Synthesis, characterization, antimicrobial, DNA binding and cytotoxic studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes of quinoline-adenine Schiff bases

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ABSTRACT

New transition metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) with the Schiff bases derived from the condensation of 9H-purin-6-amine(Adenine) with 3-formyl-2-hydroxy quinoline (ADOH) and with 3-formyl-2-mercapto quinoline(ADSH) were synthesized and characterized by elemental analysis, molar conductance, magnetic susceptibilities, UV, IR, ^{1}H-NMR, ESR and thermal studies. The elemental analysis of the complexes confirms $[M(ADOH)_2(H_2O)_2]$ and $[M(ADSH)_2(H_2O)_2]$ stoichiometry for Co(II), Ni(II), Cu(II) and Zn(II) complexes respectively. Both the ligands act as monobasic and didentate, coordinating through azomethine nitrogen, phenolic oxygen via deprotonation in ADOH and with thiolate sulphur in ADSH respectively. All the complexes exhibit octahedral geometry. The synthesized ligands and the metal complexes were screened for the antibacterial, antifungal and DNA Binding studies. The cytotoxic activity was carried by brine shrimp bioassay method for all the compounds. The results reveal that the metal complexes possess higher activity than the corresponding ligands. Among the metal complexes, Cu(II) complexes are found to be more potent than the other complexes.

Key words: Quinoline, adenine, monobasic didentate, Antimicrobial, DNA binding, Cytotoxic.
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INTRODUCTION

Quinoline a heterocyclic base has proven its potential as anti-inflammatory, analgesics, anti-convulsant, antibacterial, antipyretic, antihypertensive and interferon inducing activity [1]. Dynemicin A and Steptonigrin are naturally occurring members of the class of antitumor antibiotics, whose syntheses are based on the utilization of preformed quinoline derivatives [2]. The 8-(diethylaminohexylamino)-6-methoxy-4-methyl-quinoline is highly effective against the protozoan parasite Trypanosoma cruzi, which is the agent of Chagas disease [3] and the 2-(2-methylquinoline-4-ylamino)-N-phenylacetamide is more active than the standard antileishmnanial drug sodium antimony gluconate [4]. The synthetic applications of 2-chloro-3-formyl-quinoline have been reported by Meth-cohn et.al.[5]. B. Basavaraju et.al have reported the synthesis characterization and antimicrobial studies of metal complexes derived from 2-chloroquinoline Schiff bases [6]. P. Kubat et.al have reported the lanthanide(III) complexes with quinoline derivatives and has studied the DNA binding activities [7]. D. Maffeohave reported the europium(III) complexes using 8-benzoxyquinoline in aqueous solution and have reported the intra molecular sensitisation of the complexes [8]. T. J. Egan et.al have reported Tb(III) metal complexes and effects of solvents composition and ionic strength on the interaction with quinoline based antimicrobials [9]. Q. Yang et.al have studied the binding behavior of La(III) with quinoline derivatives in the formation of ternary complexes [10]. A. J. Prussin

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have reported the photochemical methods to assay DNA photo cleavage using super coiled pUC 18DNA and LED or Xenon arc lamp excitation [11]. L .Armelao et.al have reported a design of luminescent Lanthanide complexes derived from quinoline derivatives which are used as highly efficient photo emitting materials [12]. Min Li et.al have reported the quinoline amine reactive forms of Tb(III) and Eu(III) properties and the studies of DNA attachment and energy transfer measurements [13]. A. Canfi et.al have reported the characteristics of no self quenching of the lanthanide luminousness of quinoline derivatives [14]. H. Takalo et.al have reported the spiked emission spectrum, stoke shifts and high quantum yield using lanthanide (III) complexes of quinoline derivatives [15]. S. Mathew et.al have reported the Tb(III) and Eu(III) complexes using quinoline derivatives and have designed the ratio metric optical probes [16].

The literature survey reveals that the Schiff bases derived from quinoline and adenine derivatives and their transition metal complexes have not been reported and studied so far. Hence the present study aims for the new transition metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) with the Schiff bases derived from the condensation of 9*H*-purin-6-amine(Adenine) with 3-formyl-2-hydroxy quinoline (ADOH) and with 3-formyl-2-mercapto quinoline(ADSH).

