Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2012, 4(1):851-865

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis, Characterization and Antimicrobial studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes derived from a Schiff base of 2-[(4-Methyl-2-oxo-*2H*-chromen-7-yl)oxy]acetohydrazide with 3-formyl-2-hydroxy quinoline and 3-formyl-2-mercapto quinoline

Pulin Nath* and Sreedhar D. Dhumwad

Department of Chemistry, Karnatak University's Karnatak Science College, Dharwad, Karnataka, India

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ABSTRACT

Co(II), Ni(II), Cu(II) and Zn(II) complexes of Schiff bases of N'-[(E)-(2-hydroxyquinolin-3-yl)methylidene]-2-[(4-methyl-2-oxo-2H-chromen-7-yl)oxy] acetohydrazide(OHQZ) and 2-[(4-methyl-2-oxo-2H-chromen-7-yl)oxy]-N'-[(E)-(2-sulfanylquinolin-3-yl)methylidene] acetohydrazide(SHQZ) have been prepared. The titled Schiff-bases act as tridentate ligands coordinating through NOO and NSO donor sites via deprotonation during complexation. All the metal complexes are found to have the general formula ML_2. The complexes have been characterized by elemental analysis, molar conductance, magnetic studies, IR, ^{1}H NMR, UV-visible, ESR and thermal studies. From the above studies it is found that the complexes possess octahedral geometry. The Schiff-bases and their metal complexes have been screened for their antibacterial, antifungal and DNA cleavage studies. 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 in antibacterial, antifungal and DNA cleavage studies.

Keywords: Quinoline, monobasic tridentate, Fluorescence, Antibacterial, DNA cleavage.

INTRODUCTION

Coumarins are well-known natural products displaying a broad range of biological activities[1]. Owing to their diverse bioactivities *viz*. anticoagulant[2,3] antibacterial, antifungal[4], antibiotic[5], spasmolytic[6], anthelmintic[7], diuretic[8], anti-inflammatony[9], antitubercular agents[10], anti-histamic agents[11], antidepressant[12] and antimalerial[13]. Chelating ability of coumarin derivatives have been studied to suggest their use as a chelating agents[14,15]. Regarding their high fluorescence ability, they are widely used as fluorescent probes in biology and medicine[16,17]. More recently, coumarin derivatives have been evaluated in the treatment of human immunodeficiency virus, due to their ability to inhibit human immunodeficiency virus integrase[18,19]. The in vitro effects of coumarins on the growth of renal cell carcinoma that derived cell lines showed that coumarin and 7-hydroxycoumarin were potent cytotoxic and cytostatic agents. Interest in metal coumarin complexes has arisen from the search for novel lead compounds along with the desire to improve the pharmacological profile. For example, some interesting lanthanide complexes of coumarin derivatives like bis(4-hydroxy-3-coumarinyl) acetic acid,[20] the ligand 8,8_-[1,2-ethanediylbis(nitriloethylidyne)]bis[7-hydroxy- 4-methyl-2*H*-1-benzopyran-2-one] and coumarin-3-carboxylic acid have been reported.[21-23]. *Ajaykumar K., Sangamesh A. Patil* has synthesized La(III), Th(IV) and VO(IV) complexes of Schiff bases derived from 8-formyl-7-hydroxy-4-methylcoumarin and studied their antibacterial, antifungal and DNA cleavage properties[24]. *Sangamesh A. Patil et. al. synthesised*

Co(II), Ni(II) and Cu(II) Complexes with 4-Chloro-3- Coumarinaldehyde Schiff Bases and studied their in-vitro Antibacterial and Antifungal properties. They found that the Schiff base , Co(II) and Ni(II) complexes cleave DNA as compared to control DNA *S. aureus* and *A. niger*[25]. *Jagannadha et al.* have been synthesized and studied the synergistic behavior of the Schiff bases of 8- formyl-7- hydroxy-4-methyl-2H-1-benzopyran-2-one with aniline and p-methyl aniline and their interaction with Co(II), Ni(II), Cu(II) and Zn(II) have been also studied pH-metrically[26].

Quinoline derivatives have proven to be the potential anti-inflammatory, analgesics, anti-convulsant, antibacterial, antipyretic, antihypertensive and interferon inducing agents [27]. *Meth-cohn et. al.* have reported the synthetic applications of 2-chloro-3-formyl- quinoline[28]. Many Schiff bases derived from 2-chloro-3-formyl have been reported for their antifungal activities and as potential biodynamic agents[29]. The Schiff bases derived from 3-formyl-2-mercaptoquinoline have also proven to be important pharmaceutical agents[30]. X. Zhao et. al., have reported Cu(II) and Co(II) complexes using 8-hydroxy quinoline. It has also been reported that these complexes are stronger chelating reagents than dioxtetramine macrocycles[31]. *R. C. Maurya et. al.* have reported the synthesis of dinitrisylmolybdenum(0) complexes with 8-hydroxy quinoline sulphonamades and their biological activities[32]. *S. Mandal et. al.* have reported the metal-ion dependent oxidative DNA cleavage by transition metal complexes using quinoline derivatives, few complexes were reported to posses potent antitumor activities[33]. *Y. Shao et. al* have reported nuclease activity of Cu(II) complexes amino quinoline derivatives. These complexes have been reported to enhance the DNA cleavage[34]. *Mahammedshafi A. Paniband and Shreedhar D. Dhumwad* synthesized Co(II), Ni(II), Cu(II) and Zn(II) complexes of Schiff bases derived from 3-formyl-2mercapto quinoline and found that Cu(II) complexes have more potent antibacterial properties[35]. Narayanachar et. al. has reported the synthesis and antimicrobial studies of some transition metal complexes of 2-Marcapto quinoline[36]. *Jitendra H. et. al*. has studied the X-ray diffraction of Cu (II), Co (II), Fe (II) complexes with (RS)-4-(7-chloro-4-quinolyl amino) pentyldiethylamine diphosphate[37]. *M. K. Shivananda et. al.* studied the biological activity some 2-(2-furyl)-4-(3-aryloxymethyl-1,2,4-triazolo[3,4- b]-1,3,4-thiadiazol-6-yl)quinoline derivatives[38].

However the literature survey reveals that the Schiff bases containing 2-[(4-methyl-2-oxo-2*H*-chromen-7-yl)oxy]acetohydrazide and 3-formyl quinoline derivatives with their transition metal complexes have not been reported and studied so far. Hence the present study aims for the Synthesis, Characterization and Antimicrobial studies of Co(II), Ni (II), Cu (II) and Zn (II) complexes with novel Schiff bases derived from 2-[(4-Methyl-2-oxo-*2H*-chromen-7-yl)oxy]acetohydrazide with 3-formyl-2-hydroxy quinoline and 3-formyl-2-mercapto quinoline.

EXPERIMENTAL SECTION

2.1. *Physical measurements*

Elemental analysis (C, H and N) were performed on a Parkin-Elmer 2400 CHN elemental Analyzer Model 1106, Carloerba Strumentazione. The IR spectra of the ligands and their Cu (II), Ni (II), Cu (II) and Zn (II) complexes were recorded on a HITACHI-270 IR Spectrophotometer in the 4000-250 cm^{-1} region in KBr discs. Molar conductivity measurements were recorded on an ELICO-CM-82 T conductivity bridge with a cell having caell constant 0.51. The electronic spectra of the complexes were recorded in DMF on a VARIAN CARY 50-BIO UV-spectrophotometer in the region of 200-1100nm. The ^{1}H-NMR spectra of ligands were recorded in $CDCl_3$ and Zn(II) complexes in DMSO-d_6 on BRUKER 300 MHz spectrometer at room temperature using TMS as an internal reference. Thermogravimetric data were measured from room temperature to 1000^0C at a heating rate of 10^0C/min using PERKIN-ELMER DIAMOND TG/DTA instrument. The ESR spectra of Cu(II) complexes were recorded at room temperature on Varian E-4 X-band spectrometer using TCNE as g marker.

2.2 Materials

All the chemicals were of reagent grade and used without further purification.

2.2.1. Synthesis of 2-[(4-methyl-2-oxo-2H-chromen-7-yl)oxy]acetohydrazide.(a)

The titled compound was synthesized by the reaction of 7-hydroxy-4-methyl coumarin with ethyl chloroacetate in dry DMF followed by the treatment with Hydrazine hydrate as described by the literature.

2.2.1 Synthesis of 2-chloro-3-formyl Quinoline.(b)

This compound was synthesized by Vilsmier reaction using acetanilide, $POCl_3$ and DMF at 80^0C as per the procedure given in the literature[39]. Yellow crystals (ethyl acetate), yield= 92.24%, m.p. = 172-173^{0}C.

