Egypt. J. Chem. **Vol. 64,** No. 8 pp. 4191 - 4195 (2021)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Ex-vivo Antimalarial and *in-vitro* Biological Activities of newly synthesized Co(II) complex with Schiff base

C. Veeravel, K. Rajasekar, S. Balasubramaniyan, R. Selvarani,

PG & Research Department of Chemistry, Government Arts College, Rajaji Nagar, Ariyalur-621 713, Tamil Nadu, INDIA.
(Affiliated to Bharathidasan University, Tiruchirappalli-620024)

Abstract

The first-row transition metal complex of Schiff base has been synthesized and characterized based on physicochemical spectral and biochemical methods. The metal-ligand stoichiometry and molecular formula of the complex assessed by Elemental analysis and metal estimation-neutral, monomeric nature of the complex and paramagnetic nature also predict by the conductance and magnetic moment study. The octahedral environment around Co(II) and metal-imine bond as a whole predicted by atomic IR and Far-IR spectra. *In-vitro* antibacterial and antifungal activities of the Schiff base and its complexes compared with those for standard (Chloramphenicol & Fluconazole) by agar disc diffusion method. The *Ex-vivo* antimalarial activity of the Schiff base and its metal complex was found by using Plasmodium falciparum bacteria/fungal.

Keywords: Cinnamaldehyde; Aniline; ligand; Conductance; Chloramphenicol and Fluconazole

1. Introduction

Primary and opportunistic bacterial and fungal infections are severe to human health. The necessary production of antifungal compounds due to its need many research attentions to the derivatives of cinnamaldehyde[1]. presence of methoxyl group in the cinnamaldehyde and its derivatives to improve the antifungal activity[2,3]. Cinnamon oil is a nature antifungal substance. It is a main component of cinnamaldehyde. Cinnamaldehyde and its derivatives are mainly potent to anti-tumor and anti-diabetic properties, and also food additive and antimicrobial agent[4-6]. Schiff base are extensively studied in many areas like medicine, organic and inorganic due to thefact that C=N linkage is important in enhancing bio-potential activities[7,8]. In the present work we have proposed and characterized Co(II) complex of Schiff base. The cinnamaldehyde &aniline, condensed Schiff base were also assessed by biological activity *viz.*,antibacterial, antifungal and antimalarial.

Materials and Method

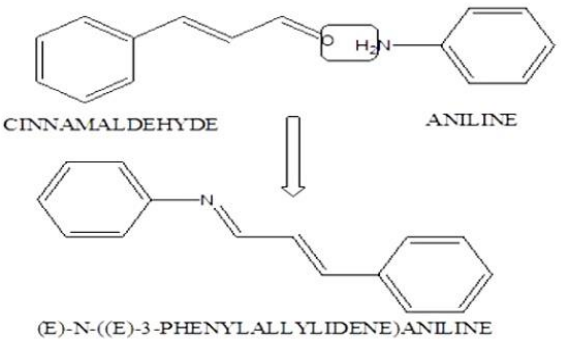
Material: All the reagents were of AnalaR grade used as such without further purification. Aniline, cinnamaldehyde, sodium oxalate were of AnalaR grade. Solvents such as methanol and ethanol were used as such without further purification.

Methods: The elemental analysis of the complex was carried out using (Thermo Finnegan make, Flash EA1112 series) CHNS(O) analyzer instrument. The molar conductance of 10^{-3} M complexes in acetonitrile was conducted using Systronic Conductivity Bridge at 300C. Absorption spectra of the Schiff base were obtained by solid state spectra (DRS-method) using JASCO model No:V-650 make UV-VIS spectrophotometer in the range of 200-800nm. The IR-spectra of Schiff base and its metal complex were recorded in the range of 4000-400cm^{-1}, using KBr pellet technique by Perkin Elmer spectrum, ONE-NO17-1159 Spectrometer. The Schiff base and its metal complex were carried out by antibacterial, antifungal, antimalarial & antioxidant activities.