MATERIALS AND METHODS

2.1. Material and methods
All the chemicals used were of analytical grade and were used without further purification.

2.2. Synthesis of ligands (ADOH and ADSH)
2-Hydroxy-3-formyl quinoline and 2-mercapto-3-formyl quinoline were prepared by the reported procedure[17]. The Schiff base ligands were prepared by condensation of 3-formyl-2-hydroxy quinoline (0.1M) with 9H-purin-6-amine(Adenine)(0.1M) in ethanol and refluxed on water bath for 5-6 hours in presence of few drops of acetic acid. The reaction mixture was cooled to room temperature. The separated Schiff base was filtered, washed with hot alcohol and recrystallized from alcohol to get a pure sample (ADOH). Similar methods were used for the preparation of the ligand (ADSH) by the condensation of 3-formyl-2-mercapto quinoline(0.1M) with 9H-purin-6-amine(Adenine). The synthesis of ligands and the structure is given in Scheme 1.

2.3. Synthesis of Co(II), Ni(II), Cu(II) and Zn(II)complexes
A solution of 0.01 mole of metal chlorides in ethanol was mixed with ethanolic solution of 0.01 mole of ligands and refluxed for 3-4 h on water bath to get clear solution. 0.5 g of excess sodium acetate was added to the reaction mixture to adjust the pH 7-8 of the solution. The reaction mixture was further refluxed for 2 h more. The resulting mixture was decomposed by pouring into 100 mL distilled water with constant stirring. The suspended solid complex was allowed to settle and collected by filtration. Then washed with sufficient quantity of distilled water and with little hot ethanol to apparent dryness and dried in a vacuum over anhydrous calcium chloride in a desiccator (Yield, 60-78 %).

2.4. Analysis
The complexes were analyzed for their metal and chloride contents by gravimetric method [18]. The results of elemental analysis and the molar conductance values are listed in Table 1.

2.5. Physical measurements
The elemental analysis(C, H and N) were performed on a Parkin-Elmer 2400 CHN elemental Analyzer Model 1106 (Carlo Erba Strumentazione). Infrared spectra of the ligand and its metal complexes in KBr pellets were recorded in the spectral range 4000-350 cm^{-1} with Perkin Elmer Spectrum one FT-IR Spectrometer using KBr pellets. Electronic spectra of the complexes were recorded in dimethylformamide (DMF) on a VARIAN CARY 50-BIO UV-spectrometer in the region 200-1100nm. Magnetic susceptibilities were measured on a Guoy Balance at room temperature using $HgCo(NCS)_4$ as calibrate. The molar conductance of the complexes were measured on ELICO CM-82T conductivity bridge in DMF solution at conc. $\sim 10^{-3}$ M. ^{1}H NMR spectra were recorded on AMX-400 NMR spectrometer, using TMS as internal standard and DMSO as a solvent. Thermogravimetric anslysis data were measured from room temperature to 1000^0C at a heating rate of 10^0C/min. the data were obtained by using a PARKIN-ELMER DIAMOND TG/DTA instrument. The Electron pair resonance (EPR) spectra of the Cu(II) complex were recorded on Variant E-4', X-band ESR Spectrometer using cylindrical quartz sample tube at room temperature. Polycrystalline diphenylpicrylhadrazyl was used as "g" marker.

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RESULTS AND DISCUSSION

All the complexes were sparingly soluble in common organic solvents but soluble in DMF, DMSO and Acetonitrile. The analytical data indicates that the complexes are agree well with 1:2 metal to ligand stoichiometry of the type $[ML_2(H_2O)_2]$ for Co(II), Ni(II) Cu(II) and Zn(II) complexes shown in Table 1. The observed molar conductance (Table 1) values measured in DMF solution fall in the range (12-20 Ohm^{-1} cm^2 mol^{-1}). These observed values of the molar conductance are well within the expected range for non electrolytic [19]. To establish whether water molecule present in the Co(II), Ni(II), Cu(II) and Zn(II) complexes coordinated to the metal ion, weighed Co(II), Ni(II), Cu(II) and Zn(II) complexes were dried over P_4O_{10} in vacuum for 1h and weighed again. No loss in weight was observed. This was further confirmed by heating the complexes for 2 h at 105^0C and no weight loss was observed. These observations suggests that the water molecules in the Co(II), Ni(II), Cu(II) and Zn(II) complexes are coordinated to the metal ion.

