Final report of work done on the Minor Research Project

(MRP(S)-1127/11-12/KAMY013/UGC-SWRO)

Synthesis and characterization of biologically active metal complexes

Submitted to

Deputy Secretary
South Western Regional Office
PK Block, Palace road, Gandinagar, Bangalore-560009

By

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UNIVERSITY GRANTS COMMISSION

BAHADUR SHAH ZAFAR MARG

NEW DELHI – 110 002.

Final Report of the work done on the Minor Research Project.

1. Project report No.	First
2. UGC Reference No.	MRP(S)-1127/11-12/KAMY013/UGC-SWRO
3. Period of report:	13-07-2012 to 30-12-2014
4. Title of research project	**S**ynthesis and characterization of biologically active metal complexes
5. (a) Name of the Principal Investigator	Dr. B.K. Kendagannaswamy
(b) Department. and University/College where work has progressed	Department of chemistry, JSS College of Arts, Commerce & Science, Ooty road,Mysore-25
6. Effective date of starting of the project	20-07-2012
7. Grant approved and expenditure incurred during the period of the report	
a. Total amount approved Rs.	Rs1,50,000/-
b. Total expenditure Rs	Rs 1,52,506/-
c. Report of the work done: (Please attach a separate sheet)-	enclosed
I. Brief objective of the project	a) Synthesis of Schiff base ligands and their metal complexes. b) Characterization of the prepared ligands by using spectroscopic studies (IR, ^{1}H-NMR and MS) elemental analyses, magnetic moments and molar conductance. c) In order to check the biological activities of the prepared ligands and their metal complexes, we have planned to conduct antibacterial, antifungal and anthelmentic studies
II. Work done so far and results achieved and publications, if any, resulting from the work (Give details of the papers and names of the journals in which it has been published or accepted for publication	We have synthesized several Schiff base ligands and their metal complexes. All the prepared compounds were characterized by spectroscopic analysis. In addition, we have also published **two** research article entitled "**Synthesis and *in vitro* activity of quinolin-5-ylamine derivatives**" in a peer-reviewed Journal "***Current Chemistry Letters***" **'Investigation of Antioxidant Activity of 3, 5-**

	Dimethoxyaniline Derivatives' in a peer reviewed *Journal of Applicable Chemistry, 2014, 3 (5):* 2131-2137(Copy is attached).
III. Has the progress been according to original plan of work and towards achieving the objective. if not, state reasons	Yes, according to the original plan of work.
IV. Please indicate the difficulties, if any, experienced in implementing the project	Not Applicable
V. If project has not been completed; please indicate the approximate time by which it is likely to be completed. A summary of the work done for the period (Annual basis) may please be sent to the Commission on a separate sheet	Not Applicable
VI. If the project has been completed, please enclose a summary of the findings of the study. Two bound copies of the final report of work done may also be sent to the Commission	Status of the project- completed Summary of the findings of the enclosed. Two bound copies of the final report of work done is enclosed
VII. Any other information which would help in evaluation of work done on the project. At the completion of the project, the first report should indicate the output, such as (a) Manpower trained (b)Ph.D awarded (c) Publication of results (d) Other impact, if any	Students trained. Two papers Published

SIGNATURE OF THE
PRINCIPAL INVESTIGATOR

SIGNATURE OF THE
PRINCIPAL

Summary report about proposed research project:

Introduction

Modern trends in the area of coordination chemistry involve studies on the synthesis, structure and applications. The role of metal ions in living systems is well established in recent years. It has been recognized that inorganic biochemistry is a bridge between the academic disciplines *viz*., biochemistry and inorganic chemistry. In fact, biochemistry has been considered as the coordination chemistry of living systems **[1]**. This dependence is well exemplified by the observation that one third of all enzymes have a metal ion as essential component **[2]**. Several reviews, monographs etc., are available on the inorganic aspects of biochemistry **[3-5]**. As metal ions play such an important role in biological systems it is to be expected that the various aspects of coordination will be studied with intense interest.

The reasons for the persistent interest in the complexes are many, but the important among them must be their role in various biochemical, pharmaceutical, industrial and chemical processes. Certain coordination compounds, which are occur in nature of biological importance. The participation of metallo proteins in respiratory, photosynthetic, nitrogen fixation, biosynthetic and metabolic processes is essential to the foundations of life. Several cobalt complexes are important as models to oxygen binding involved in biological systems, cobalt is also present in enzymes related to vitamin B_{12}. A number of copper proteins including enzymes such as ascorbic acid oxidase, cytochrome oxidase etc., have been isolated.

Coordination complexes have a long history of use as chemotherapeutic agents. The successful application of inorganic complexes as drugs involves the recognition of their bioinorganic modes of action coupled with the traditional pharmacokinetic parameters of uptake, distribution and excretion. Further, the rational approaches to chemotherapy and particularly the notion of selective toxicity **[6, 7]** must be placed in an inorganic context. The concept of selective toxicity, and its scientific basis, is of particular use in describing the actions of drugs on an invading organisms, be it viral, bacterial, parasitic or ultimately malignant tumours caused by the cancerous growth of the host's cells. The achievement of some form of selectivity is critical to the successful use of any agent as a drug or modifier of biological response.

Bacterial, viral and malignant tumour (cancer) remains the most life threatening, refractory and global killer diseases around the world. Present therapy involving organic moieties as therapeutic agents is increasingly getting marginalized due to rapid emergence of drug resistance, limited target specificity and difficult to achieve therapeutic drug levels. Consequently metallo drugs offer unique advantages in overcoming these difficulties. These are the compounds incorporating biologically relevant transition metal ions an integral part of their structural scaffold and possess clinical and therapeutic value. They can provide synergized bioavailability through

increased liposolubility, enhanced biological activity and selective targeting of certain proteins/ receptors and activity against drug-resistant species.

The predominant role of DNA in cellular replication and transmission of genetic information makes the nucleic acids a primary target for drug action, and many drugs are considered to act fundamentally at this level. In the case of metals (metal-aqua complexes) and other metal complexes, the subject of their interaction with DNA is relevant for a number of reasons. These systems range from *in vivo* aspect such as the endogenous presence in the nucleus of metal ions, the role of zinc in RNA polymerase, the mutagenesis and eventual carcinogenesis of metal ions, the diverse uses of metal ions as probes of polynucleotide structure, as well as the cytotoxic effects of metal-complexes.

There has been an increasing interest in the synthesis of novel model metal coordination compounds to mimic biological reactions. These investigations constitute one of the major lines of pursuit in bioinorganic chemistry concept. These model studies have been useful to understand the role of metal ions in specified coordination geometries dictating the course and nature of reaction in biological systems. One of the successful routes to tackle this problem is through the investigations on structure-property correlation of new complexes. It is, therefore, worthwhile t study on the synthesis of some biologically active ligands and also the isolation of their novel metal complexes.

