OPEN ACCESS Freely available online

ISSN 2737-5323
Volume 2, Issue 3
https://www.iikii.com.sg/journal/AFM
Applied Functional Materials

Research Article

Novel Schiff Base Co(II) Complexes: Potential Biological Applications

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Received: Aug 22, 2022; **Accepted:** Sep 22, 2022; **Published:** Sep 30, 2022

Abstract: Cobalt (Co) complexes with the N_2O_2 category have been created synthetically by the reaction of salicylaldehyde / 3,4-diamino benzophenone with acetylacetone and glutaric anhydride respectively. The ligands and individual Cobalt (II) complexes were recognized through spectroscopical data (Fourier Transform Infrared, Ultra Violet-visible, proton and carbon-13 NMR, & Mass). Non-electrolytic in nature of the complex found from their molar conductivities ($\Omega^{-1}cm^2mol^{-1}$) in DMSO of 10^{-3}M solution. The ESR revealed the geometry of the complexes to be octahedral. The Schiff base Cobalt (II) complex was characterized by anticancer activity and cytotoxicity.

Keywords: Glutaric anhydride Anticancer activity, Cytotoxicity, Morphological study

1. Introduction

Nowadays, with the medicine resistance property of bacteria, cancer was becoming a major worldwide problem. Therefore, there was needed to design a suitable potent medicine that overcame resistance and was one of the most critical areas of research [1]. The massive literature reported that directed towards the growth of new chemical compounds to postpone or converse the development of cancer [2,3]. In our body, the biomolecules such as vitamins, enzymes, and amino acids were existing in the arrangement of a mutual ligand-metal (Fe, Cu, Co, and Mg) coordinated system [4]. There were biologically active against numerous pathogenic microorganisms and have enlarged applications and activities *in vivo* processes [5-7]. Cobalt (Co) was an organically energetic metal for living organisms. There have extensive applications in our bodies [8]. Although Co has excellent applications for living things, perhaps long exposure leads to toxicity towards tissue and cells [9]. At present, the investigation revealed that was offered probable medicinal privileges [10]. There was keeping in the assessment of these facts, the research was quintessence cobalt-based complexes for active applications.

2. Experimental

Most of the Chemicals were procured from Sigma- Aldrich and used. Cobalt nitrate hexahydrate was bought from E. Merck.

The potassium bromide pellets were used to study FTIR. Perkin Elmer Lambda 3B Spectrophotometer was used to study Ulta-violet - Visible spectra. Dimethyl sulphoxide (0.001 M) was used to find the Conductivity (Cell constant 1.05 cm^{-1}) at 25^0C through an Elico CM-180 Conductivity meter and Elico type CC-03 Conductivity cell. The NMR spectra of the ligand were recorded in Joel 500 MHz NMR spectrometer using DMSO-D6. The molecular weight of ligands was logged using JEOL GC hyphenated mass spectrophotometer. Gouy balance was used to study the magnetic susceptibility utilizing copper sulfate pentahydrate as a calibrant.

The surface morphological (SEM and EDX) studies were achieved on (Philips XL-30) functioning at 20 kV. Anticancer activity and cytotoxicity were recorded in the A549 cell line (Vero line for Cytotoxicity) attained from NCCS, Pune. The cells were kept alive in DMEM supplemented with 10% FBS, (100 U/ml of penicillin, and 100 g/ml of streptomycin) at 37 °C in a humidified environment containing 50 g/ml CO_2.

2.1. Preparation of Ligand L_1/L_2

A hot alcoholic solution of an equimolar mixture of acetylacetone / glutaric anhydride and salicylaldehyde were used to create Schiff base ligands (L1/L2). The content was assorted slowly with spontaneous stirring followed by the incorporation of an ethanolic solution of 3,4-diamino benzophenone. The temperature was upheld at 70^0C for 2.30 hours Con.HCl. The crystalline compound was extracted after cooling the substance for one day at 0^0C [11–13]. The ligands were separated by filtration, washed with ethanol, and then dried.