3.1. Magnetic susceptibility

The magnetic susceptibility measurements of the complexes were performed at room temperature (Table 1). The magnetic moment value for Cu(II) complexes of the ligands fall in the range 1.87-1.97 B.M. The copper atom is less than the normal value[20](1.84-2.20 B.M.). The lowered magnetic moment value observed for Cu(II) complex under present study is due to distorted octahedral geometry[21,22]. On the other hand Ni(II) and Co(II) complex have shown magnetic moment value 2.97 and 4.88 B.M respectively. This indicates octahedral geometry[23] for their Ni(II) and Co(II) complexes.

3.2. Electronic spectra

The electronic spectral data of Co(II), Ni(II), Cu(II) and Zn(II) complexes were recorded in DMF as shown in Table 2-4**.** They have been studied with the view to obtain more information on stereochemistry of the complexes and to procure more support for the conclusion, deduced with the help of magnetic data. The light green colored Cu(II) complex exhibits a broad asymmetric band in the region 16528-12422 cm^{-1} (table 4)with maxima at 14470 cm^{-1} in an distorted octahedral geometry[24]. The broadness of the band may be due to dynamic Jahn-Teller distortion and is assigned to $^2T_{2g}$ - ^2E_g transitions.

The Co(II) complex (light purple) of the electronic absorption bands appears at 9992 and 20085 cm^{-1}, due to $^4T_{1g}$(F) - $^4A_{2g}(\nu_1)$ and $^4T_{1g}$(F) - $^4T_{1g}$(P)(ν_3) transition, respectively, in an octahedral environment. The bands due to the $^4T_{1g}$(F) - $^4A_{2g}$(F)(ν_2) transition could not observed because of its very low intensity. However the position of the ν_2 band has been computed (15439 cm^{-1}) by the equation. $\nu_2 = \nu_1 + 10Dq$. The intense band around 30000 cm^{-1} may be a charge transfer band. The ligand field parameter such as Dq, B', β and β % have been calculated by using band-fitting equation given by Underhill and Billing[25]. The crystal field splitting energy (Dq) value at 825 cm^{-1}. These values are well within the range reported are most of the octahedral Co(II) complexes. The Co(II) complex under present investigation process interelectronic repulsion parameter (B') 930 cm^{-1}. The Racha parameter (B) is less than free ion value (971) suggesting a considerable orbital overlap and delocalization of electrons on the metal ion. The nephelauxetic ratio (β) for the present Co(II) complex (0.95). This is less than one, suggesting partial covalency in the metal ligand bond. The values Dq, β% LFSE and ν_2/ν_1(Table **2**) suggest the octahedral geometry for Co(II) complex[26]. The electronic spectrum of Ni(II) complex shows two bands at 15151 and 25316 cm^{-1} assignable to $^3A_{2g}$ - $^3A_{1g}$(F)(ν_2) and $^3A_{2g}$ - $^3T_{1g}$(P) (ν_3) transitions respectively, in an octahedral environment[27]. The lowest band ν_2 (10 Dq) was not observed due to limited range of the instrument used. However, it is calculated by using equation suggested by Billing and Underhill. Racha parameter B^1 is less than the free ion value of 1040 cm^{-1} indicating the covalent character of the complex. The ratio ν_2/ν_1 and β% are further support the octahedral geometry around the Ni(II) ion[28].(table 3)