In coordination chemistry, Schiff bases have a significant role as ligands still a century after their discovery [**8**]. The importance of Schiff bases and their metal complexes are important as biochemical, electrochemical, analytical, antifungal and antibacterial activities and redox catalysts. A comprehensive review [**9**] covers much of the Schiff base chemistry known up to 2007 and it has been followed by others. Structure and mechanism of the formation of metal complexes and stereochemistry of four coordinate chelate compounds from Schiff bases and their analogues have been discussed in a review [**10**] with 250 references.

Schiff-base metal complexes have been known since the mid nineteenth century and even before the general preparation of Schiff base ligands themselves. Metal complexes of Schiff bases have occupy a central place in the development of coordination reaction chemistry, the work Jorgense and Werner. Ettlings isolated a dark green crystalline product from the reaction of cupric acetate, salicylaldehyde and aqueous ammonia. Schiff has synthesized complexes of metal-salicylaldehyde with primary amines. Subsequently, Schiff isolated complexes from the condensates of urea and salicylaldehydes. Delepine has prepared complexes by reacting metal acetate salicyladehydes and a primary amine in an alcohol and demonstrated a 2:1 stoichiometry. However, there was no comprehensive, systematic study until the preparative work of Pfeiffer and associates.

Apart from biological applications of metal complexes, the coordination compounds of azo, formazan, azomethine, nitroso, anthraquinone and phthalocyanine ligands find important applications in the field of photography, catalysis and some modern high technology industries, such as electronics. Chromium and cobalt complexes of azo-dye stuffs were largely used in the homogeneous and asymmetric catalysis. Other metal complexes were used as catalysts in olefin hydroxylation, hydrogenation, cyclopropanation , cyclo addition and allylic alkylation reactions. Recently reported review article has covered all aspects of metal-based catalyst preparation, physical properties and its applications [**11**].

Though significant advances have been made in the field of coordination chemistry, there is still scope on the study of complexes whose structures and reactivity are less understood. It is, therefore, considered worthwhile to study on the synthesis, structural elucidation and biological activity of a new series of complexes of biological importance.

Synthesis of ligands

In the present investigation, we have synthesized Schiff's base ligands of quinazolinone and also characterized by elemental analysis, Infrared, ^{1}H-NMR and mass spectral studies.

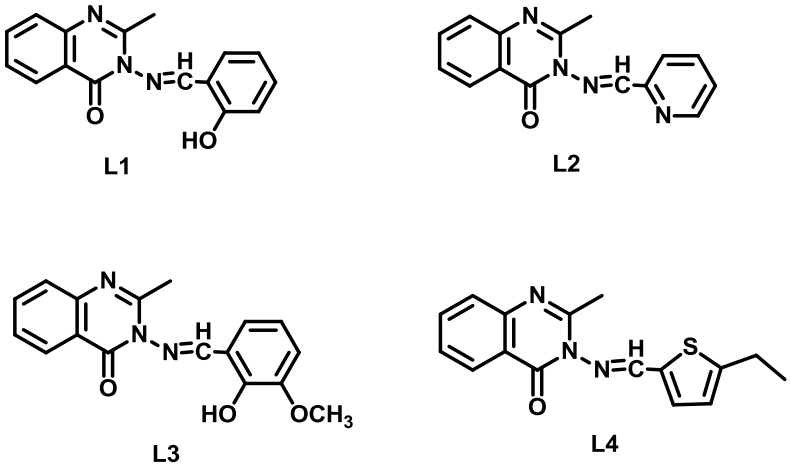
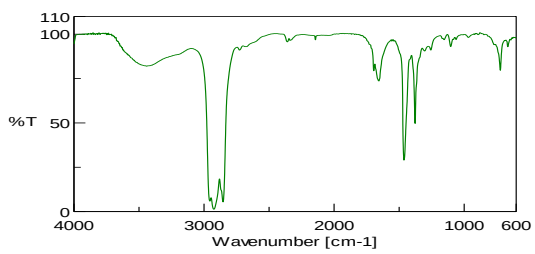


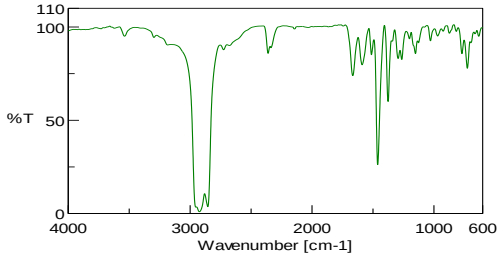
Figure 1: Structures of synthesized Schiff base.

Table 1: Analytical and physical data of quinazolin-4(*3H*)-one Schiff base ligands.

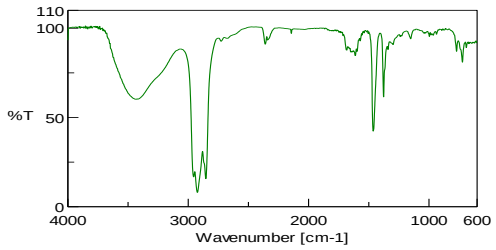
Compound	Ligand Molecular Formula (Mol. Wt)	Melting Point (°C)	Yield (%)	Elemental found (calculated)			
				C (%)	H (%)	N (%)	S(%)
L_1	$C_{16}H_{13}N_3O_2$ (279)	167-169	71	68.43 (68.5)	4.58 (4.61)	14.9 (15.02)	-
L_2	$C_{15}H_{12}N_4O_2$ (264)	175-177	63	68.18 (68.27)	4.28 (4.31)	21.22 (21.32)	-
L_3	$C_{17}H_{15}N_3O_3$ (309)	215-217	61	66.01 (66.12)	4.93 (5.03)	13.58 (13.79)	-
L_4	$C_{16}H_{15}N_3OS$ (297)	183-185	79	64.62 (65.13)	5.08 (5.14)	14.13 (15.61)	10.77 (10.91)