*Corresponding author e-mail: *cveeravel.ml@gmail.com*, *yokkesh111@gmail.com*.
Receive Date: 26 December 2020, Revise Date: 12 February 2021, Accept Date: 18 April 2021
DOI: 10.21608/EJCHEM.2021.55320.3166

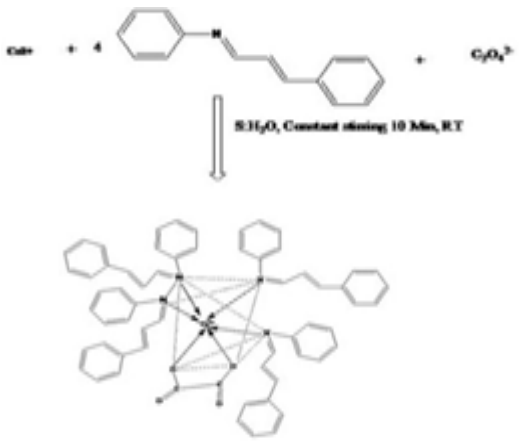
Synthesis of Schiff base: A solution of Benzenamine 0.462g (4.90 mmole) in 10 ml ethanol, 0.668g (5.05 mmole) of (2E)-3-phenylprop-2-enol in 10 ml Diethyl ether was mixed in a beaker, add a 15 ml water as a catalyst. The whole mixture was stirred for 10minutes at room temperature. The pale yellow precipitated powder was formed and then the reaction mixture was filtered, washed with water, dried in desiccators, kept in an airtight glass container. The Schiff base is soluble in ethanol.

Fig -1: synthesis of Schiff base



Synthesis of Co(II) complex: The Co(II) complex were synthesized by mixing the Schiff base ligand 2.849g (13.70 mmole) in 35ml ethanol with 1.0g (3.40 mmole) of metal nitrate in 10ml methanol and then sodium Oxalate 0.460g (3.40mmol) in 25ml water respectively was mixed and the whole mixture was stirred at 10min at a room temperature on a green route synthesize method 15 ml water as a catalyst. The precipitated brown-greenish colored complexes were filtered, washed with water and dried in desiccators and kept in an air tight glass container. The metal complex is soluble in ethanol.

Fig-2: Synthesis of metal complex



Result and Discussions

Elemental analysis: The prepared metal complex is colored; its melting point shows the stability of them. The carbon, hydrogen, nitrogen & oxygen in the ligand and its complexes were measured from elemental analysis. The values are confirmed by the molecular formula of the complex. It is further indicates that the metal and ligand ratio 1:1:1 for the Co(II) complex which is further confirmed by metal estimations by volumetric/colorimetric method. The Schiff base complexes are stable by air and moisture at room temperature. They are non-electrolyte, neutral in nature because they have low molar conductance. The physical properties such as Color, melting point, molar conductance values are given in the Table-1[9].

Mass spectrum of Schiff base:

The ESI mass spectrum fragmentation of Schiff base shows the m/z value at 207 indicating the formula and molecular weight of them, the other two m/z values of 115 and 89 indicating the fragment of $C_9H_8^+$ and $C_6H_7N^-$.

Electronic spectra: The electronic spectra of Schiff base shows the absorption bands in the region of 261 & 388 nm corresponding to n-π* and π-π* transitions confirmed by the presence of C=N bond.The absorption band of Co(II) complex exhibit three transitions at 519 nm , 388nm and 319 nm is due to three transitions $^4T_{1g} \rightarrow {}^4T_{2g}$, $^4T_{1g} \rightarrow {}^4T_{1g}(P)$ and $^4T_{1g} \rightarrow {}^4A_{2g}$ indicating the octahedral geometry of cobalt complex which is further confirmed by magnetic moment at 4.90 BM [10-12].