3.3 Infrared Spectra

The broad band observed at 3435 cm^{-1} in the IR spectra of the ligand (ADOH) assigned to ν(OH), which were found to have disappeared in all their respective complexes, thereby indicating the involvement of phenolic oxygen is bonding with metal ions through deprotonation. A strong sharp band observed at 1659 cm^{-1} is assigned to quinoline ring ν(C=O), which was shifted to 33-57 cm^{-1} in all complexes, indicates the involvement of adenine ring carboxyl in complexation with metal ion, the band at 1600 cm^{-1} is assigned to the azomethine ν(C=N) group, lowering of ν(C=N) 24-43 cm^{-1} in the complexes as compared to its ligand is due to reduction of double bond character carbon-nitrogen bond of the azomethine group. The band observed at 1273 cm^{-1}, of the ligand is attributed to phenolic ν(C–O) ,This band is shifted to higher frequency and is found in the region 1301-1316 cm^{-}1 for the complexes. Thus, this

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further confirms the involvement of phenolic OH in the complex formation. The low frequency skeletal vibrations due to M–O and M–N stretching provide direct evidence for complexation. In the present investigation, the bands in the 534-525 cm^{-1} and 445-425 cm^{-1} region for νM–O and νM–N vibration respectively. The bands due to ν(M–S) were observed in the 364-352 cm^{-1} region and are characteristic of s atom in Sulphur atom in Co(II), Ni(II), Cu(II) and Zn(II) complexes for ADSH ligand.(table 5)

3.4 ^{1}H NMR spectra
Spectrum of ^{1}H NMR in DMSO-d$_6$ solvent used. In ligand (ADOH) showed sharp peak at d 12.2 (S, 1H) due to OH at 2-position of phenyl ring of quinoline moiety has resonated, but in the case of Cu(II) complex which has been disappeared indicating the involvement of phenolic oxygen in the coordination via deprotonation. The peak appears at d 8.8 (S, 1H, –CH=N) due to the azomethine group in ligand but in case of Zn(II) complex the peak observed at 8.6 (S, 1H, –CH=N). The aromatic protons due to adenine and quinoline rings have resonated in region d 7.0-8.6 (m, 14H, Ar-H) as a multiplet in Zn(II) complex the fourteen aromatic protons have been observed in the region d 6.92-8.42 (m, 14H, Ar-H) as multiplet.(table 6)

3.5 ESR Spectrum
ESR spectrum of Cu(II) complexes of ligand ADOH scanned at room temperature using DPPH as a standard showed a broadened feature without hyperfine splitting due to the dipolar interaction from the ESR spectrum of a set of magnetic parameter g‖ 2.053 and g⊥2.0276. The observed ESR spectrum is characteristic of distorted octahedral geometry g value averaged to overall directions and G which is measure of extent of exchange interaction between metal ion have been calculated. In present case the value of G was found to be 4.028 according to Hathway. If G value is greater than 4, the spin exchange interaction is negligible where as G value less than 4 indicate considerable interaction between metal ions in solid complex clearly indicate that Cu(II) ion in the complex is mono-nuclear nature of the complex.

3.6 Antimicrobial Activity
Antimicrobial activity was carried out using the cup-plate method. The antimicrobial activity results of the screened compounds are given in the Table 7. The ligands and their Co(II), Ni(II), Cu(II) and Zn(II) complexes have been tested for their antibacterial activity, against E. coli and S. aureus and antifungal activity against *A. Niger* and *C. Albicans* at 100 μg/0.1cm^3 concentration. The standard drugs *Gentamycine* and *Flucanazole* were also tested for their antibacterial and antifungal activity at the same concentration under the conditions similar to that of the test compounds. The antibacterial activity results revealed that the ligand and its complexes shown weak to good activity. The ligand and its Co(II) and Ni(II) complexes shows weakly active with the zone of inhibition 11-19 mm against the both organisms when compared to the standard drug *Gentamycine*. The Cu(II) and Zn(II) complexes shows active and moderate activity as compared to its ligand with zone of inhibition 14-24 and 17-25 mm respectively. The antifungal activity results revealed that the ligand and its Co(II), Ni(II), Cu(II) and Zn(II) complexes have exhibited weak to good activity. The ligand and its Cu(II) and Co(II) complexes shows weak activity when compared to the standard drug *Flucanazole*. The Ni(II) and Zn(II) complexes shows active and moderate activity as compared to its ligand with the zone of inhibition 15-25 and 17-23 mm respectively.