2.2.3. Synthesis of 2-hydroxy-3-formyl Quinoline.(c)
2-Chloro-3-formyl Quinoline(0.1mol) was refluxed for 10h in HCl(4M) and allowed to cool to room temperature. The reaction mixture was poured into crushed ice to get yellow product[40]. Recrystallized from aqueous acetic acid. Yield=89%, m.p.= 295-297^{0}C.

2.2.4. Synthesis of 2-Marcapto-3-formyl Quinoline.(d)
A mixture of 2-Chloro-3-formyl Quinoline (5.73g, 29.98mmol) and sodium sulphide (8.4g, 9.2mmol) was refluxed for 10min on a water bath in ethanol (50ml). Conc. HCl (15ml) was added dropwise to the reaction mixture. The marcapto compound precipitates as a yellow crystalline solid which was further filtered, washed with ethanol, dried and crystallized from ethyl acetate and benzene (8:2) [41]. Yield= 84%, m.p. = 193^{0}C.

2.2.5. Synthesis of Schiff bases (OHQZ and SHQZ):
The Schiff base OHQZ was synthesized by the condensation of 2-[(4-methyl-2-oxo-2*H*-chromen-7-yl)oxy]acetohydrazide**(a)**(0.1M) and 2-hydroxy-3-formyl Quinoline(c) (0.1M) in ethanol under reflux for 6 hours at a pH of 5.5-6.0 using acetic acid. The purity was checked by TLC (Hexane: Ethyl acetate).The Schiff base SHQZ was also synthesized by the above said method using 2-[(4-methyl-2-oxo-2*H*-chromen-7-yl)oxy]acetohydrazide(a) (0.1M) and 2-mercapto-3-formyl Quinoline(d) (0.1M).

2.2.6. Synthesis of Co(II), Ni(II) Cu(II) and Zn(II)complexes:
For the Synthesis of transition metal complexes, hot ethanolic solution of the respective metal(II) chlorides(0.01mol) and the Schiff bases(OHQZ and SHQZ)(0.02mol) were refluxed for 4h on a water bath at the pH 7.0-7.7 and further filtered, washed successively with ethanol and ether and finally dried over fused $CaCl_2$ in vacuum. Yield of all the complexes lie in the range of 67-73%.

2.3 Pharmacology
2.3.1. In Vitro antibacterial and antifungal assay.
The synthesized Schiff bases and their Co(II), Ni(II), Cu(II) and Zn(II) complexes were studied for their antibacterial and antifungal activities by potato dextrose agar diffusion method and nutrient agar method. The antibacterial and antifungal activities were done at 100, 50 and 20 mgL^{-1} concentrations in DMF solvent using two bacteria (*Escherichia coli* and *Staphylococcus aureus)* and two fungi(*Aspergillus niger and Penecillium chrysogenum*) strains by minimum inhibitory concentration (MIC) method[42].These bacterial and fungi strains were incubated for 24h and 48h at 37^{0}C respectively. Standard antibacterial (*Steptomycin*) and antifungal drugs (*Nyastatin*) were used for comparison under similar conditions. Activity was determined by measuring the diameter of the zone of inhibition (mm). The results of antibacterial and antifungal activity are given in table-1.

2.3.2 DNA cleavage experiment.
2.3.2.1. Preparation of culture media
DNA cleavage experiments were carried out according to the literature [43, 44]. Nutrient broth (peptone, 10 g l^{-1}; yeast extract, 5 g l^{-1}; NaCl, 10 g l^{-1}) was used for the culturing of *E. coli*. The 50mL medium was prepared and autoclaved for 15 min at 121^{0}C under 15-lb pressure. The autoclaved medium was inoculated with the seed culture. The *E. coli* was incubated for 24 h.

2.3.2.2. Isolation of DNA
The fresh bacterial culture (1.5 mL) was centrifuged to obtain the pellet, which was then dissolved in 0.5 mL of lysis buffer (100 mM Tris pH 8.0, 50 mM EDTA, 10 % sodium dodecyl sulphate (SDS)). To this, 0.5 mL of saturated phenol was added and incubated at 55 ^{0}C for 10 min. It was then centrifuged at 10,000 rpm for 10 min, and to the supernatant, an equal volume of chloroform: isoamyl alcohol (24:1) and 1/20th volume of 3 M sodium acetate (pH 4.8) were added. Then, this solution was centrifuged at 10,000 rpm for 10 min and to the supernatant, 3 vol of chilled absolute alcohol was added. The precipitated DNA was separated by centrifugation and the pellet was dried and dissolved in a TAE buffer (10 mM Tris pH 8.0, 1 mM EDTA) and stored in cold conditions.

2.3.2.3. Agarose gel electrophoresis
Cleavage products were analyzed by the agarose gel electrophoresis method.Test samples (1 mg mL−1) were prepared in DMF. The samples (25 μg) were added to the isolated DNA of *E. coli.* The samples were incubated for 2 h at 37^{0}C. Then 20 μL of DNA sample (mixed with bromophenol blue dye at a 1:1 ratio) was loaded carefully into the electrophoresis chamber wells along with a standard DNA marker containing TAE buffer (4.84 g Tris base, pH

8.0, 0.5 MEDTA per 1 L) and finally loaded on agarose gel and a constant electricity of 50V was passed for around 30 min. The gel was removed and stained with 10.0 μg mL^{-1} ethidium bromide for 10–15 min and the bands observed under Vilberlourmate Gel documentation system and photographed to determine the extent of DNA cleavage. Then, the results were compared with that of a standard DNA marker.

RESULTS AND DISCUSSION

The synthesized complexes are colored and are insoluble in water, methanol and ethanol, totally soluble in DMF and DMSO. The elemental analyses (table-2) are consistent with the type ML_2. The conductivity measurement in DMF/DMSO at the 10-3M concentrations is too low to account for any dissociation of the complex in DMF/DMSO. Hence, the complexes may be regarded as non-electrolytes. In order to establish whether the water molecule present in the synthesized complexes coordinated to the metal ion, weighed complexes were dried over P_4O_{10} in vacuum for 1 h and weighed again. No loss in weight was observed. This was confirmed by heating the complex for 2 h at 105^0C and no weight loss was considered for the water of hydration. These observations suggest that, no water molecules in the Co(II), Ni(II), Cu(II) and Zn(II) complexes are coordinated to the metal ion.

3.1 *Infrared spectra*

The IR spectra (table-3) of the Schiff bases show characteristic bands due to ν(NH), ν(OH) and ν(SH) in the region 3145-3179cm^{-1}, 3428-3489cm^{-1} and 2362-2382cm^{-1} respectively. The strong band in the region 1635-1676, 1615-1628 and 1387-1394 cm^{-1} in the IR spectra of the Schiff bases are assigned to ν_{amide}(C=O), ν(C=N) and phenolic ν(C-O) vibrations respectively. A high intensity band at 1700- 1730cm^{-1} was assigned to ν(C=O) (Lactone carbonyl) which remains almost unaltered in the complexes indicating the non involvement in the coordination. However the band due to ν_{amide}(C=O) at 1635-1676cm^{-1} in the Schiff bases exhibited downword shift by 5-20cm^{-1} indicating that amide oxygen is coordinated to the metal ions.

In the case of Co(II), Ni(II), Cu(II) and Zn(II) complexes we observed the following changes. The bands appeared around 1615-1628cm^{-1} due to ν(C=N) in Schiff bases shifted to 1590-1603 cm^{-1}, showing the shift of the band to lower wave numbers and indicating that the azomethine group of the ligands has co-ordinated to the metal ion through nitrogen. IR spectra of ligand (OHQZ) show a broad medium intensity band in the region 3428-3489cm^{-1} due to phenolic-OH, absence of this band in complexes suggested that coordination through oxygen of phenolic-OH via deprotonation. The deprotonation of the thiol group in (SHQZ) is indicated by the absence of a band in the metal complexes at 2362-2382 cm^{-1}, which is due to ν(SH) of Schiff bases, indicating that, the Schiff bases are coordinated to the metal ion through the thiolate sulphur atom. This is further supported by the lower frequency band appeared in the region 752-762 cm^{-1} in the metal complexes due to ν (C-S). The new bands in the region of 469-478cm^{-1} 430-470cm^{-1} and 341-378 cm^{-1} in the spectra of the metal complexes are assigned to stretching frequencies of (M-N), (M-O) and (M-S) bond formation respectively. A representative IR Spectrum of $[Ni(SHQZ)]_2$ complex is shown in figure-1.