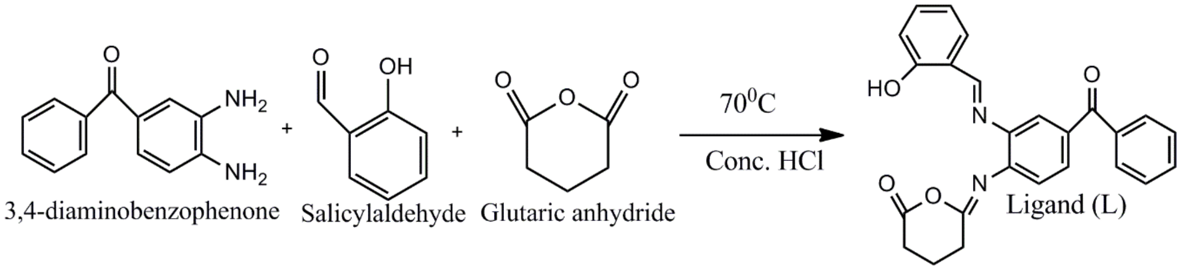
2.2. Preparation of metal complexes (ML_1/ ML_2)

In a round bottom flask, there made a hot alcoholic solution of Schiff base ligands (L1/L2) and metal salt in an equal molar mixture and refluxed at 70^0 C for 2.30 hours. The initial volume of the content was reduced by about one-fourth. Thus, the precipitate once formed subjected to workup using ethyl alcohol and dried over $CaCl_2$ [11-13]. The solubility of Cobalt complexes was plaid with different solvents. The complexes were insoluble in H_2O, $CHCl_3$, CCl_4, and CH_3CN moderately soluble in diethyl ether, alcohol, and spontaneously soluble in DMF and dimethyl sulphoxide.

3. Results

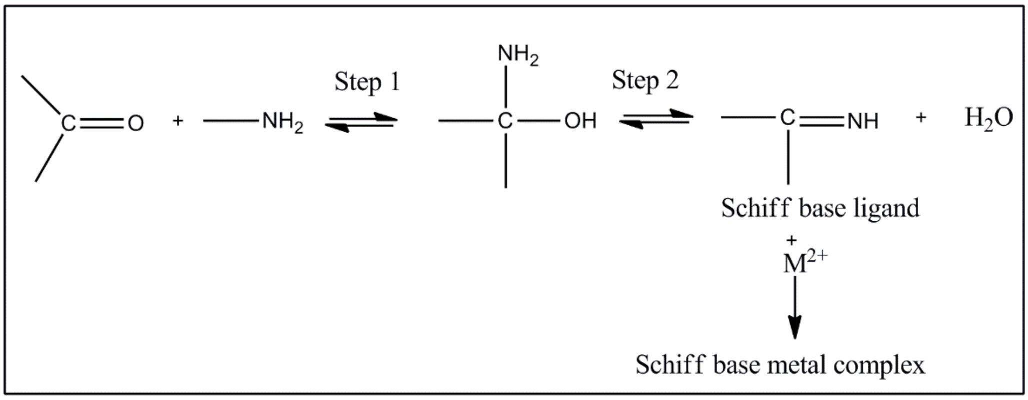
Salicylaldehyde-based metal complexes found that have extensive applications. The schematic representation of Scheme.1 was presented as follows.

3.1. Scheme.1 Schiff base ligands



Scheme.1 Preparation of ligand (L)

3.2. Scheme. 2: Preparation of Schiff base



Scheme. 2 Preparation of Schiff base

4. Discussion

4.1. ESI Mass spectra

The purity of two ligands L_1 and L_2 about 99 % has been confirmed by HPLC. Figure 1 and 2 represents the mass spectrum of the ligand (L_1 / L_2) with molecular ion peaks (M+) $m/z = 398$ and 412 correspondingly. A base peak of ligands was found that was 85% ($m/z = 315$) implying cationic species with three benzene ring-like structures. The results were determined by calculated and observed values.