3.7 DNA binding studies
3.7.1 Electronic absorption titration
Electronic absorption spectroscopy is one of the most powerful experimental techniques for probing metal ion–DNA interactions. Binding of the macromolecule leads to changes in the electronic absorption spectrum of the metal complex. Base binding is expected to perturb the ligand field transition of the metal complex. Intercalative mode of binding usually results in hypochromism and bathochromism due to the strong stacking interaction between an aromatic chromophore and the base pairs of DNA. The extent of hypochromism parallels the strength of intercalative binding. On the other hand, metal complexes, which bind non-intercalatively or electrostatically with DNA, may result in hyperchromism or hypochromism. The electronic absorption titration of complex [M(ADSH)$_2$(H$_2$O)$_2$], M= Co(II), Ni(II), Cu(II) and Zn(II) has been carried out at a fixed concentration of complexes (100 μM) in aqueous media at 25^{0}C, while varying the concentration of DNA (0-150 μM). The absorption spectra of the complex [M(ADSH)$_2$(H$_2$O)$_2$] in the absence and presence of DNA is depicted in the Figure 1. Addition of increasing amount of DNA results in an appreciable decrease in absorption intensity of LMCT band at 392 nm with insignificant shift in wavelength. The complex [M(ADSH)$_2$(H$_2$O)$_2$] showed hypochromism (24%) and the K$_b$ value is 2.1 x 10^4 M^{-1}. Isosbestic points are observed near 292 nm for [M(ADSH)$_2$(H$_2$O)$_2$], while binding to DNA,

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suggesting that the complex has a single mode of binding to DNA. Determinations of intrinsic binding constant, K_b, based upon these absorption titrations may be made with the following equation.

$$[DNA]/ (\varepsilon_A-\varepsilon_F) = [DNA]/ (\varepsilon_B-\varepsilon_F) + 1/K_b (\varepsilon_B-\varepsilon_F)$$

Arrow shows the absorbance change upon the increase of DNA concentration where ε_A, ε_F, and ε_B correspond to Aobsd/[complex], the extinction coefficient for the free complex and the extinction coefficient for the complex in the fully bound form, respectively. The slope and y intercept of the linear fit of [DNA]/(εA-εF) *versus* [DNA] give $1/(\varepsilon B-\varepsilon F)$ and $1/Kb(\varepsilon B-\varepsilon F)$ respectively. The intrinsic binding constant, K_b can be obtained from the ratio of slope to the intercept. The K_b values observed here are lower than those observed for typical classical intercalators (ethidium-DNA, 7.0×10^7 M^{-1} in 40 mM Tris-HCl buffer, pH 7.9, and 1.4×10^6 M^{-1} in 40 mM NaCl-25 mM Tris-HCl; proflavin with *Escherichia coli* DNA, 50% GC content, 4.1×105 M-1 in 0.1 M Tris-HCl) with a proven DNA-binding mode involving the complete insertion of the planar molecules between the base pairs. This is indicative of binding of the complex $[M(ADSH)_2(H_2O)_2]$ with DNA host with lower affinity than the classical intercalators.

Table 1. Analytical, magnetic and conductance data of the Schiff bases and their Cu (II), Ni (II), Cu (II) and Zn (II) complexes along with molar conductance and magnetic moment data.