Infrared spectra:

The IR spectral data of the Schiff base and their complexes are summarized in table-3. The IR spectra of the ligands show characteristic >C=N bands at 1621cm^{-1} region which are shifted to higher frequencies in Co(II) at 1623 cm^{-1} which is confirmed the imine group (>C=N) coordinated to the metal ions through 'N' atom. The negative and positive shift of this band is an obvious indication of the involvement in the azomethine nitrogen atoms in complex formation. In the single aromatic at C-H band at 3053cm^{-1} which is present in the complex for higher frequencies at 3351cm^{-1}respectively, similarly aromatic C-C and aliphatic C-C frequencies are shifted to higher/lower frequencies in complexes, all these facts supported by coordination of ligands.

Table-1:Elemental analysis

S.	Complex/Ligand	%C	%H	%N	%O	%Metal
1	($C_{15}H_{13}N$)	86.30	06.27	06.75	-	-
		(86.01)	(06.45)	(07.00)		
2	$[Co(C_{15}H_{13}N)_4(C_2O_4)]$	76.22	05.32	05.70	06.55	06.00
		(76.09)	(05.31)	(05.69)	(06.54)	(06.10)

*Theoretical values are given in parenthesis

Table-2 :conductance and magnetic and spectral data

S.No	Complex/Ligand	Color	Melting Point (°C)	Yield (%)	Molar Conductance Ohm^{-1} cm^{2}mol^{-1}	μ_{eff} [BM]	λ_{max} (nm)
1	$C_{15}H_{13}N$	pale yellow	125	71.42	1.00	-	261 388
2	$[Co(C_{15}H_{13}N)_4(C_2O_4)]$	Pale pink	165	79.41	1.40	4.9	519 319 388

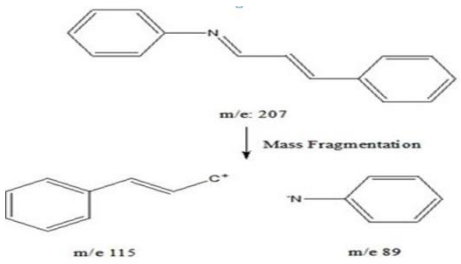


Fig - 3 mass Fragments

The appearance of bands at 473 cm^{-1}corresponding to the stretching vibration of M─N bond of imine group is coordinate to the metal ion. The bands at 350cm^{-1}and 326 cm^{-1}correspond to two M─O stretching vibrations oxalate ion coordinate to metal ion by bidentate mode[13-15].

Antibacterial and Antifungal activities

Antimicrobial assay: The newly synthesized compounds were screened for their antibacterial and antifungal activity against four bacterial strains namely *Escherichia coli* (MTCC 732), *Staphylococcus aureus* (MTCC 3160), *Bacillus subtilis* (MTCC 441) and *Pseudomonas aeruginos* (MTCC 1035) and *Candida Albicans* (MTCC 183), *Aspergillusniger* (MTCC 10180) for fungal strains were obtained from Microbial type culture collection (MTCC) at the institute of Microbial Technology (IMTECH), Chandigarh, India. The discs measuring 6.0 mm in diameter were punched from Whatman No.1 filter paper. Petri plates were prepared by pouring 30 ml of Nutrient agar (NA) medium and Potato dextrose agar (PDA) medium. The plates were incubated at 37 ºC for 24 hour for the bacteria and 48 hour. for fungal strains. Each sample was tested in triplicate. The Standard drug as Chloramphenicol for bacteria and Fluconazole for fungi separately. The zones of inhibition of the tested microorganisms by the samples were measured using a millimetre scale.The Schiff base ligand was less effective activate against for *E.coli, S.aures, B.subtilis, p.aeruginos* but the Cobalt complex has moderate activity again *E.coli* only otherwise has resistant[16-17].