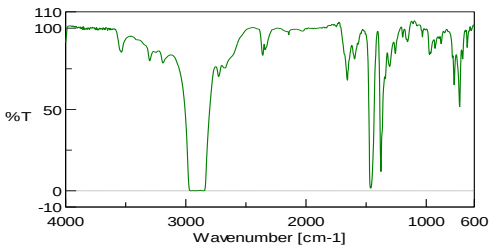
L_1



L_2

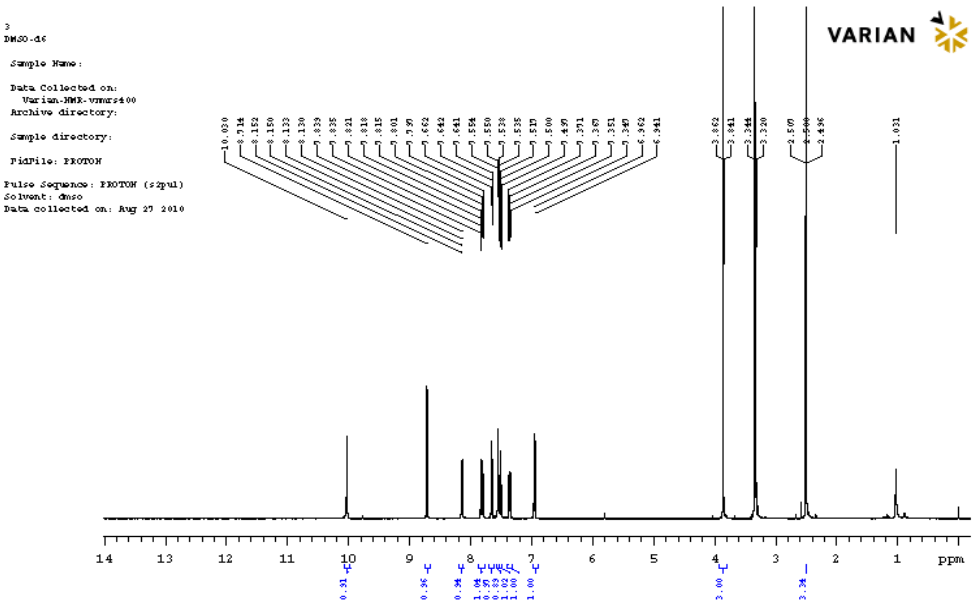


L_3



L_4

Figure 2: IR spectra of synthesized ligands.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DMSO-d6
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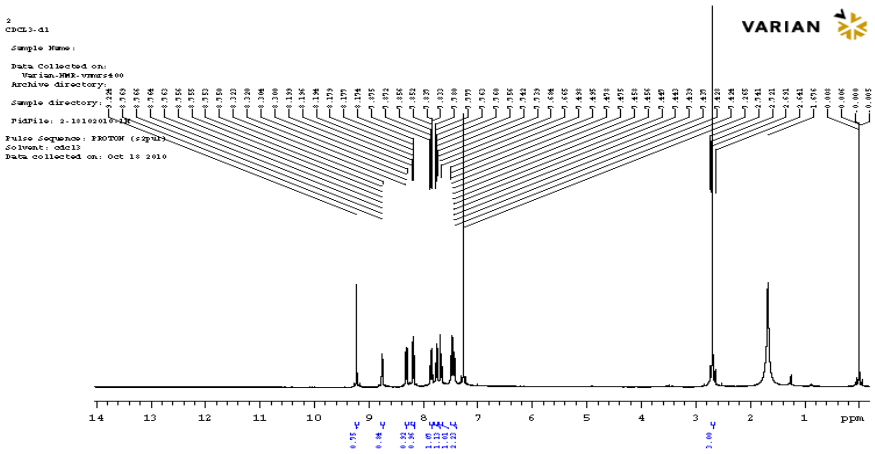
Solvent: dmso
Data collected on: Aug 27 2010
ppm

L_1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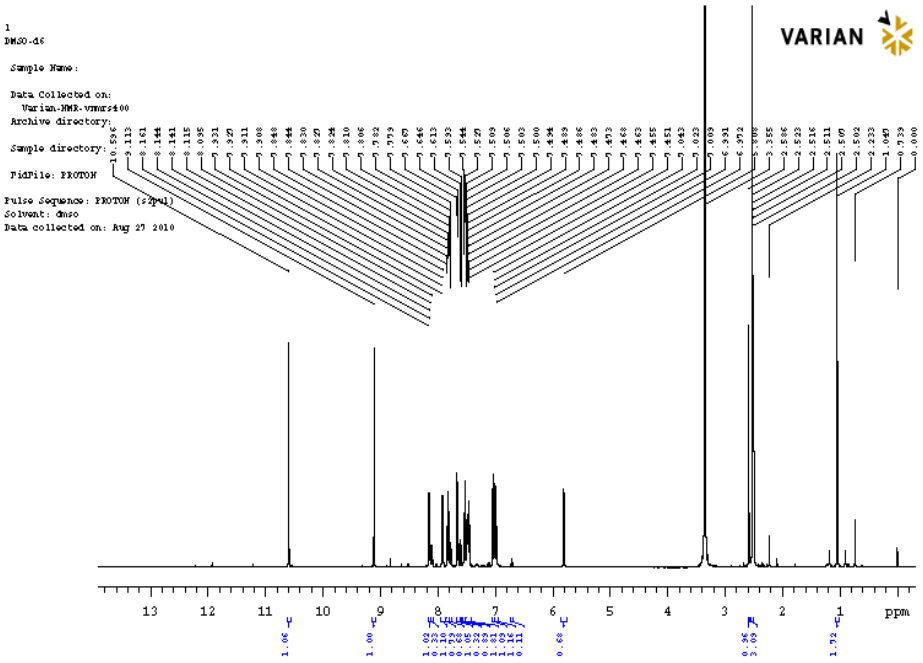
L_2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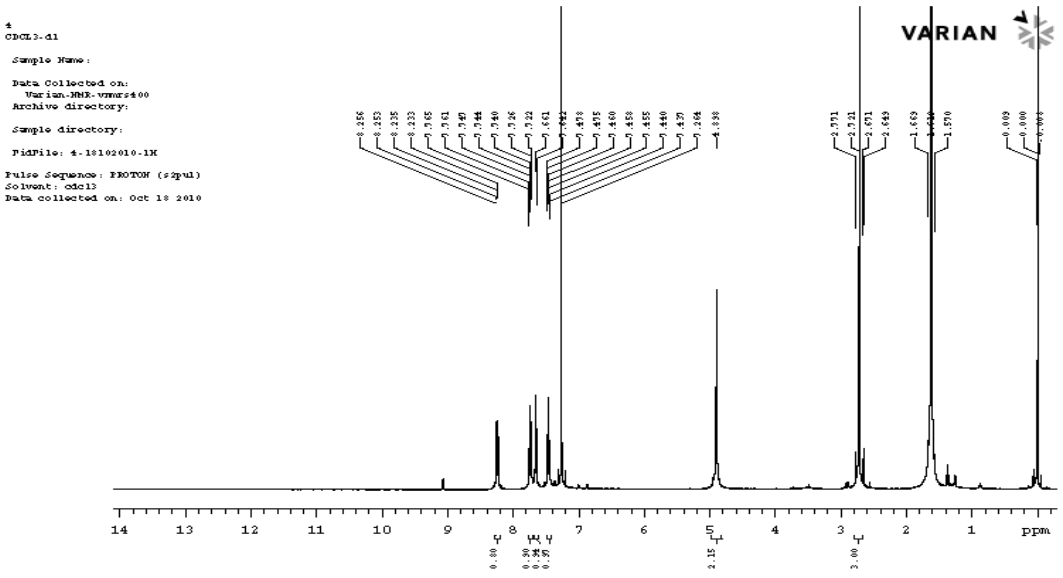
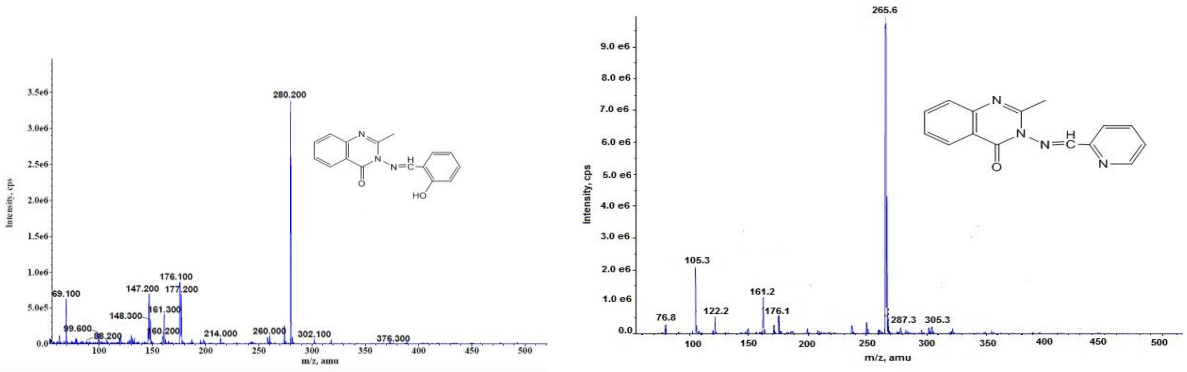
Data collected on: Aug 27 2010
ppm