Code	Ligand/complex	C% Calc. (Found)	H% Calc. (Found)	N% Calc. (Found)	S% Calc. (Found)	M% Calc. (Found)	Molar condt. Ohm^{-1} cm^{-2} mole^{-1}	μ_{eff} (BM)
L$_1$	ADOH	62.06 (63.10)	3.47 (3.12)	28.95 (27.58)	-	-	-	-
1	[Co(ADOH)$_2$(H$_2$O)$_2$]	53.50 (53.12)	3.29 (2.87)	24.96 (23.43)	-	8.75 (8.56)	8.31 (8.23)	4.80 (4.12)
2	[Ni(ADOH)$_2$(H$_2$O)$_2$]	53.52 (53.38)	3.29 (3.07)	24.96 (23.45)	-	8.72 (8.53)	6.08 (6.32)	3.20 (3.29)
3	[Cu(ADOH)$_2$(H$_2$O)$_2$]	53.14 (53.20)	3.27 (3.29)	24.79 (24.20)	-	9.37 (9.20)	8.12 (8.30)	1.77 (1.50)
4	[Zn(ADOH)$_2$(H$_2$O)$_2$]	52.99 (53.20)	3.26 (3.20)	24.72 (24.50)	-	9.62 (9.44)	7.17 (7.30)	Dia
L$_2$	ADSH	58.81 (59.30)	3.29 (2.93)	27.43 (27.30)	10.47 (10.38)	-	-	-
5	[Co(ADSH)$_2$.2H$_2$O]	51.06 (50.85)	3.14 (2.97)	23.82 (23.34)	9.09 (9.34)	8.35 (8.30)	7.42 (7.24)	5.02 (4.89)
6	[Ni(ADSH)$_2$.2H$_2$O]	51.08 (51.78)	3.14 (2.98)	23.83 (24.08)	9.09 (8.78)	8.32 (8.30)	6.33 (5.78)	3.28 (3.37)
7	[Cu(ADSH)$_2$.2H$_2$O]	50.73 (50.28)	3.12 (3.35)	23.66 (22.46)	9.03 (8.94)	8.95 (7.79)	7.31 (7.30)	1.79 (1.56)
8	[Zn(ADSH)$_2$.2H$_2$O]	50.60 (50.12)	3.11 (3.14)	23.60 (23.28)	9.01 (9.28)	9.19 (9.38)	7.92 (7.49)	Dia

Table 2. Electronic spectral data of octahedral Co(II) complexes (in DMF solution)

Code	Complex	ν_1	ν_2	ν_3	Dq	B'	B	ν_2/ν_1	LFSE Kcal/mol
1	[Co(ADOH)$_2$(H$_2$O)$_2$]	10152	16260	20618	869	945	0.973	1.601	14.89
5	[Co(ADSH)$_2$(H$_2$O)$_2$]	10146	16250	20605	868	944	0.972	1.602	14.88

Free ion value for Co(II) = 971cm^{-1}; LFSE = 12Dq

Table 3. Electronic spectral data of Ni(II) complexes in DMF solution.

Code	Complex	ν_1	ν_2	ν_3	Dq	B'	B	ν_2/ν_1	LFSE Kcal/mol
2	[Ni(ADOH)$_2$(H$_2$O)$_2$]	11049	15302	26115	933	895	0.860	1.385	31.98
6	[Ni(ADSH)$_2$(H$_2$O)$_2$]	10256	15455	24691	866	830	0.798	1.506	29.68

Free ion value for Ni(II)=104cm^{-1}; LFSE=12Dq; 350 cm^{-1} Kcal

3.8 Cytotoxicity Bioassay (in vitro):
The Schiff base and complexes were screened for their cytotoxicity (brine shrimp bioassay) using protocol of Meyer et al (Table-8). Brine shrimp (Artemia salina leach) eggs were hatched in a shallow rectangular plastic dish (22x32 cm) filled with artificial seawater, which was prepared with a commercial salt mixture and doubly-distilled water. An unequal partition was made in the plastic dish with the help of a perforated device. Approximately 50 mg of eggs were sprinkled into the large compartment, which was darkened while the minor compartment was open to ordinary

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light. After two days, nauplii were collected by a pipette from the lighted side. A sample of the test compound was prepared by dissolving 20 mg of each compound in 2 ml of DMSO. From this stock solutions 100, 50 and 10 μg ml^{-1} were transferred to 9 vials (three for each dilution were used for each test sample and LD$_{50}$ is the mean of three values) and one vial was kept as control having 2 ml of DMSO only. The solvent was allowed to evaporate overnight. After two days, when shrimp larvae were ready, 1mL of seawater and 10 shrimps were added to each vial (30 shrimps/dilution) and the volume was adjusted with seawater to 5 ml per vial. After 24 h the number of survivors was counted. Data were analyzed by a Finney computer program to determine the LD$_{50}$ values.