3.2 *1H-NMR spectra*

Spectrum of ^{1}H NMR in DMSO-d_6 solvent was recorded at room temperature(table-4). The ligand (OHQC) showed sharp peak at d 13.8 (S, 1H) due to OH at 2-position of phenyl ring of 2-hydroxy quinoline moiety, but in the case of Zn(II) complex which has been disappeared indicating the involvement of phenolic oxygen in the coordination via deprotonation. A singlet corresponding to one proton observed at 10.92ppm is probably due to SH group in the ligand (SHQC). Hydrogen bonding leads to deshielding and an increase in the frequency of the PMR signal of the hydrogen bonded proton. The Schiff bases exhibit the characteristic resonance at 8.7 ppm due to the azomethine proton. The sharp multiplet signals of the phenyl protons are found in the region 7.46-9.45ppm. Co(II), Ni(II) and Cu(II) complexes being paramagnetic in nature were ^{1}H-NMR inactive. The peak due to SH group in ligand L_2 appeared at 10.92 ppm in the ligand was not observed in the Zn(II) complexes. This confirmed the involvement of thiolate Sulphur in coordination with the metal via deprotonation. The downfield shift of the azomethine proton from 8.7 ppm in the ligand to 9.23ppm in the complexes indicated the participation of azomethine nitrogen in the coordination[45]. The 1HNMR spectrum of $[Zn(SHQZ)_2]$ is given in figure-2.

3.3 *Electronic spectra*

The electronic absorption spectra of the metal complexes were recorded in freshly prepared solutions in DMF at room temperature. (Figure-3). The Cobalt(II) complexes exhibited two distinct bands in the region 9920-9938 cm^{-1} and 18860-20660 cm^{-1} corresponding to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ (ν_1) and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ (ν_3) transitions respectively

which suggests an octahedral geometry around the cobalt(II) ion [46]. The ν_2 band that involves a two-electron transition is not observed in spectra because of its proximity to strong ν_3 transition. The electronic spectra of nickel(II) complexes showed d-d bands in the region 10450-10790 cm^{-1}, 16333- 16889 cm^{-1} and 26824-27620 cm^{-1} respectively. These are assigned to the $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ (ν_1), $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ (ν_2) and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ (ν_3) transitions respectively, which indicate an octahedral geometry around Ni(II) ion(table-5). The ligand field parameters are given in table-4. The value of ν_2/ν_1 is found to be around 1.53, and the μ_{eff} value is around 3.18, which is within the range of 2.8-3.5 BM, suggesting the octahedral environment. The values of the naphelauxetic parameter, β, indicate the low covalent character of the metal-ligand σ bonds [47].(table-6).

The electronic spectra of Cu(II) complexes display two prominent bands. A low-intensity broad band of around 14,392 cm^{-1} is assignable to $^2T_g \leftarrow {}^2E_g$ transition and another high intensity band at 25,548 cm-1 is due to symmetry forbidden ligand → metal charge transfer. On the basis of electronic spectra distorted octahedral geometry around Cu(II) ion is suggested[48](table-7).

3.4 *Magnetic data*

The magnetic susceptibility measurements of the complexes were performed at room temperature (Table-1). The magnetic moment value for Cu(II) complexes of the ligand OHQC and SHQC are 1.97 B.M and 1.99 B.M. respectively. The copper atom is less than the normal value(1.84-2.20 B.M.). The magnetic moment value observed for Cu(II) complexes under present study indicates octahedral geometry around Cu(II) complexes. 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 for their Ni(II) and Co(II) complexes[49].

3.5. ESR spactra

The ESR spectrum of one representative Cu(II) complex (figure-was recorded at room temperature (300 K) and at liquid nitrogen temperature(77 K) which has exhibited unresolved broad signals giving only one g value, i.e., g_{iso} (g_{iso} at 300 K is 2.066 respectively). The shape of ESR indicates that the present complexes may have distorted octahedral geometry [50].(figure-4)

3.6. Thermal studies of the metal complexes.

In the present investigation TGA and DTG studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes have been carried out in static air at a limiting temperature of 1000^0C using the heating rate of 10^0C min^{-1}. The spectrum of one representative Ni(II) complex is presented in (Table-8). The decomposition of the complexes showed that the two Coumarin and two Quinoline moieties were lost in the regions of 215-245, 310-345, 350-395 and 420-475^0C corresponding to mass losses of 23.16% (cal.23.55%), 20.84(calc. 21.06%), 21.44%(calc. 21.72%) and 23.92%(calc. 24.04%). Finally, the formation of metal oxide took place above 500^0C (figure-5).

3.7 UV-Fluorescence Spectra

The UV-Vis and fluorescence spectra of ligands and their complexes were determined in 200– 800 nm region in DMSO and DMF.(table-9)

For ligand (SHQC) and its complexes, two absorption maxima were observed in the range 250-290 and 304-424 nm due to π– π* and n– π* transitions, respectively. In fluorescence spectra emission were observed in the range 413-467 nm, the highest emission was observed for ligand 467 nm which decreases on complexation with metals in DMSO solvent.

Similarly in DMF solvent, two absorption maxima were observed in the range 250-290 and 302-422 nm due to π– π* and n– π* transitions, respectively. In fluorescence spectra emission were observed in the range 439-472 nm, the highest emission was observed for Cu-complex 472 nm (figure-6) [51, 52].

3.9 DNA cleavage studies.

The representative Schiff base SHQZ, Co(II), Ni(II), Cu(II) and Zn(II) complexes (figure-7) were studied for their DNA cleavage activity by agarose gel electrophoresis method. Lanes L_2, C_1 and C_2 represents the cleavage activity of the Schiff base SHQZ**,** Co(II) and Ni(II) complexes respectively on the isolated DNA of *E. coli* and the difference in the migration was observed compared to the control DNA of *E. coli* (Lane Ct1). The cleavage activity of Cu(II) and Zn(II) complexes on isolated DNA of *S. aureus* represented by Lanes C_3 and C_4 of respectively, the migration was observed compared to the Lane Ct2 ie., control DNA of *S. aureus.*

Table-1. Antibacterial and antifungal activity of ligands OHQC, SHQC and their Co(II), Ni(II), Cu(II) and Zn(II) complexes (zone of inhibition in mm)

code	Compound	Conc. µg/L	Antifungal		Antifungal	
			A.niger	*C. albicans*	*E. coli*	*B. cirroglagellous*
OHQZ	$C_{22}H_{17}N_3O_5$	100	17	16	19	18
		50	08	09	12	11
		25	--	--	02	03
SHQZ	$C_{22}H_{17}N_3O_4S$	100	20	19	22	23
		50	12	11	16	15
		25	05	04	09	10
1	$[Co(OHQZ)_2]$	100	19	18	22	21
		50	08	09	15	14
		25	--	01	03	07
2	$[Ni(OHQZ)_2]$	100	21	22	26	25
		50	11	12	18	19
		25	--	--	--	--
3	$[Cu(OHQZ)_2]$	100	25	24	27	26
		50	08	09	15	14
		25	07	07	08	07
4	$[Zn(OHQZ)_2]$	100	18	17	20	21
		50	10	09	13	15
		25	03	04	07	08
5	$[Co(SHQZ)_2]$	100	21	20	24	25
		50	14	12	15	17
		25	07	06	09	10
6	$[Ni(SHQZ)_2]$	100	19	18	22	21
		50	08	09	15	14
		25	--	01	08	07
7	$[Cu(SHQZ)_2]$	100	23	24	27	28
		50	14	13	19	20
		25	07	08	10	11
8	$[Zn(SHQZ)_2]$	100	20	18	22	23
		50	11	08	14	15
		25	02	02	08	09
9	Gentamycine	100	--	--	28	28
		50	--	--	21	21
		25	--	--	13	13
10	Flucanazole	100	22	22	--	--
		50	14	14	--	--
		25	07	07	--	--
11	DMF	100	11	09	12	08
		50	06	05	06	03
		25	02	--	--	02

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

Table 2. 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)
OHQZ	$C_{22}H_{17}N_3O_5$	65.50 (64.87)	4.25 (4.11)	10.42 (9.67)	-	-	-	-
1	$[Co(OHQZ)_2]$	61.19 (60.88)	3.73 (3.44)	9.73 (9.58)	-	6.82 (6.62)	8.31	4.80
2	$[Ni(OHQZ)_2]$	61.20 (60.78)	3.74 (3.11)	9.73 (10.14)	-	6.80 (6.99)	6.08	3.20
3	$[Cu(OHQZ)_2]$	60.86 (61.12)	3.71 (2.97)	9.68 (9.96)	-	7.32 (7.45)	8.12	1.77
4	$[Zn(OHQZ)_2]$	60.73 (60.23)	3.71 (4.11)	9.66 (10.21)	-	7.52 (7.32)	7.17	Dia
SHQZ	$C_{22}H_{17}N_3O_4S$	63.00 (64.17)	4.09 (3.87)	10.02 (9.63)	7.64 (7.47)	-	-	-
5	$[Co(SHQZ)_2]$	58.99 (59.16)	3.60 (3.12)	9.38 (8.79)	7.16 (6.97)	6.58 (5.98)	7.42	5.02