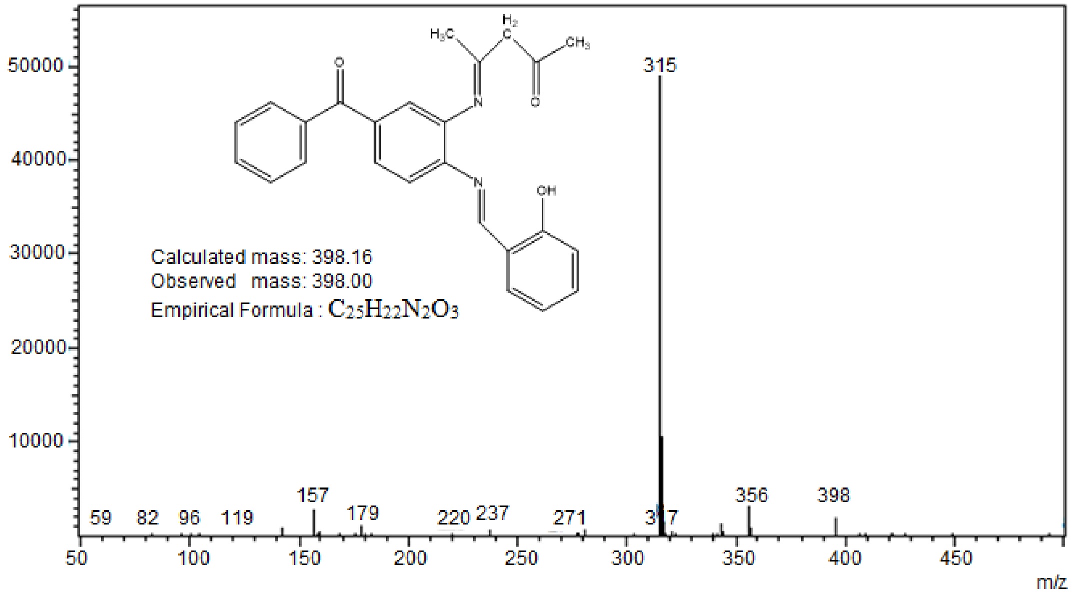


Figure 1: ESI Mass spectrum of Ligand (L_1)

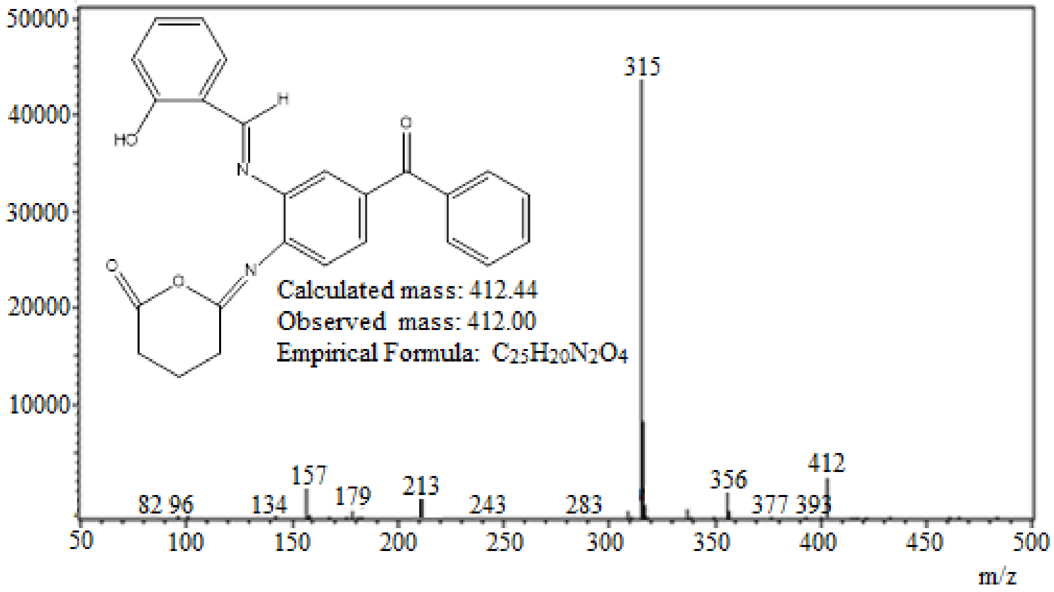


Figure 2: ESI Mass spectrum of Ligand (L_2)

4.2. FTIR spectroscopy

FTIR spectra of Schiff base ligands and Cobalt (II) complexes were displayed in Table 1. Accordingly, the stretching vibration ν(C=N) mode has appeared at 1530-1607cm^{-1}. FTIR spectrum of ligand exhibited characteristic stretching at 3291 cm^{-1} υ(–OH) [14-15], upon complexation, the observed band disappears which indicated the deprotonation of the phenolic –OH by metal complex. FTIR has shown that the hydrated complex was about 3420-3320 cm^{-1} [16] which was due to the significant coordination of water molecules in the υ (H_2O) cobalt complex. Metal-ligand coordination was further established by the appearance of moderate intensity peaks formed by (Co-N) bonds and (Co-O) bonds in the range of 465-478 and 522-536 cm^{-1}, respectively [17]. The Free nitrate existed in 1375-1390 cm^{-1} so nitrate did not coordinate with metal ions and was the escape layer of the complex [18].

Table 1: FTIR studies on Schiff Base and metal complex

Compound	Stretching C=N	Stretching (C-O)	Stretching (Co-N)	Stretching (Co-O)	Ionic nitrate
Ligand (L_1)	1607	1085	-	-	-
Ligand (L_2)	1547	1097	-	-	-
$[Co(L_1)(H_2O)_2](NO_3)_2$	1575	1090	475	536	1383
$[Co(L_2)(H_2O)_2](NO_3)_2$	1530	1102	465	536	1384

4.3. Electronic Spectra

The electron spectral information of the ligand demonstrated that the two absorption bands at 252, 345 nm were due to the π-π* transition to the azomethine chromosphere of L1, while 267, 350 nm were due to the n-π* transition of L2, respectively [19]. Due to the coordination of the nitrogen atom, the absorption band was red-shifted relative to the free ligand. Table 2 listed the electronic spectroscopic facts of the ligands and metal complexes.