Table 4. Electronic spectral data of Cu(II) complexes in DMF solution

Complex Code	Complex	λ_{max} nm	λ_{max} cm^{-1}	Assignment
3	[Cu(ADOH)$_2$(H$_2$O)$_2$]	584	17123	$^2T_{2g} \leftarrow {}^2E_g$ Ligand
		342	29240	
		297	33670	
		258	38760	
7	[Cu(ADSH)$_2$(H$_2$O)$_2$]	658	15198	$^2T_{2g} \leftarrow {}^2E_g$ Ligand
		385	25974	
		332	30121	
		264	37879	

Table 5. Infrared spectral data of Schiff bases and their metal complexes in cm^{-1}

Code	Ligand/complex	υ_{OH}/H$_2$O	υ_{SH}	$\upsilon_{C=O}$ Lactone	$\upsilon_{C=O}$ amide	υ_{NH}	$\upsilon_{C=N}$	υ_{M-N}	υ_{M-O}	υ_{M-S}
L$_1$	ADOH	3260b	-	1718	1680	3160	1614	-	-	-
1	[Co(ADOH)$_2$(H$_2$O)$_2$]	-	-	1721	1676	3145	1610	508	450	-
2	[Ni(ADOH)$_2$(H$_2$O)$_2$]	-	-	1709	1645	3137	1609	485	467	-
3	[Cu(ADOH)$_2$(H$_2$O)$_2$]	-	-	1710	1654	3159	1608	510	468	-
4	[Zn(ADOH)$_2$(H$_2$O)$_2$]	-	-	1712	1651	3160	1611	495	450	-
L$_2$	ADSH	-	2634	1708	1635	3144	1617	-	-	-
5	[Co(ADSH)$_2$(H$_2$O)$_2$]	-	-	1702	1645	3148	1588	488	456	434
6	[Ni(ADSH)$_2$(H$_2$O)$_2$]	-	-	1711	1638	3154	1576	511	466	428
7	[Cu(ADSH)$_2$(H$_2$O)$_2$]	-	-	1705	1639	3160	1601	479	464	422
8	[Zn(ADSH)$_2$(H$_2$O)$_2$]	-	-	1709	1648	3164	1589	486	458	433

Table-6. The important ^{1}HNMR data of Schiff bases and Zn(II) complexes

Code	Empirical formula	OH	SH	H-C=N-	O=C-N-H	C-H (Ph)
L$_1$	ADOH	12.5	-	8.9	10.5	6.2
L$_2$	ADSH	-	10.92	8.7	10.4	6.1
4	[Zn(ADOH)$_2$(H$_2$O)$_2$]	-	-	8.2	10.0	6.6
8	[Zn(ADSH)$_2$(H$_2$O)$_2$]	-	-	8.4	10.1	6.7

Figure 1: UV absorption spectra of copper(II) complex in the absence and presence of DNA

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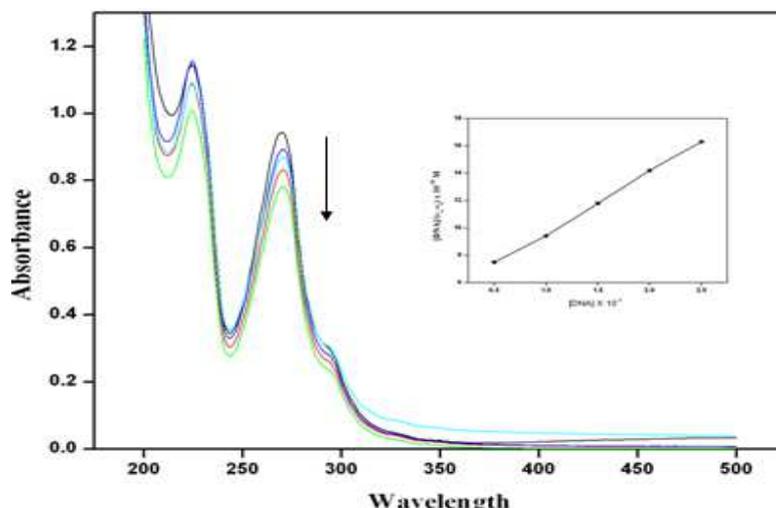
Table 7. Antibacterial and antifungal activity of Quinoline derivatives and their metal complexes (zone of inhibition in mm)

