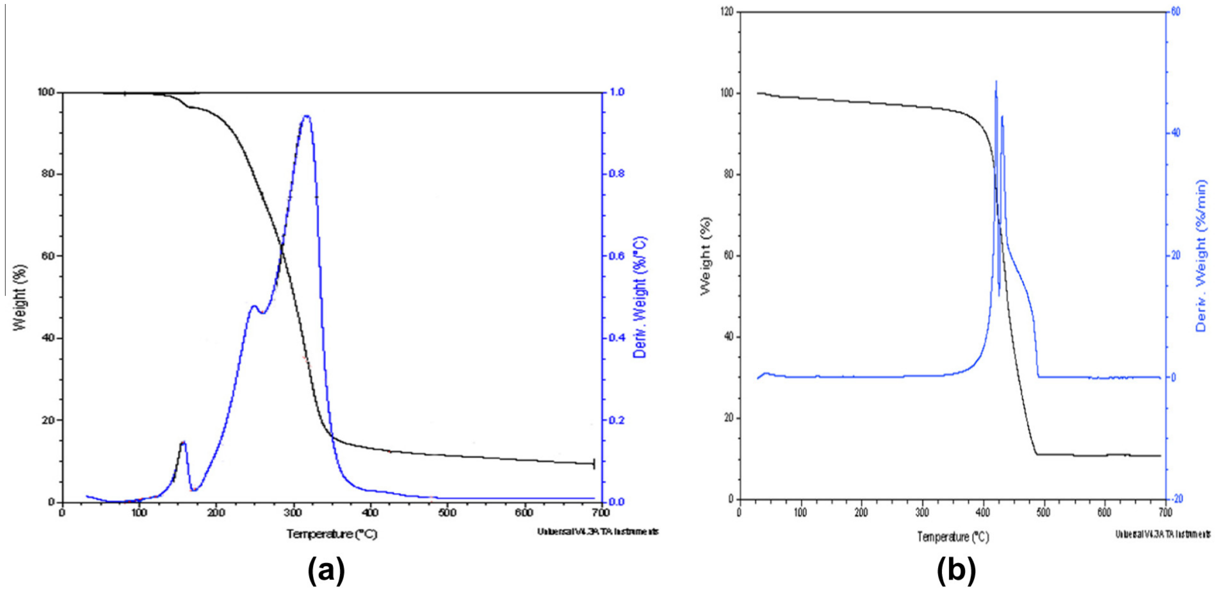


Figure 1. TG curves of metal complexes (a) **6a**, (b) **6c**.

Table 5
The influence of the amount of catalyst (Schiff base Cu complex)

Catalyst wt (mmol)	Time (h)	Temp (K)	Benzyl alcohol (mmol)	H_2O_2 (mmol)	Conversion (%)
10	3	343	30	45	17.68
20	3	343	30	45	30.55
30	3	343	30	45	39.50
40	3	343	30	45	40.30

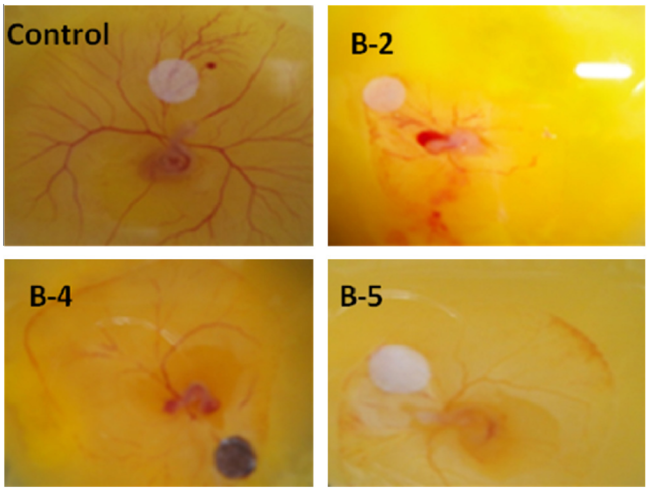


Figure 2. Suppression of angiogenesis in vivo by synthetic novel B2, B4 and B5 in shell less CAM assay. Decreased vasculature was observed in treated groups compared to control.

conformation. Synthetic molecules, which could induce DNA deformations, such as bending, 'local denaturation' (over winding and under winding), intercalation, micro loop formation and subsequent DNA shortening lead to a decrease in the molecular weight of DNA. Gel electrophoresis is an extensively used technique for the study of binding of compounds with nucleic acids: in this method segregation of the molecules will be on the basis of their relative rate of movement through a gel under the influence of an electric field. DNA is negatively charged and when it is placed in an electric field, it migrates toward the anode; the extent of migration of DNA is decided by strength of electric field, buffer, and density of agarose gel and size of the DNA. Generally it is seen that mobility of DNA is inversely proportional to its size. Gel electrophoresis picture is shown in Figure 1. The photographs show the bands with different band widths and brightnesses compared to the control. The difference observed in the band width and intensity is the criterion for the evaluation of binding/cleavage ability of synthetic molecule with calf thymus DNA. Figure 1 shows the bands with different band widths and brightnesses compared to control. There is a significant binding/cleavage of DNA in lanes 2, 3, and 5. Lanes 4 and 6 are showing more florescence when compared to the control indicating that these molecules are strongly bound to the DNA by inserting themselves between the two stacked base pairs and exhibiting their original property of fluorescence. Lanes 2, 3 and 5 (treated with synthetic molecule: B2, B3

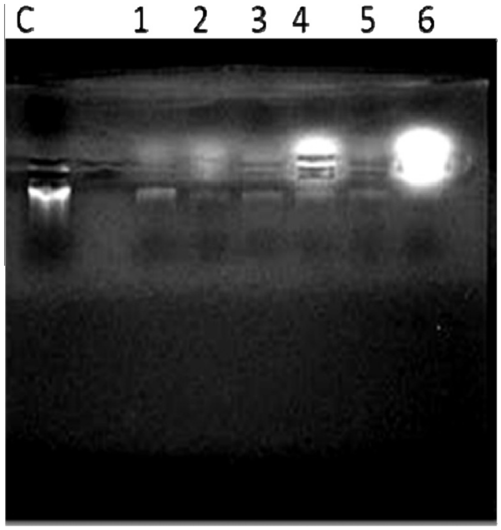


Figure 3. Photograph showing the effects of synthetic molecules on calf thymus DNA. Lane C: Untreated DNA, Lane 1: B1, Lane 2: B2, Lane 3: B3, Lane 4: B4, Lane5: B5. Lane 6: B6.

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and B5) showed less intense DNA indicating degradation when compared with lane 1(B1-Ligand) and control lane, the molecule B2 has degraded the DNA compared to other molecules indicating a better cleavage activity of all.

Conclusion

The analytical and physico-chemical techniques confirmed the geometries of the newly synthesized compounds. The coordination ability of the Schiff base has been proved in complexation reaction with metal(II) ions. Electronic and magnetic moment data support the octahedral geometry around cobalt whereas square planar geometry around copper, nickel, Zinc and cadmium metal ions. Results of antiangiogenesis activity screening indicated that the ligand has no angiogenesis effects at the tested concentrations, while compounds B-2(Zn complex), B-4(Cu complex) and B-5(Cd complex) have potent antitumor efficacy and activation of a binding of synthesized complexes with calf thymus DNA (CT DNA) was significant in lanes 2, 3, and 5. Lanes 4 and 6 are showing more florescence when compared to the control. Antiangiogenesis could be one of the possible underlying mechanisms of tumor inhibition. Synthesized complexes can be used as a good catalyst for the conversion of benzyl alcohol to benzaldehyde.

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