L_3



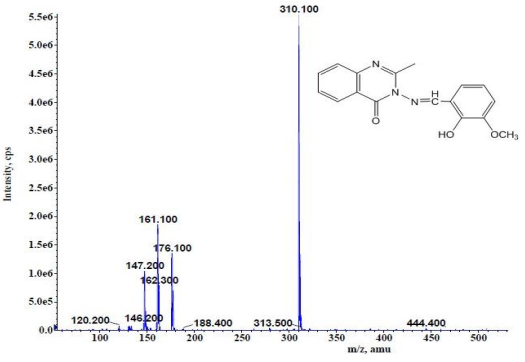
L_4

Figure 3: ^{1}H-NMR spectra of ligands.

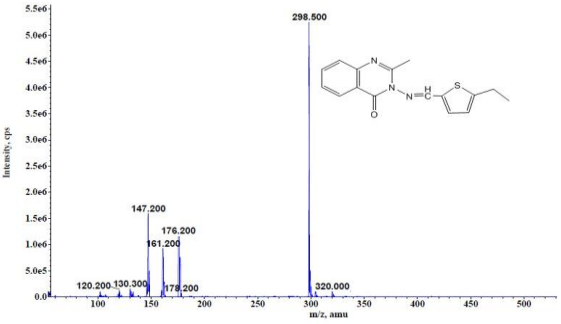


L_1

L_2



L_3

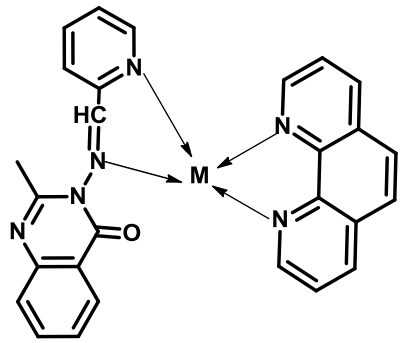


L_4

Figure 4: Mass spectra of ligands.

Synthesis of metal complexes

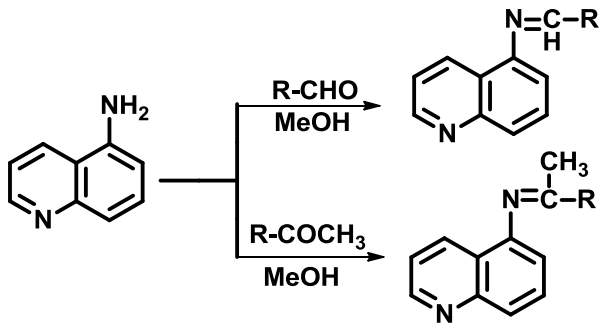
The metal complexes were prepared in 1:2 ratio using above prepared Schiff base ligands and 1,10-phenanthroline.



M=Cu(II), Co(II), Cr(III),Zn(II).

Figure 6: Structure of metal complex.

Synthesis of Schiff bases of quinolin-5-ylamine with different aldehydes



Scheme 1: Synthetic route of quinolin-5-ylamine derivatives.

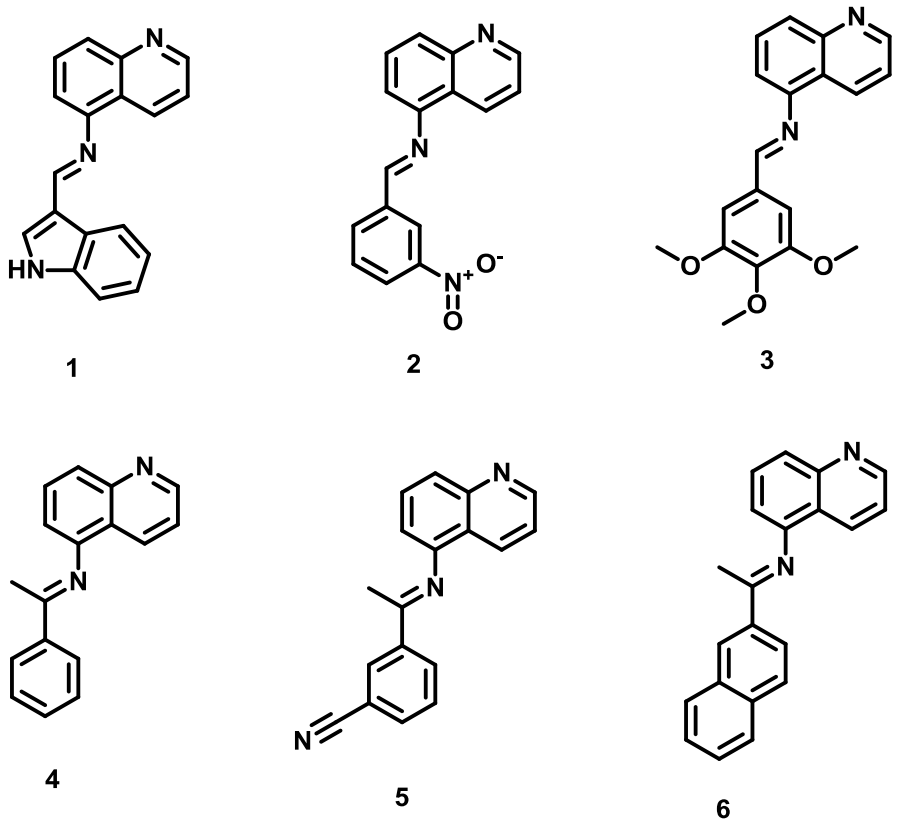


Figure 5: Structures of synthesized quinolin-5-ylamine analogues.

This part of work has been published in ***CURRENT CHEMISTRY LETTERS***. In this article we have shown the antioxidant activities of quinolin-5-ylamine analogues. All the compounds showed DPPH radical scavenging activity.