Code	Compound	Conc. mg/L	Antifungal		Antibacterial	
			A.niger	*C. Albicans*	*E.coli*	*S. aureus*
L_1	ADOH	100	17	16	19	18
		50	08	09	12	11
		25	03	02	07	06
1	$[Co(ADOH)_2(H_2O)_2]$	100	20	19	22	23
		50	12	11	16	15
		25	05	04	09	10
2	$[Ni(ADOH)_2(H_2O)_2]$	100	19	18	22	21
		50	08	09	15	14
		25	--	01	08	07
3	$[Cu(ADOH)_2(H_2O)_2]$	100	21	22	26	25
		50	11	12	18	19
		25	05	06	11	12
4	$[Zn(ADOH)_2(H_2O)_2]$	100	18	17	20	19
		50	08	09	15	14
		25	--	01	08	07
L_2	ADSH	100	18	17	20	21
		50	10	09	13	15
		25	03	04	07	08
5	$[Co(ADSH)_2(H_2O)_2]$	100	21	20	24	25
		50	14	12	15	17
		25	07	06	09	10
6	$[Ni(ADSH)_2(H_2O)_2]$	100	19	18	22	21
		50	08	09	15	14
		25	--	01	08	07
7	$[Cu(ADSH)_2(H_2O)_2]$	100	23	24	27	28
		50	14	13	19	20
		25	07	08	10	11
8	$[Zn(ADSH)_2(H_2O)_2]$	100	20	18	22	23
		50	11	08	14	15
		25	02	02	08	09
	Gentamycine	100	--	--	28	28
		50	--	--	21	21
		25	--	--	13	13
	Flucanazole	100	22	22	--	--
		50	14	14	--	--
		25	07	07	--	--

Less than 10mm----------Inactive
Less than 10-15mm------Weakly active
Less than 15-20mm------Moderately active
More than 20mm---------Highly active

Table 8. Brine shrimp bioassay data of the some active compounds

Compound Code	LD_{50} (M/ml)
ADSH	4.819×10^{-3}
$[Co(ADSH)_2(H_2O)_2]$	4.034×10^{-4}
$[Ni(ADSH)_2(H_2O)_2]$	4.218×10^{-3}
$[Cu(ADSH)_2(H_2O)_2]$	3.657×10^{-3}
$[Zn(ADSH)_2(H_2O)_2]$	4.722×10^{-3}

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Scheme-1: synthesis of Ligands and metal complexes

Novel transition metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) with the Schiff bases derived from the condensation of 9*H*-purin-6-amine(Adenine) with 3-formyl-2-hydroxy quinoline (ADOH) and with 3-formyl-2-mercapto quinoline(ADSH) were synthesized and characterized by elemental analysis, molar conductance, magnetic susceptibilities, UV, IR, ^{1}H-NMR, ESR and thermal studies. The elemental analysis of the complexes confirms $[M(ADOH)_2(H_2O)_2]$ and $[M(ADSH)_2(H_2O)_2]$ stoichiometry for Co(II), Ni(II), Cu(II) and Zn(II) complexes respectively. Both the ligands act as monobasic and didentate, coordinating through azomethine nitrogen, phenolic oxygen via deprotonation in ADOH and with thiolate sulphur in ADSH respectively. All the complexes exhibit octahedral geometry. The synthesized ligands and the metal complexes were screened for the antibacterial,

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antifungal and DNA Binding studies. The cytotoxic activity was carried by brine shrimp bioassay method for all the compounds. The results reveal that the metal complexes possess higher activity than the corresponding ligands. Among the metal complexes, Cu(II) complexes are found to be more potent than the other complexes.

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