Table-3

Bio-potential activities of the Schiff base complexe

Sample dose (100µl)	***E. coli* (mm)**	***S. aureus* (mm)**	***B. subtilis* (mm)**	***P.aeruginos* (mm)**	***C. Albicans* (mm)**	***A. Niger* (mm)**
Control	01.6	1.33	01.0	01.3	01.0	0.66
CV	09.0	08.6	07.6	08.4	07.1	06.8
V5	07.3	06.6	06.0	05.0	03.6	03.3
Std	15.6	15.0	14.3	14.8	13.6	13.4

Antimalarial activities: Ex vivo antimalarial activities at different concentrations (25, 50, 100, 200 and 400µg/mL) of Schiff base and Co(II) complex carried out, the result were compared with that from control groups treated with distilled water (containing dimethylsulfoxide 10%, as solvent of compound). The reference groups were treated with standard drugs (Chloroquine). Blood sample (group: O^+) with mono infection of *Plasmodium falciparum* was collected from malaria patient in citrate dextrose containing vial. The i.p. administrations of donor mice blood contain about 1×10^6 parasites induced Malaria infection in mice. Ex vivo study against *Plasmodium falciparum* were conducted by testing the compound into infected albino mice blood. The preparation of blood smears collected from tail of each mice at 24 hour. Parasitized erythrocytes of the blood sample films were determined by staining with Giemsa's stain. Three times of the treatments were conducted as replications. The results were observed as inhibition of parasitaemia in mice blood cells. The estimating the percentage of parasitaemia in a thin blood film is by expressing the number of infected cells as a percentage of the red blood cells. Decreased levels of parasitaemia and percentage of inhibition were expressed as antimalarial activity observed by calculating the parasitaemia percentage after 24 hour observation.

$$\text{Percentage parasitaemia} = \frac{\text{Total number of parasitized RBCs}}{\text{Total number of RBCs}} X\ 100$$

$$\text{Percentageof inhibition} = \frac{(\text{Parasitaemia of negative control} - \text{parasitaemia of treated group})}{\text{Mean parasitaemia of negative control}} X\ 100$$

The Schiff base produced parasitaemia reduction as compared to the negative control. However, only 400 µg/mL of Schiff base demonstrated lowest reduction (33.33%) of parasitaemia as compared to the respective negative control (63.88%) and the positive control of parasitaemia was 19.35%. The percentage inhibition was directly proportional to the concentrations.

The highest inhibition was 47.82 at 400 µg/mL while the lowest inhibition was 11.94 at 25µg/mL. The positive control inhibition was 69.70%. LC_{50} value of compound was 397.60 µg/mL[18].

Table-4 :Antimalarial activity of CV compound

S. No.	Concentrations (µg/mL)	Parasitaemia level (%)	Percentage (%) of inhibition
1	Negative control	63.88	0.00
2	Positive control (Chloroquine: 25µg/mL)	19.35	69.70
3	25	56.25	11.94
4	50	50.00	21.72
5	100	46.42	27.33
6	200	40.00	37.38
7	400	33.33	47.82
	LC_{50} (µg/mL)		397.67

Conclusion

The synthesized new transition metal complex of Co(II) with novel Schiff base complex prepared are stable under ordinary conditions. They are evaluating for their spectral and bio potential activities. It was possible to rationalize the trend in the biological data on the basis of specific structural properties of the examined complexes. Thus, the present findings are useful in advancing the efforts towards achieving a systematic prediction of the absolute biological effects in a rational way. Such information is currently in high demand to the biological and medicinal communities.

Reference

[1]. Khan.MSA, Ahmed.I,Antifungal activity of essential oils and their synergy with fluconazole against drug-resistant strains of Aspergillus fumigatus and Trichophytonrubrum, Appl. microbial. Biotechnolgy. 90, 1083-1094(2011).

[2]. Gan.F.F, Chua. Y.S, Scar magnani.S, palaniappan.P, Franks. M, poobalasingam.T, BradshawTD, Westwell .A.D. and Hagen. T, Structure–activity analysis of 20 -modified cinnamaldehyde analogues as potential anticanceragents,Biochem.Biophys.Res.coo municacation.387, 741-747(2009).

[3]. Babu.P.S, Prabuseenivasan.S, and IgnacimuthuS,Cinnamaldehyde—A potential antidiabetic agent, Phytomedicine.14, 15-22(2007).

[4]. Sharma.U. k, SoodS, Sharma.N, Rahi.P, Kumar. R, SinhaA.K, and gulatiA, Synthesis and SAR investigation of natural phenylpropenederivedmethoxylatedcinnama ldehydes and their novel Schiff bases as potent antimicrobial and antioxidant agents, Med.chem.ref.22, 5129-5140(2013).