References:

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Investigation of Antioxidant Activity of 3,5-Dimethoxyaniline Derivatives

INTRODUCTION

In recent years, there has been an increased interest in the application of antioxidants to medical treatment as information is constantly gathered linking the development of human diseases to oxidative stress. Free radicals play a role in the pathogenesis of chronic degenerative diseases including cancer, autoimmune, inflammatory, cardiovascular and neurodegenerative diseases and aging [1-4]. It is also known that oxidative stress can be induced by a wide range of environmental factors including UV stress, pathogen invasion, herbicide action and oxygen shortage [5]. Owing to these facts, synthetic and natural compounds with potential antioxidant activity are receiving increased attention in biological research, medicine and pharmacy [6].

Schiff bases are characterized by the imine group which is important in elucidating the mechanism of transamination and racemisation reactions in biological systems [7]. Due to the great flexibility and diverse structural aspects, a wide range of Schiff bases have been synthesized and their complexation behaviors have been studied [8]. They have been synthesized from a variety of compounds such as amino thiazoles, 2-hydroxy-1-napthalaniline, amino sugars, aromatic aldehydes, ketones, isatin, triazole ring, thiosemicarbazides, amino acids and pyrazolone [9, 10]. Antibacterial, antifungal, antitumor and anticancer activities of some Schiff bases have been reported and they are active against a wide range of organisms [11]. Some Schiff bases bearing aryl groups or heterocyclic residues possessing excellent biological activities have attracted the attention of many researchers in recent years [12]. The Schiff bases formed from aromatic aldehydes, ketones and their derivatives are quite stable. Many Schiff bases are known to be medicinally important and are used to design medicinal compounds [13]. Treatment of 1,2-indanedione with 3,5-dimethoxybenzenamine in benzene afforded several products have been reported [14]. Synthesis of poly(2,5-dimethoxyaniline) and poly(aniline-Co-2,5-dimethoxyaniline) has been reported [15]. Crystal structure of some novel compounds from 3,5-dimethoxyaniline have been reported [16]. In this respect, the present paper reports the preparation and antioxidant activity of a new class of Schiff bases, 3a-g.

MATERIALS AND METHODS

All solvents and reagents were purchased from Sigma-Aldrich Chemicals Pvt. Ltd., India. Melting points were determined using SELACO-650 hot stage melting point apparatus and were uncorrected. Elemental analyses were recorded on VarioMICRO superuser V1.3.2 Elementar. The UV spectra were recorded using Analytik Jena Specord 50 UV–vis spectrophotometer. FT-IR spectra were recorded using a Jasco FTIR-4100 series. ^{1}H-NMR spectra were recorded on Shimadzu AMX 400-Bruker, 400 MHz spectrometer using DMSO-d_6 as a solvent and TMS as internal standard (chemical shift in δ ppm). All the compounds 3a-g was prepared according to the reported procedure [17].

General procedure for the preparation of 3,5-dimethoxyaniline derivatives 3a-g: Equimolar concentrations of different aldehydes (0.003 mol) and 3,5-dimethoxyaniline (0.003 mol) were stirred for 4-6 hr at room temperature in absolute ethanol (25 ml) and then 2-3 drops of concentrated sulfuric acid was added to the mixture. The progress of the reaction was monitored by TLC until the reaction was complete. It was cooled to 0 °C, and the precipitate was filtered, washed with diethyl ether and the residue was recrystallized from methanol.

N-(2-Chloro-6-fluorobenzylidene)-3,5-dimethoxybenzenamine (3a): The general experimental procedure described above afforded 3a, and the product obtained from 3,5-dimethoxybenzenamine (1) (0.50 g) and 2-chloro-6-fluorobenzaldehyde (2a) (0.47 g). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.65 (s, 1H, HC=N), 7.42-7.40 (m, 3H, Ar-H), 6.53-7.12 (s, 3H, Ar-H), 3.31 (s, 6H, OCH_3). Anal. Calcd. for $C_{15}H_{13}ClFNO_2$: C, 61.34; H, 4.46; N, 4.77; Found: C, 61.22; H, 4.58; N, 4.56 %.

2-((3,5-Dimethoxyphenylimino)methyl)phenol (3b): The general experimental procedure described above afforded 3b, and the product obtained from 3,5-dimethoxybenzenamine (1) (0.50 g) and 2-hydroxybenzaldehyde (2b) (0.37 ml). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.60 (s, 1H, HC=N), 7.921-7.86 (m, 4H, Ar-H), 6.61-7.10 (s, 3H, Ar-H), 6.42 (s, 1H, OH), 3.34 (s, 6H, OCH_3). Anal. Calcd. for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44; Found: C, 70.25; H, 5.78; N, 5.56 %.

4-((3,5-Dimethoxyphenylimino)methyl)-2-methoxyphenol (3c): The general experimental procedure described above afforded 3c, and the product obtained from 3,5-dimethoxybenzenamine (1) (0.50 g) and 4-hydroxy-3-methoxybenzaldehyde (2c) (0.46 g). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.68 (s, 1H, HC=N), 7.97 (s, 1H, Ar-H), 7.84 (d, 1H, Ar-H), 7.75 (d, 1H, Ar-H), 6.61-7.11 (s, 3H, Ar-H), 6.54 (s, 1H, OH), 3.35 (s, 9H, OCH_3). Anal. Calcd. for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88; Found: C, 66.72; H, 5.78; N, 4.66 %.

4-((3,5-Dimethoxyphenylimino)methyl)phenol (3d): The general experimental procedure described above afforded 3d, and the product obtained from 3,5-dimethoxybenzenamine (1) (0.50 g) and 4-hydroxybenzaldehyde (2d) (0.37 g). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.53 (s, 1H, HC=N), 7.94 (d, 2H, Ar-H), 7.44 (d, 2H, Ar-H), 6.72-7.22 (s, 3H, Ar-H), 6.42 (s, 1H, OH), 3.31 (s, 6H, OCH_3). Anal. Calcd. for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44; Found: C, 70.25; H, 5.78; N, 5.36 %.

N-(4-Ethoxybenzylidene)-3,5-dimethoxybenzenamine (3e): The general experimental procedure described above afforded 3e, and the product obtained from 3,5-dimethoxybenzenamine (1) (0.50 g) and 4-ethoxybenzaldehyde (2e) (0.41 ml). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.81 (s, 1H, HC=N), 8.44 (d, 2H, Ar-H), 7.99 (d, 2H, Ar-H), 7.85 (s, 1H, Ar-H), 7.55 (s, 1H, Ar-H), 7.28

(s, 1H, Ar-H), 4.13 (q, 2H, CH_2),2.92 (s, 6H, OCH_3), 2.36 (t, 3H, CH_3). Anal. Calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91; Found: C, 71.75; H, 6.78; N, 4.76 %.