6	$[Ni(SHQZ)_2]$	59.01 (60.32)	3.60 (2.76)	9.38 (9.24)	7.16 (6.77)	6.55 (6.19)	6.33	3.28
7	$[Cu(SHQZ)_2]$	58.69 (59.22)	3.58 (2.65)	9.33 (8.79)	7.12 (6.84)	7.06 (7.91)	7.31	1.79
8	$[Zn(SHQZ)_2]$	58.57 (59.11)	3.57 (3.14)	9.31 (8.66)	7.11 (6.88)	7.25 (8.42)	7.92	Dia

Table-3. Infrared spectral data of Schiff bases and their metal complexes in cm^{-1}

Code	Ligand/complex	υ_{OH}	υ_{SH}	$\upsilon_{C=O}$ Lactone	$\upsilon_{C=O}$ amide	υ_{NH}	$\upsilon_{C=N}$	υ_{M-N}	υ_{M-O}	υ_{M-S}
OHQZ	$C_{22}H_{17}N_3O_5$	3360b	-	1728	1684	3160	1614	-	-	-
1	$[Co(OHQZ)_2]$	-	-	1722	1650	3145	1610	508	450	-
2	$[Ni(OHQZ)_2]$	-	-	1708	1645	3137	1609	485	467	-
3	$[Cu(OHQZ)_2]$	-	-	1713	1654	3159	1608	510	468	-
4	$[Zn(OHQZ)_2]$	-	-	1712	1651	3160	1611	495	450	-
SHQZ	$C_{22}H_{17}N_3O_4S$	-	2410	1718	1675	3144	1617	-	-	-
5	$[Co(SHQZ)_2]$	-	-	1709	1645	3148	1588	488	456	434
6	$[Ni(SHQZ)_2]$	-	-	1711	1638	3154	1576	511	466	428
7	$[Cu(SHQZ)_2]$	-	-	1715	1639	3160	1601	479	464	422
8	$[Zn(SHQZ)_2]$	-	-	1719	1648	3164	1589	486	458	433

Table-4. 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	OHQZ	12.5	-	8.9	10.5	6.2
L_2	SHQZ	-	10.92	8.7	10.4	6.1
4	$[Zn(OHQZ)_2]$	-	-	8.2	10.0	6.6
8	$[Zn(SHQZ)_2]$		-	8.4	10.1	6.7

Table 5. 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	$[Co(OHQZ)_2]$	10152	16260	20618	869	945	0.973	1.601	14.89
5	$[Co(SHQZ)_2]$	10146	16250	20605	868	944	0.972	1.602	14.88

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

Table 6. 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	$[Ni(OHQZ)_2]$	11049	15302	26115	933	895	0.860	1.385	31.98
6	$[Ni(SHQZ)_2]$	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

Table 7. Electronic spectral data of Cu(II) complexes in DMF solution.

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

This shows that, the control DNA alone does not show any apparent cleavage where as Schiff base SHQZ**,** Co(II), Ni(II) and Cu(II) complexes have showed. However, the nature of reactive intermediates involved in the DNA cleavage by the complexes has not been clear. The results indicated that, the important role of metal ions in these isolated DNA cleavage reactions. From these results we infer that, the Schiff base SHQZ, Co(II), Ni(II) and Cu(II)

complexes act as a potent nuclease agent. As the compound was observed to cleave the DNA, it can be concluded that, the compound inhibits the growth of the pathogenic organism by cleaving the genome.

Table 8. Thermal data of complexes

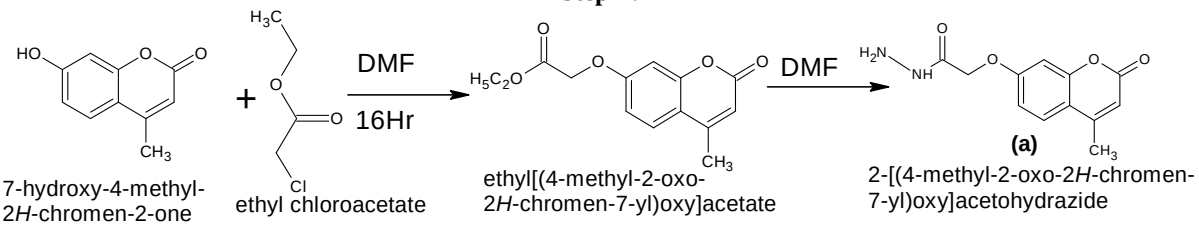
Complex code	Complex	Temp (°C)	% weight loss	Proposed chemical change	Metal %
1	$[Co(OHQZ)_2]$	236	25.72 (25.94)	Coumarin moiety	9.21 (9.46)
		392	61.41 (61.64)	Quinoline Moiety	
2	$[Ni(OHQZ)_2]$	239	32.41 (32.63)	Coumarin moiety	8.79 (9.03)
		387	58.19 (58.37)	Quinoline Moiety	
3	$[Cu(OHQZ)_2]$	232	34.46 (33.63)	Coumarin moiety	8.79 (9.03)
		378	57.19 (58.32)	Quinoline Moiety	
4	$[Zn(OHQZ)_2]$	238	32.41 (32.63)	Coumarin moiety	9.29 (10.03)
		377	58.17 (57.37)	Quinoline Moiety	
5	$[Co(SHQZ)_2]$	239	31.49 (32.73)	Coumarin moiety	8.79 (9.13)
		357	59.17 (57.37)	Quinoline Moiety	
6	$[Ni(SHQZ)_2]$	229	32.41 (32.63)	Coumarin moiety	8.97 (10.03)
		377	58.19 (58.37)	Quinoline Moiety	
7	$[Cu(SHQZ)_2]$	235	35.46 (34.63)	Coumarin moiety	9.89 (10.73)
		383	58.49 (57.97)	Quinoline Moiety	
8	$[Zn(SHQZ)_2]$	239	39.79 (40.63)	Coumarin moiety	9.99 (10.77)
		374	60.19 (58.22)	Quinoline Moiety	

Table 9. Emission spectral data of Schiff base (OHQZ) and its Ni(II), Cu(II) and Zn(II) complexes in DMSO.

Solvents	Compound code	(EX) nm	(EM) nm
DMF	OHQC	370	516
	$[Ni(OHQZ)_2]$	370	508
	$[Cu(OHQZ)_2]$	370	513
	$[Zn(OHQZ)_2]$	370	519
DMSO	SHQZ	362	510
	$[Ni(SHQZ)_2]$	362	502
	$[Cu(SHQZ)_2]$	362	507
	$[Zn(SHQZ)_2]$	362	514

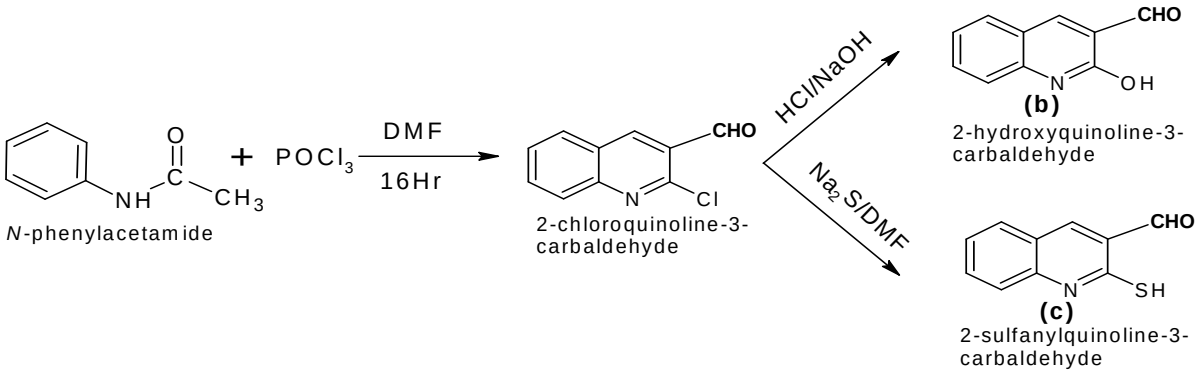
Scheme

Step-1:



7-hydroxy-4-methyl-2*H*-chromen-2-one + ethyl chloroacetate → ethyl[(4-methyl-2-oxo-2*H*-chromen-7-yl)oxy]acetate → 2-[(4-methyl-2-oxo-2*H*-chromen-7-yl)oxy]acetohydrazide

Step-2:



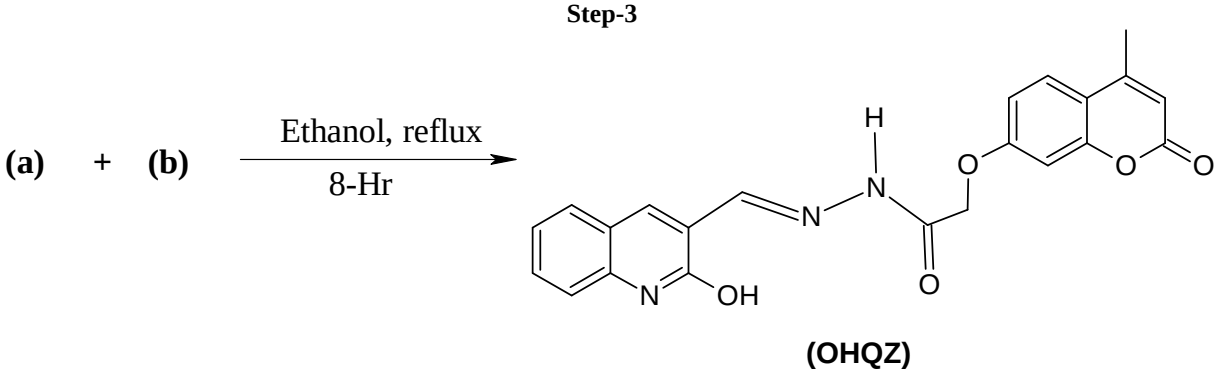
N-phenylacetamide

2-chloroquinoline-3-carbaldehyde

2-hydroxyquinoline-3-carbaldehyde

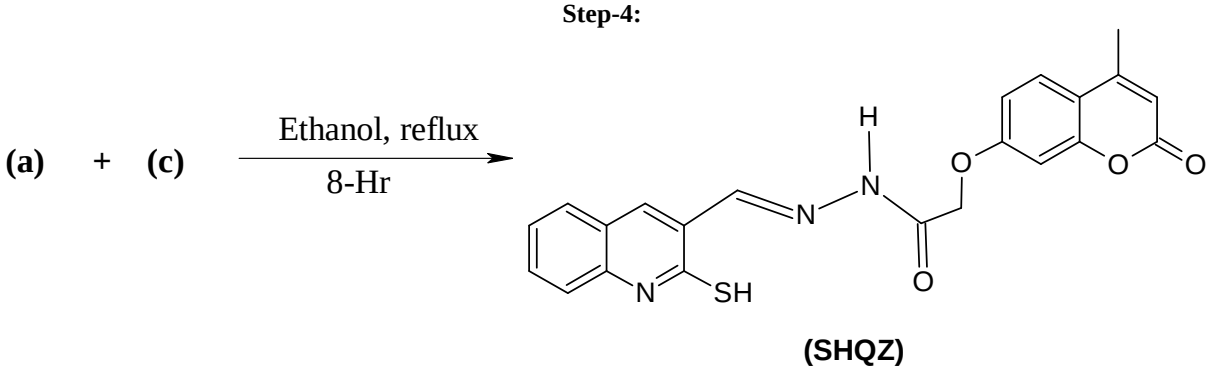
2-sulfanylquinoline-3-carbaldehyde

Step-3



(OHQZ)

Step-4:



(SHQZ)

Step-5:

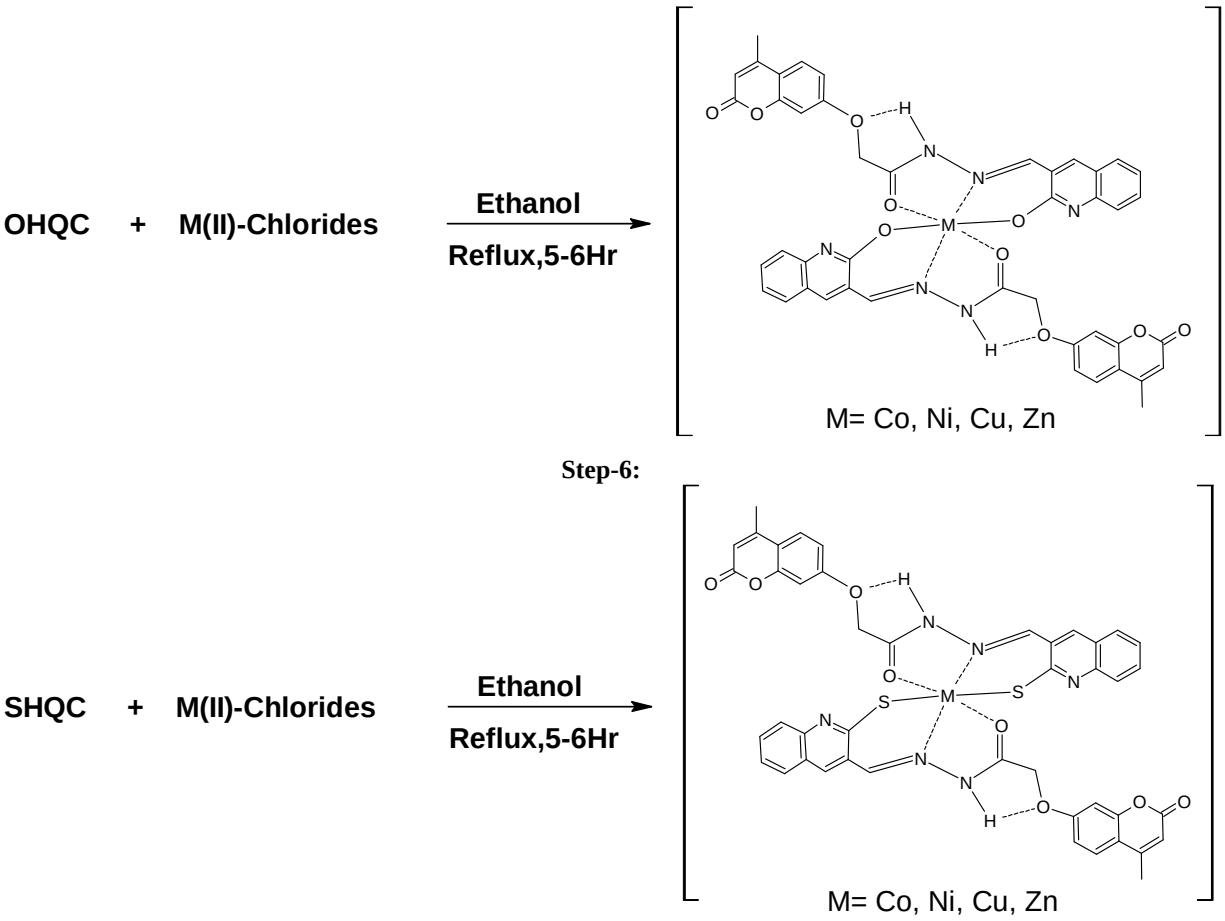


Figure-1: IR-Spectrum of [Ni(SHQZ)$_2$] complex:

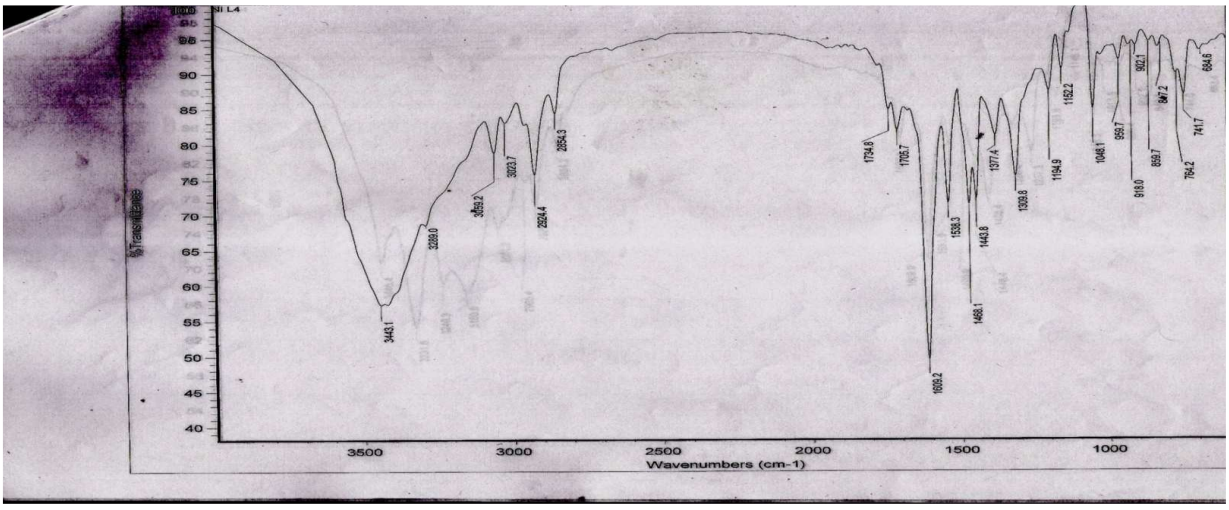


Figure-2: ^{1}HNMR spectrum of [Zn(SHQZ)$_2$] complex:

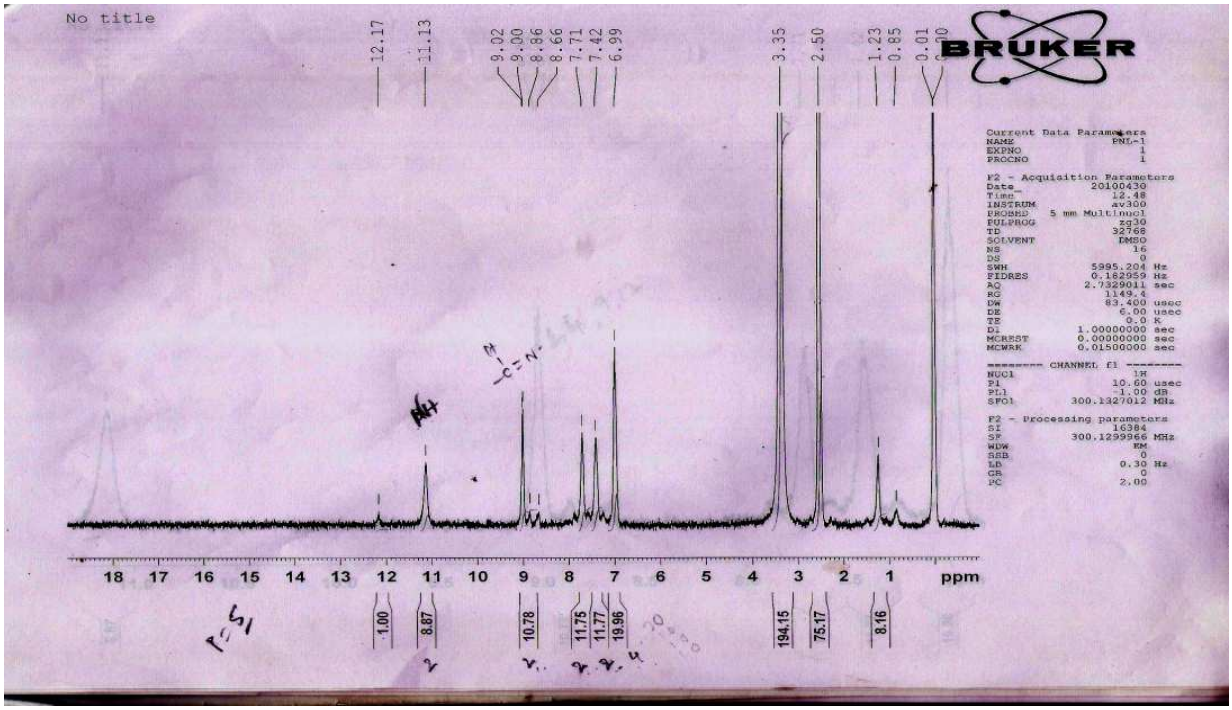
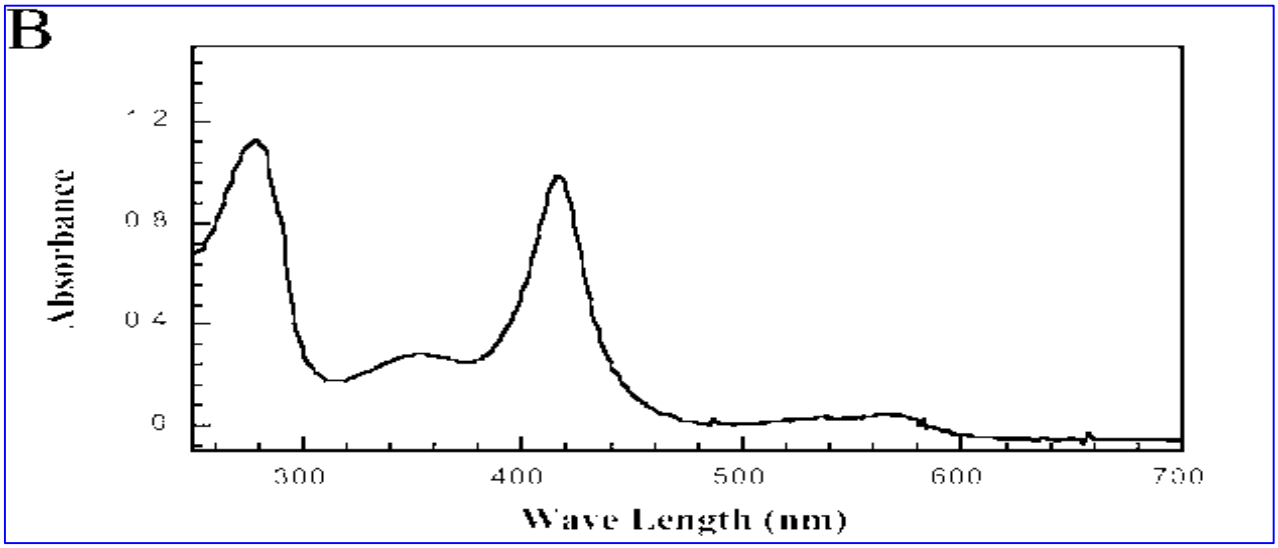


Figure-3. Electronic Spectrum of [[Co(SHQC)$_2$]complex:



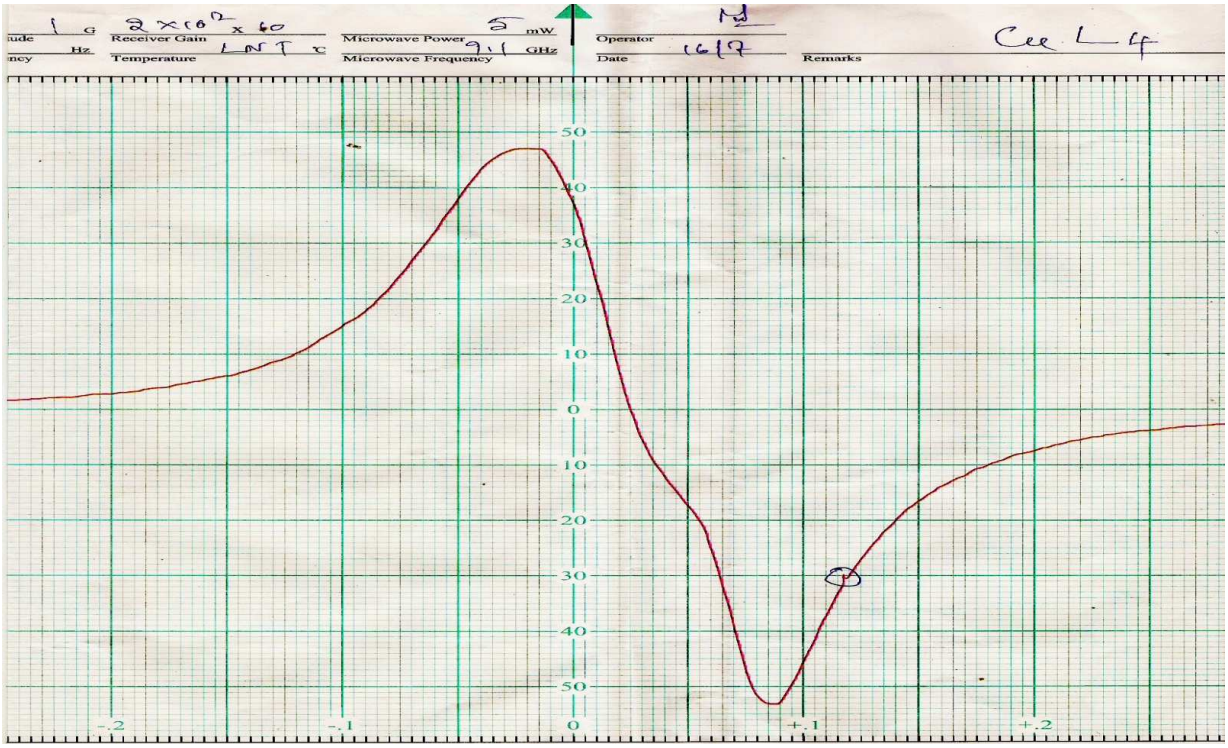


Figure-5. TG/DTA curve of [Co(SHQC)$_2$] complex

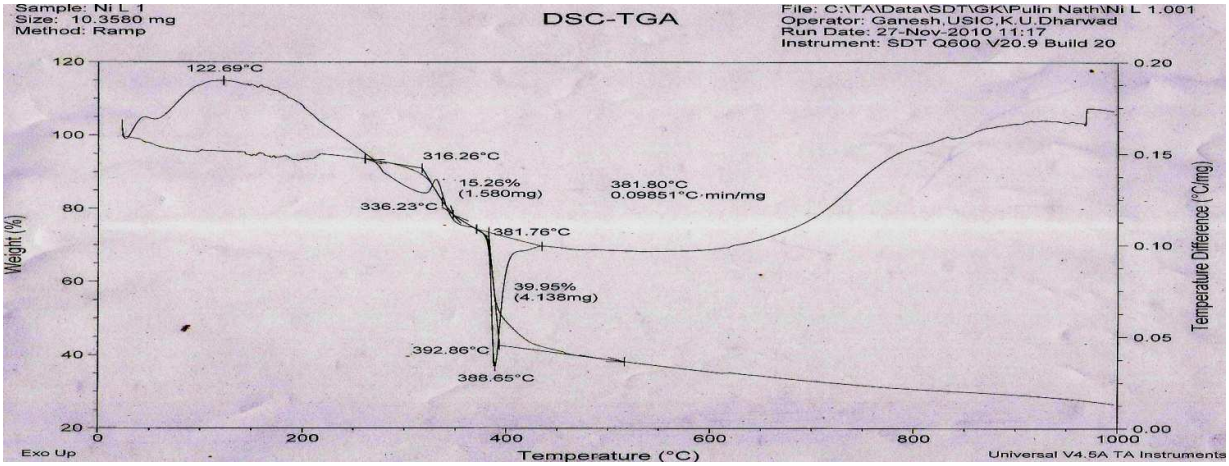
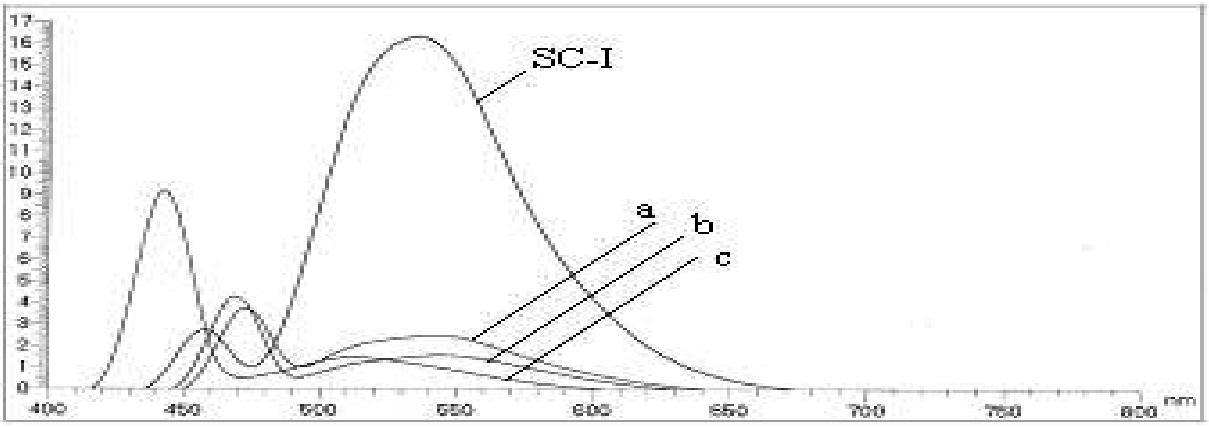
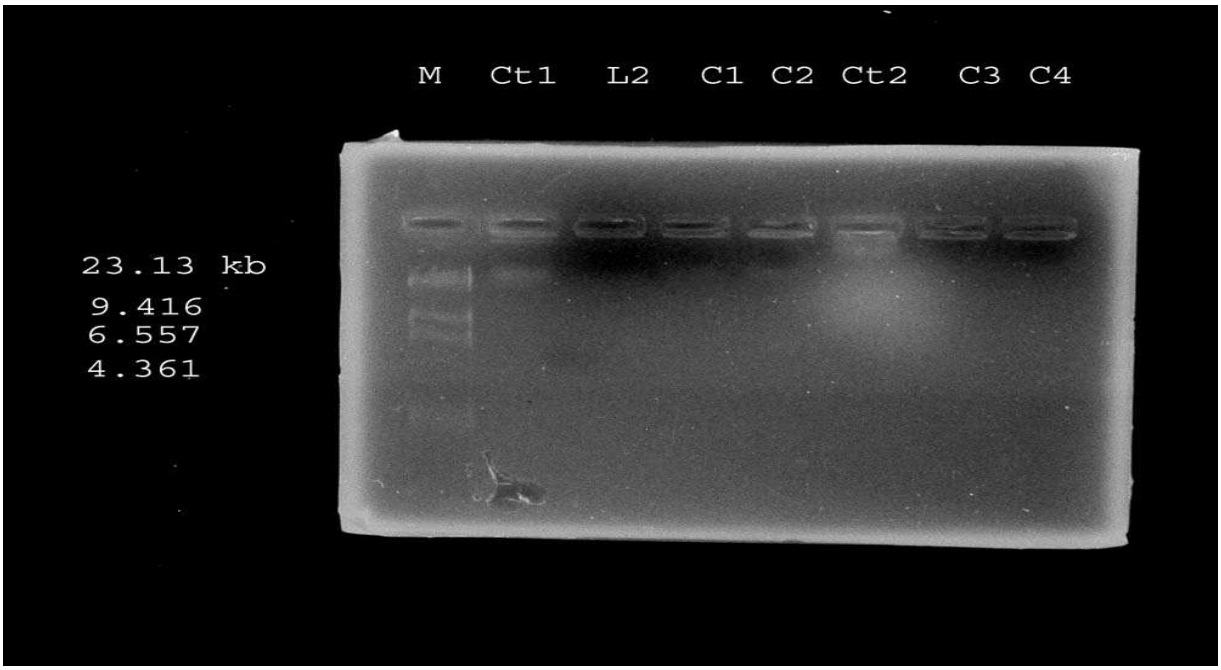


Figure-6. Emission spectra of Schiff base-1, Co(II), Ni(II) and Cu(II) in DMF



*SC-I: Schiff base **I**; a: Co(II) (**1**); b: Ni(II) (**3**); c: Cu(II) (**5**)*

Figure -7. DNA cleavage study on genomic DNA of E. coli and S. aureus



***Lane M**= standard molecular weight marker; **Lane Ct$_1$**=control DNA of E. coli; **Lane L$_2$**= E. coli DNA treated with SHQZ; **Lane C1**= E. coli DNA treated with[Co(SHQZ)$_2$]; **Lane C2**,=E. coli DNA treated with [Ni(SHQZ)$_2$]; **Lane Ct$_2$**= control DNA of S. aureus; **Lane C3**= S. aureus DNA treated with [Cu(SHQZ)$_2$]; **Lane C4**= S. aureus DNA treated with [Zn(SHQZ)$_2$].*

CONCLUSION

Due to insolubility in water and common organic solvents, all the complexes are thought to be polymeric in nature. The tentative structures of all the complexes are based on elemental analysis, IR, 1NMR, electronic, magnetic measurements, thermal studies and mass spectra. On the basis of different techniques, it is proposed that all the complexes possess octahedral geometry (figure-8) and the Schiff bases act as versatile tridentate ligands coordinated to metal ion trough carbonyl oxygen, nitrogen and sulphur atoms.

The electrochemical properties of the metal complexes investigated in DMF showed most significant two-electron transfer processes. From the in vitro antibacterial and antifungal activity against representative bacterial and fungal

strains, it is evident that the Cu(II) complexes are most active towards the bactericidal activity at lower MIC concentrations. The Schiff base SHQZ, Co(II), Ni(II) and Cu(II) complexes have the potent DNA cleavage property.

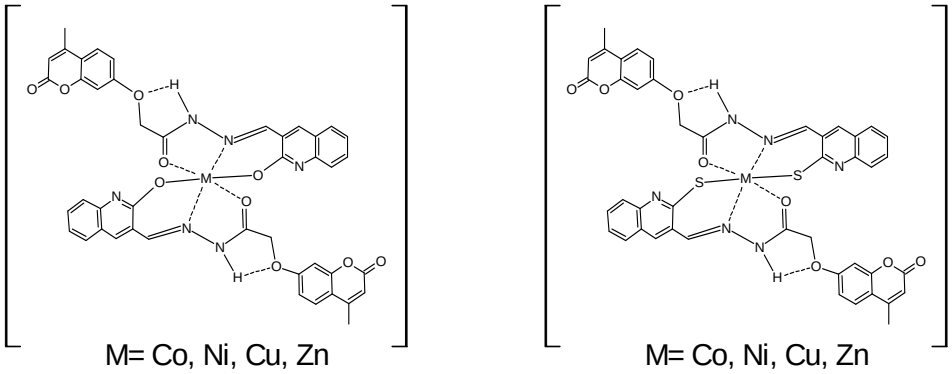


Figure-8: Proposed Structure of the complexes

Acknowledgement
Authors are thankful to Karnatak Science College, Dharwad for providing necessary facilities for the research and to University Sophisticated Instrumentation Centre (USIC), Karnatak University Dharwad for the recording the spectral data. Authors extend their thanks to IICT, Hyderabad for providing mass spectra, IIT Bombay for the ESR spectra. Authors are also thankful to the Biogenics of Hubli for biological studies.