[5]. QinS, XingK, JiangJ-H, Xu L-H &Li W.J,Biodiversity, bioactive natural products

and biotechnological potential of plant-associated endophyticactinobacteria, Apply.microbial.Biotecnol.89, 457-473(2011).

[6]. Feng K, Wen P, XangH,LiN, LouWY, Zony M.H and WuH, Enhancement of the antimicrobial activity of cinnamon essential oil-loaded electrospunnanofilm by the incorporation of lysozyme ,Rsc Adv.7,1572-1580(2017)

[7]. Pritiyadav ,Anjanasarkar and Amit Kumar, synthesis and biological activities of Schiff bases and their derivatives: a review of recent work,Journal of Basic and Applied Engineering Research. 6(1),62-65,(2019)

[8]. SadeekA.Sadeek,Synthesis,thermogravimetric analysis, infrared, electronic and mass spectra of Mn(II), Co(II) and Fe(III) norfloxacin complexes, Journal of molecular structure, 753(1-3), 1-12 (2005),

[9]. Carmen M, Sharaby, Preparation, characterization and biological activity of Fe(III), Fe(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and UO2(II) complexes of new cyclodiphosph(V)azane of sulfaguanidine, Spectrochimica Acta Part A62, 326–334(2005)

[10]. CottonFA, WilkinsonG, MurilloCA, BochmannM. Advanced in Schiff base chemistry. 6th Ed. New York: Wiley (1999)

[11]. Mustafa Dolaz, Vickie McKee, SerhanUrus, NecmettinDemir, Ali E. Sabik,MehmetTumer, Synthesis, structural characterization, catalytic, thermal and electrochemical investigations of bidentate Schiff base ligand and its metal complexes, Spectrochimica Acta Part A.76, 174–181(2010)

[12]. NzikayelS, AkpanIJ and AdamsEC, Synthesis, FTIR and Electronic Spectra Studies of Metal (II) Complexes of Pyrazine-2-Carboxylic Acid Derivative, Med Chem.7, 11(2017)

[13]. Mariana LoredanaDianu, Angela Kriza, NicolaeStanica and Adina Magdalena Musuc, Transition metal M(II) complexes with isonicotinic acid 2-(9-anthrylmethylene)-hydrazide, J. Serb. Chem. Soc.75(11), 1515–1531(2010).

[14]. RaiB. K, Vineeta Singh, Puja Sinha, VidyarthiS. N, ShashiBhushanSahi, Ashok Pandey and Amit, Synthesis and Characterization of Cobalt(II), Nickel(II) and Copper(II) Complexes with Nitrogen-Oxygen Donor Ligand, Oriental Journal Of Chemistry. 30,3(2014)

[15]. Khlood.Abou-MelhaS., Octahedral Co(II) and Ni(II) complexes of Schiff bases, semicarbazone and thiosemicarbazone, synthesis, biological, spectral, and thermal studies, Journal of Coordination Chemistry. 61(13), 2053–2067(2018)

[16]. ZahidH., Chohani,.ArifM, ZahidShafiq, Muhammad Yaqub, and Cclaudiu, SupuranT., In vitro antibacterial, antifungal & cytotoxic activity of some isonicotinoylhydrazide Schiff ’s bases and their cobalt (II), copper (II), nickel (II) and zinc (II) complexes, Journal of Enzyme Inhibition and Medicinal Chemistry. 21, 95–103,(2006)

[17]. Peter A. Ajibade and Gabriel A. Kolawole, Cobalt(III) Complexes of Some Antimalarial Drugs: Synthesis, Characterization, and in-vitro Antiprotozoal Studies, Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry. 40,273–278(2010)

[18]. Adediji J. Femi,JoshuaObaleye, Co(II) Complex of Mefloquine Hydrochloride: Synthesis, Antimicrobial Potential, Antimalaria and Toxicological Activities, E-Journal of Chemistry. 9, 4(2012).