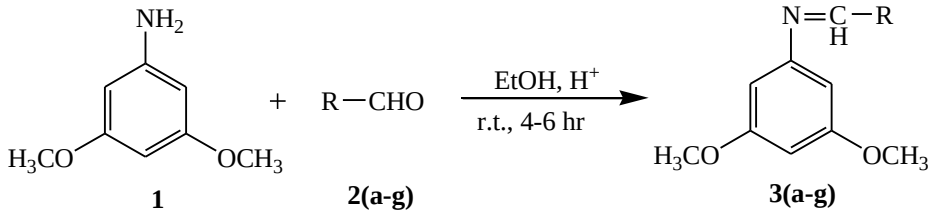
(3,4-Dimethoxy-benzylidene)-(3,5-dimethoxy-phenyl)-amine (3f): The general experimental procedure described above afforded 3f, and the product obtained from 3,5-dimethoxyaniline (1) (0.50 g) and 3,4-dimethoxybenzaldehyde (2f) (0.50 g). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.40 (s, 1H, HC=N), 7.10 (d, 1H, Ar-H), 7.03 (s, 1H, Ar-H), 6.75 (d, 1H, Ar-H), 6.28 (s, 3H, Ar-H), 3.64 (s, 12H, OCH_3). Anal. Calcd. for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65; Found: C, 67.85; H, 6.28; N, 4.46 %.

(3,5-Dimethoxy-phenyl)-(3,4-dimethyl-benzylidene)-amine (3g): The general experimental procedure described above afforded 3g, and the product obtained from 3,5-dimethoxyaniline (1) (0.50 g) and 3,4-dimethylbenzaldehyde (2g) (0.40 g). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.42 (s, 1H, HC=N), 7.12 (d, 1H, Ar-H), 7.00 (s, 1H, Ar-H), 6.81 (d, 1H, Ar-H), 6.26 (s, 3H, Ar-H), 3.60 (s, 6H, OCH_3), 2.30 (s, 6H, CH_3). Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20; Found: C, 75.85; H, 7.28; N, 5.36 %.

Antioxidant activity: The free radical scavenging activity of the compounds was studied *in vitro* by 1, 1-diphenyl-2-picrylhydrazyl (DPPH) assay method [18]. Stock solution of the drug was diluted to different concentrations in the range of 100-200 μg/ml in methanol. Methanolic solution of the compounds (2 ml) was added to 0.003 % (w/v) methanol solution of DPPH (1 ml). The mixture was shaken vigorously and allowed to stand for 30 min. Absorbance at 517 nm was determined and the percentage of scavenging activity was calculated. Ascorbic acid was used as the standard drug. The inhibition ratio (I %) of the tested compounds was calculated according to the following equation: $I\ \% = (Ac\text{-}As) / Ac \times 100$, where *Ac* is the absorbance of the control and *As* is the absorbance of the sample. The concentration of compounds providing 50 % scavenging of $DPPH^{\cdot}$ (IC_{50}) was calculated from the plot of percentage inhibition against concentration (μg/mL). All tests and analyses were done in triplicate and the results were averaged.

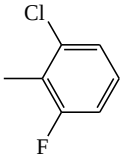
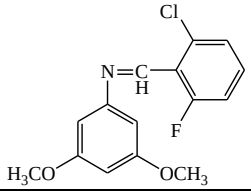
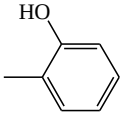
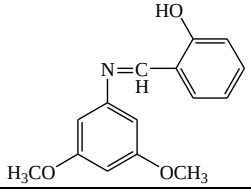
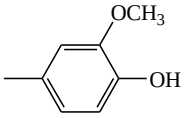
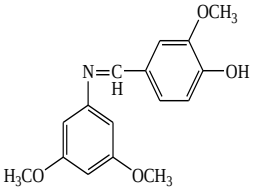
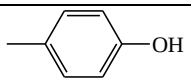
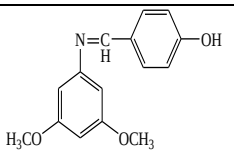
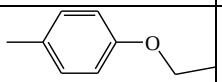
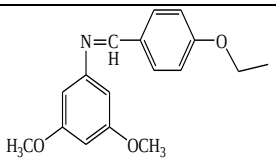
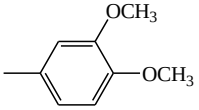
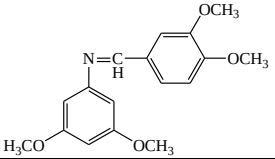
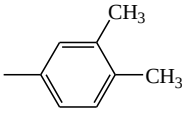
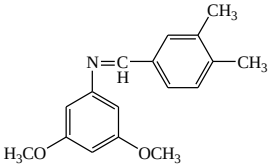
RESULTS AND DISCUSSION

The reaction of 3,5-dimethoxyaniline (1) with different aldehydes, were carried out in the presence of ethanol as solvent with a good yield ranging from 70- 82 %. Compounds were characterized by UV-visible, FT-IR and ^{1}H NMR spectral studies. The chemical structures and physical data of all the compounds are given in Table 1. The electronic absorption spectra of the compounds showed new bands, and the appearance of longer wavelength absorption band in the UV-visible region confirms the formation of compounds. The synthetic route of the compounds is outlined in Scheme 1.



Scheme 1

Table-1: Chemical structures and physical data of 3a-g

Compound	R	Structure	Mol. Wt.	Yield (%)	UV-visible	M.R (°C)
3a			293.7	70.0	450	107-109
3b			257.3	72.4	410	102-104
3c			287.3	79.0	460	105-107
3d			257.3	82.0	397	110-112
3e			285.1	78.4	373	116-118
3f			301.4	78.4	398	156-158
3g			269.3	80.2	425	128-130

The absence of NH_2 and C=O absorption bands in the IR spectra confirmed that the compounds were obtained. The appearance of a medium to strong absorption band at around 1600 cm^{-1} is due to the stretching vibration of C=N bond formation in the Schiff base compounds. IR spectral data of 3a-g was depicted in Table 2. The proton spectral data agree with respect to the number of protons and their chemical shifts with the proposed structures. The proton spectral data

of 1 shows resonance at δ 5.45 ppm (s, 2H, NH_2). In all the new compounds, the above resonance disappeared and additional resonances assigned to the -CH=N- (δ 8.81 – 8.40 ppm) was observed, which confirmed the products.