REFERENCES

[1] R. D. Murray, J. Mendez and S. A. Brown, Edited by R. Murray, J. Mender and S Brown, *The Natural Coumarins: Occurrence, Chemistry and Biochemistry*, John Wiley and Sons, New York, NY, (**1982)**, 227.
[2] M. S. Y. Khan and P. Sharma, *Indian J. Chem.*, (**1993)**, 32B, 374.
[3] M. S. Y. Khan and Sharma P, *Indian J Chem.*, **(1995)**, 32B, 237.
[4] J. A. A. Miky and A. A. Farrang, *Indian J Chem.*, **(1997)**, 36B, 357.
[5] A. K. Mishra, S. K. Sharma, A. Taneja and D. S. Seth, *Proc Nat Acad Sci India Sect.* **(1998)**, 68(2), 129.
[6] L. L. Andreani and E. Lapi, *Bull Chem Farm.*, **(1960)**, 99, 583.
[7] Y. L. Zhang, B. Chen, K. Zheng, M. Xu, L. Zhang and X. Lei, *Yao Xue Xue Bao*, 1982, 17,17; *Chem Abstr.*, **(1982)**, 96, 135383.
[8] L. Bonsignore, G. Loy, D. Secci and L. Calignano, *Eur J Med Chem.*, **(1993)**, 28, 517.
[9] M. V. Kulkarni, B. G. Pujar and V. D. Patil, *Arch Phram.*, **(1981)**, 316(1), 15.
[10] J. R. Marchant and A. S. Gupta, *Indian J Chem.*, **(1979)**, 22, 158.
[11] D. R. Buckle, D. G. Outred, J. W. Ross, H. Smith, R. J. Smith and B. A. Spicer, *J Med Chem.***(1979)**, 22,158; *Indian J Chem.*, **(1979)**, 17B, 410.
[12] K. Hino, Y. Nagai and H. Uno, *Chem Pharm Bull.*, **(1987)**, 35, 2819.
[13] G. S. Bajwa, K. E. Hartman and M. M. Joullie, *J Med Chem.*, **(1973)**, 16, 134.
[14] Bucc-Hole Hg-Pn, N. D. Xuong, F. Binon and N. Nam, *Compt Rend.*, **(1995)**, 235, 329.
[15] M. Kaytal and H. B. Singh, *Talanta*, **(1968)**, 15, 1043.
[16] R. P. Haugland,*"Handbook of Fluorescent Probes and Research Products,"* 9th ed., Molecular Probes, Eugene, **(2002)**.
[17] G. R.Green, J. M.Evans, A. K.Vong, A.Katritzky, C. W.Rees, E. F. V.Scriven, *"Pyrans and their Benzo Derivatives: Applications, Comprehensive Heterocyclic Chemistry II,"* 1st ed., Pergamon, Oxford, **(1996)**.
[18] Kurkjian, T Tonnaire., *Farmaco.*, 57, 703—708 **(2002)**.
[18] D. Yu, M. Suzuki, L. Xie, S. L. Morris-Natschke, K. H. Lee, *Med. Res. Rev.*, 23, 322—345 **(2003)**.
[20] G. B. Bagihalli, P. G. Avaji, S. A. Patil, P. S. Badami, *Eur. J. Med. Chem.*, 43, 2639—2649 **(2008)**.
[21] R. Deng, J. Wu, L. Long, *Bull. Soc. Chim. Belg.*, 101, 439—443 **(1992)**.
[22] G. P. Pokhariyal, *Proc. Natl. Acad. Sci. India*, 58A, 369—373 **(1988)**.
[23] G. P. Pokhariyal, *Indian J. Chem.*, 28A, 922—923 **(1989)**.
[24] A. K. Kulkarni, S. A. Patil , P. S. Badami, *European Journal of Medicinal Chemistry* 44 **(2009)** 2904-2912.

[25] S. A. Patil, S. N. Unki, A. D. Kulkarni, V. H. Naik, U. Kamble and P. S. Badami *Journal of Coordination Chemistry*, Manuscript ID: GCOO-2010-0297.
[26] K. J. Charyulu, K. L. Omprakash, A.V. Chandra Pal, M.L.N Reddy, *J. Indian Chem. Soc.* LXII **(1985)**121.
[27] R. A. Morton and E. Rogers. *J. Chem. Soc.* 127, 2698 **(1925).**
[28] O. Meth-Cohn, B. Tarnowski, R. hayear, A. Keyzad and S. Rhousati, *J. Chem. Soc. Parkin Trans.* 1, 2509 **(1981).**
[29] I. S. Chen, H. C. chen, M. J. Cheng, Y. L. Cheng and I. L. Tsai. *Nat. Prod. Rep.*, 19, 748 **(2002).**
[30] V. Pande, S. Tusi, Z. Tusi, M Joshi and S. A. Bajpai. *Acta. Pharm.*, 54, 1 **(2004).**
[31] X. Zhao, X. Su, E. Yang, H. Lin, S. Zhu and H. Sun. *Ind. J. Chem.*, 43A, 793 **(2004).**
[32] R. C. Maurya, A. K. Singh and S. Rajput., *Ind J. Chem.*, 43A, 551, **(2004).**
[33] S. S. Mandal, N Vinaykumar Uvarshney, S. Bhattacharya., *J. Inorg. Biochem.*, 63(4), 265 **(1996).**
[34] Y. Shao, J. Zhang, C. Tu, Q. Dai, Z. Guo., *J. Inorg Biochem.*, 99(7), 1490 **(2005).**
[35] V. S. V. Satyanarayana, P. Sreevani, A. Sivakumar, and V. Vijayakumar., *ARKIVOC* **(2008)** (xvii) 221-233.
[36] Narayanachar, S. D. Dhumwad, *J. Chem. Pharm. Res.*, 3(4) 504-517 **(2011).**
[37] J. H. Deshmukh, M. N. Deshpande**,** *J. Chem. Pharm. Res.*, 2011, 3(3):706-712.
[38] M. K. Shivananda, Shet Prakash M , *J. Chem. Pharm. Res.*, 2011, 3(5), 61-66.
[39] O. Meth-Cohn, B. Tarnowski, R. Hayear, A. Keyzad and S. Rhousati, *J. Chem. Soc.* Parkin Trans. 1, 2509 **(1981).**
[40] S. D. M. Basavarajaiah and B.H. Mruthyunjayaswamy, *Chem. Pharm. Bull*. 57(6) 557—560 **(2009).**
[41] B. P. Nandeshwarappa, D. B. Aruna Kumar, H. S. Naik, D. M. Mahadevan, Phos, Sulphur, Silicon., 181, 1997**(2006).**
[42] Z.H. Chohan, M. Arif, M.A. Akhar, C.T. Supuran, *Bioinorg. Chem. Appl*. 1 (**2006**) 8313.
[43] T.A. Brown, *Essential Molecular Biology: A Practical Approach, Vol. I;* Oxford University Press: NewYork, **(1990)**; pp 51–52.
[44] A. Kulkarni, S.A. Patil, P.S. Badami, *Eur. J. Med. Chem*. 44 (**2009**) 2904–2912.
[45] N.C. Saha, R.J. Butcher, S. Chaudhari, N. Saha, *Polyhedron* 22 (**2003**) 383.
[46] A. B. P. Lever. *Inorganic Electronic Spectroscopy, Elsevier, New York*., **(1984)**.
[47] J. T. Makode , A. S. Aswar. *J. Indian Chem. Soc.*, **80**, 44**(2003)**.
[48] H. Liu, H. Wang, F. Gao, D. Niu, Z. Lu. *J. Coord. Chem*.,**60**, 2671-2678**(2007).**
[49] D.P. Singh, R. Kumar, V. Malik, P. Tyagi, *Trans. Met. Chem*. 32 (**2007**) 1051–1055.
[50] M. Valko, R. Boca, R. Klement, J. Kozisek, M. Mazur, P. Pelikan, H. Morris, H. Elias, L. Muller, *Polyhedron* 16 (**1997**) 903.
[51] E.S. Freeman, Corroll, *J. Phys. Chem*. 62 (**1958**) 394.
[52] Z. Shirin, R.M. Mukherjee, *Polyhedron* 11 (**1992**) 262