Table-2: IR data of Schiff bases 3a-g

Compound	N-H	O-H	Aromatic C-H	C=N	C-F	C-O	C-Cl
1	3392	-	3064	-	-	-	-
3a	-	-	3081	1601	1302	1155	722
3b	-	3419	3082	1606	-	1156	-
3c	-	3420	3061	1615	-	1153	-
3d	-	3447	3075	1600	-	1158	-
3e	-	-	3065	1610	-	1152	-
3f	-	-	3035	1604	-	-	-
3g	-	-	3064	1612	-	-	-

Percentages of DPPH radical scavenging activity was tabulated in Table 3. The *in vitro* scavenging assay of DPPH radicals was performed spectrophotometrically [19] with ascorbic acid as positive control (Figure 1). The percentage scavenging effects of the compound 3b at 100, 150, 200 µg/ml are 57.1, 64.8, 78.1 and compound 3d at 100, 150, 200 µg/ml are 51.1, 60.7, 71.4, respectively (Fig. 1). The percentage inhibition of the compound 3c at 100, 150, 200 µg/ml are 50.2, 60.4, 70.0, respectively. Ascorbic acid presented a scavenging effect of 98.2 % at the concentration of 200 µg/ml. The moderate inhibition of 3e and 3f showed 64.5 %, 63.8 % and 64.1 % at 200 µg/ml. Compounds, 3a and 3g exhibited lower inhibition.

Table-3: DPPH radical scavenging activity of the tested compounds

Compound	Scavenging effect (%)		
	Concentration of the tested compounds (µg/ml)		
	100	150	200
3a	30.1	40.5	48.8
3b	57.1	64.8	78.1
3c	50.2	60.4	70.0
3d	51.1	60.7	71.4
3e	42.2	54.8	64.5
3f	42.2	53.0	64.1
3g	30.2	40.0	48.3
Ascorbic acid	73.0	85.3	98.2

Electron donating hydroxyl group in 3b and 3d showed more antioxidant activity.[20] The hydroxyl group in 3b produces enhanced activity probably by *o*-position compared to the *p*-position in 3d. This indicates the positional requirement of hydroxy group on phenyl ring for enhanced activity. The compound 3c showed good radical inhibition activity due to the presence of hydroxyl group and methoxy group in the aromatic ring.[21,22] Compound 3g bear a methoxy groups, 3e bearing an electron donating ethoxy group at para position showed similar antioxidant activity. The aromatic ring system with halogens in 3a was found to be less active than 3g.

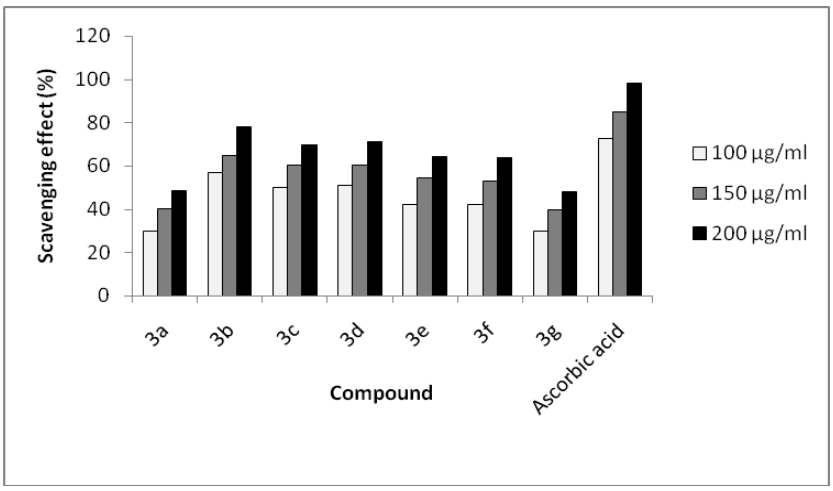


Fig. 1

CONCLUSION

In conclusion, a series of new 3,5-dimethoxyaniline derivatives 3a-g were prepared in good yield, characterized by different spectral studies and their antioxidant activity have been evaluated. Compounds 3b, 3c and 3d demonstrated good antioxidant activity. The structural activity relationship studies reveal that, the substituents on phenyl ring are responsible for antioxidant activity. On the basis of their activity, these derivatives were identified as viable leads for further studies.

This part of work has been published in ***Journal of Applicable Chemistry, 2014, 3 (5): 2131-2137***. In this article we have shown the antioxidant activities of **3,5-Dimethoxyaniline Derivatives.** All the compounds showed DPPH radical scavenging activity.

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Synthesis and characterization of chromium(III) complexes of 4(3*H*)-quinazolinone-derived Schiff base: Antimicrobial studies

Introduction

Transition metal complexes of Schiff bases have attracted much attention due to their potent biological activities such as antifungal, antibacterial, anticancer and herbicidal applications [1]. Investigations on the interaction between transition metal complexes and DNA have created interests due to their importance in cancer therapy and molecular biology [2].

In the present work, we describe the synthesis and antimicrobial, abilities of Cr (III) complexes with a Schiff base ligand derived from3-amino-2-methyl-4(*3H*)-quinazolinone.

Material and Methods

Chemicals used: 3-amino-2-methyl-4(3H)-quinazolinone and 2-benzofuran carboxaldehyde was obtained from Aldrich. Chromium(II) salts and solvents were commercially available of high purity.

Synthesis of 3-(isobenzofuran-1-ylmethyleneamino)-2-methylquinazolin-4(3H)-one (L)

A 1:1 equimolar solution of 3-amino-2-methyl-4(3*H*)-quinazolinone (0.350 g, 2 mmol) and 2-benzofuran carboxaldehyde (0.263 g, 2 mmol) were mixed in 30 mL methanol and gently heated for 3 h with constant stirring. The characteristic yellow precipitate of Schiff base obtained by condensation was filtered and crystallized using ethanol.

Yield: 83%, IR (nujol mulls, cm-1): 3088.4, 2924.5, 2161.8 (C-H), 1684.2 (C=O), 1597.0 (C=N), 1H-NMR (400 MHz, DMSO-d6) δ: 2.72 (s, CH3, 3H, C8), 8.9 (s, CH, 1H, N=CH-), 7.4-8.2 (m, Ar-H, 8H, Aromatic protons), Mass (m/z): 265 [M++1], Anal: Calcd. For C15H12N4O: C 68.18, H 4.28, N 21.22, Found: C 68.27, H 4.3, N 21.32 %. Based on these data, the following molecular structure has been assigned to the Schiff base (Figure 1).

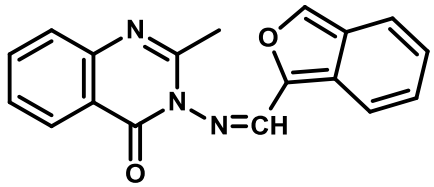


Figure1: Structure of 3-(isobenzofuran-1-ylmethyleneamino)-2-methylquinazolin-4(*3H*)-one (L).

Synthesis of metal complexes

The Cr(III) complexes of Schiff base ligand were prepared in 1:2 [metal:ligand] and 1:1:1 [metal:ligand:1,10-phenanthroline] ratios.

To a 20 ml hot methanolic solution of metal chloride (0.170 g, 1 mmol), Schiff base ligand solution was added (L, 2 mmol) to obtain 1:2 complex and a methanolic solution of 1,10-phenanthroline (0.198 g, 1 mmol) was added slowly in the presence of 1 mmol of L with continuous stirring to obtain 1:1:1 complex. The resulting mixture was stirred under reflux for 4 h to obtain the precipitated complex. It was collected by filtration, washed with hot water, then diethyl ether and dried in air.

Result and discussion

The Schiff base ligand was obtained by the 1:1 condensation of 3-amino-2-methyl-4(*3H*)-quinazolinone with 2-pyridine carboxaldehyde. The formation of the Cr(III) complexes was achieved by reaction of the ligand with Cr(III) salts in 1:2 [M:L] and 1:1:1 ratio. The analytical and physical data are presented in Table 1.

Table 1: Analytical and physical data of the Cr(III) complexes.

Compound	Molecular formula	Yield (%)	Calcd. (found), %				μ_{eff} B.M.	Molar conductance $\Omega^{-1}cm^2mol^{-1}$
			C	H	N	M		
1	$C_{36}H_{30}N_6O_6ClCr$	66	59.25 (59.49)	4.12 (4.17)	11.50 (11.91)	7.10 (7.27)	3.78	12.5
2	$C_{30}H_{25}N_5O_4ClCr$	61	59.40 (59.57)	4.12 (4.26)	11.55 (11.79)	8.58 (8.82)	3.75	14.2

IR spectra of Cr(III) complexes:

Important IR spectral bands of Cr(III) complexes.

Compound	ν(C=N)	ν(C=O)	ν(M-O)	ν(M-N)
L	1597	1684	---	---
1	1587	1642	467	565
2	1582	1648	474	537

Conductivity measurements

The molar conductance values of the Cr(III) complexes in DMF (10^{-3} M solutions) were measured at room temperature and the results are listed in Table 1. The conductance values of Cr(III) complexes fall in the range 14.5-12 $Ohm^{-1}cm^2mol^{-1}$, indicating the non-electrolytic nature of complexes (Geary 1971).

The electronic absorption spectra of the Schiff base metal complexes in DMF were recorded at room temperature. Both the complexes 1 and 2 exhibit an absorption band in the range 360-390 nm, which are assigned to charge transfer transition from the pπ-orbitals of the donor atoms to the d-orbitals of the metal. In addition, complexes exhibit d-d transition in the 617-724 nm range.

Biology activity

Antimicrobial activity

The data pertaining to the antimicrobial potential of ligand and its Cr(III) complexes are presented in Table 3. The ligand has poor activity against both bacteria and fungi. This activity may be due to the presence of imine group which imparts in elucidating the mechanism of transformation reaction in biological systems. The results indicate that the complexes show more activity than the ligand against same microorganisms under identical experimental conditions. This would suggest that the chelation could facilitate the ability of a complex to cross a cell membrane and can be

explained by Tweedy's chelation theory. All the test compounds show lesser activity than the standard antibiotics.

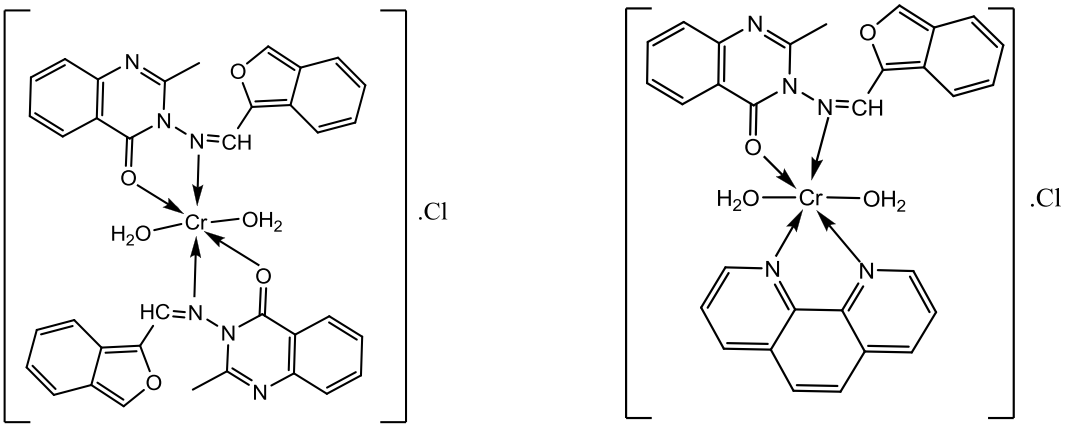
Table 3: Antimicrobial activity of Schiff base and its Cr(III) complexes.

Compound	Zone of inhibition (in mm)*			
	Antibacterial activity		Antifungal activity	
	S.aureus	*E.coli*	*A.niger*	*F.oxysporum*
L	07	09	03	07
1	18	19	16	23
2	21	23	19	27
Chloramphenicol	32	29	-	-
Griseofulvin	-	-	27	36

*average of three replicates

Conclusion

Based on the data obtained, following structures are assigned for the complexes.



1 **2**

Figure 3: Structures of chromium(III) complexes.

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Annexure-VIII

Submission of information on the final report of the work done on the project

1	Name and address of the Principal Investigator	Dr.B.K.Kendagannaswamy Assistant Professor, Dept.of Chemistry. JSS College of Arts, Commerce and Science Ooty road, Mysore-25
2	Name and address of the Institution	JSS College of Arts, Commerce and Science Ooty road, Mysore-25
3	UGC approval No and date	MRP(S)-1127/11-12/KAMY013/UGC-SWRO
4	Date of implementation	20-07-2012
5	Tenure of the Project	18 Months with Extension
6	Total grants released	Rs 1,50,000/-
7	Total grants received	Rs 1,42,000/-
8	Final expenditure	Rs 1.52,506/-
9	Title of the Project	**S**ynthesis and characterization of biologically active metal complexes
10	Objectives of the Project	Synthesis of ligands and synthesis of complexes. Characterization of the synthesized ligands and complexes. Study of the biological activity of the ligands and complexes
11	Whether the objectives were achieved	YES
12	Achievements from the Project	Two papers were published
13	Summary of the findings	Schiff bases have a significant role as ligands. The importance of Schiff bases and their metal complexes are important as biochemical, electrochemical, analytical, and redox catalysts. Apart from this they show antifungal and antibacterial activities as evident from the present work. The molecules synthesized were purified and they are characterized by IR and NMR. The molecules show very good antioxidant activity. The scope of the work is very large as we can synthesize still many more different ligands and complexes.
14	Contribution to the society	In the present project we have synthesized new series of ligands and metal complexes. These compounds (ligands) show good antioxidant property. The ligands which are synthesized can be used to synthesize metal complexes with other transition metals also.. So it is of great biological importance. The transition metal complexes play an important role in cancer therapy and molecular biology
15	Whether any Ph.D enrolled/ produced out of the project.	Students can be registered for their Ph.D. As soon as I get recognized as guide, from university of Mysore I will take up the work of guiding them using the ligands that I have synthesized for the formation of complexes with different metals.
16	No. of publications out of the Project	Two Papers published

Dr.B.K.KENDAGANNASWAMY
PRINCIPAL INVESTIGATOR

Prof.M.B.MALLIKARJUNA PANDITH
PRINCIPAL