4.4. NMR Spectra

^1H and ^{13}C NMR spectral data of ligands and Cobalt (II) complexes were illustrated in Table 3. ^1H NMR signals at 8.10 – 8.20 ppm related to Ph-CH=N [20]. A sharp multiplet signal at 7.03-7.81 ppm was Ph-H. A singlet corresponding to proton around 10.25-10.30 ppm was matched to Ph- OH. The chemical shift was detected for the OH protons in the ligands [21], however, there was not observed in the cobalt (II) complexes.

4.5. Molar conductance and Magnetic moment

Molar conductometric measurements of the cobalt complex in DMSO [22] (Table 2) indicated that the complex is non-electrolytic. Hence, the complexes were articulated as $[Co(L_1)(H_2O)_2](NO_3)_2$ and $[Co(L_2)(H_2O)_2](NO_3)_2$ where L_1 is (E)-4-((5-benzoyl-2-((E)-(2-hydroxybenzylidine) amino) phenyl)imino)pentan-2-one and L_2 was (E)-6-((4-benzoyl- 2-((E)-(2-hydroxybenzylidine)amino)phenyl)imino) tetrahydro-2H-pyran- 2-one. The magnetic moments of these two complexes at room temperature lie in the array of 4.98-5.09 B.M. There exhibited paramagnetism with three unpaired electrons slightly above the spin value. There was elucidated in terms of the expected orbital contributions of high spin states in the octahedral complex of cobalt ions [23].

Table 2: Physical and spectral parameters of metal complexes

Compound	Molar conductance $\Omega^{-1}cm^2mol^{-1}$	Color	M.P (°C)	Yield (%)	Λ max (nm)
Ligand(L_1)	-	White	237	68	252, 345
Ligand(L_2)	-	White	221	62	267, 350
$[Co(L_1)(H_2O)_2](NO_3)_2$	16.23	Brown	>300	82	268, 365, 462, 535
$[Co(L_2)(H_2O)_2](NO_3)_2$	18.40	Brown	>300	80	270, 368, 425, 550

Table 3: NMR Spectra of Cobalt complexes

Compound	^{1}H NMR			^{13}C NMR		
	Ar-OH	CH=N	H_2O	C=O	CH=N	C-CH_2
Ligand(L_1)	10.30	8.10	-	195.5	158.4	40.5
Ligand(L_2)	10.25	8.20	-	195.9	158.4	40.5
$[Co(L_1)(H_2O)_2](NO_3)_2$	-	8.02	4.80	195.6	158.7	48.5
$[Co(L_2)(H_2O)_2](NO_3)_2$	-	8.06	4.20	195.9	157.5	40.5

4.6. Surface morphological study

The identification and determination of the speciation of macrocyclic complexes were undoubtedly established by SEM-EDX. The SEM image of the Cobalt (II) complex of ligand (L_1) has shown that the cobalt complex particles have a sponge-like rock morphology, as shown in Figure 3. The surface morphology of the cobalt complex of the ligand (L_2) was found to be a single-phase morphology, as shown in Figure 4.

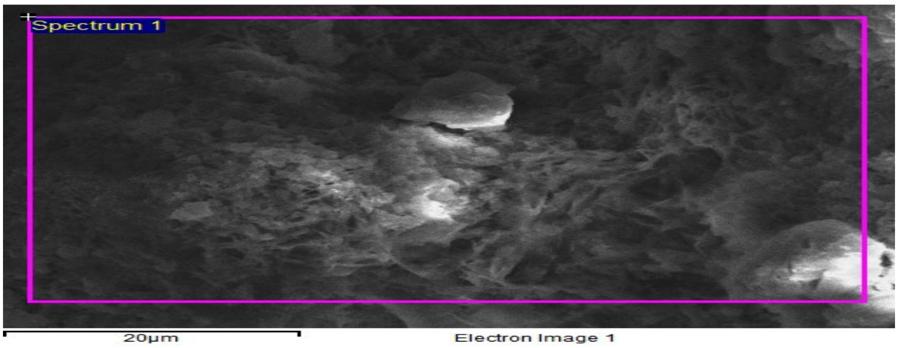


Figure 3: Scanning Electron Microscope image of Cobalt complex of (E)-4-((5-benzoyl-2-((E)-(2-hydroxybenzylidene)amino) phenyl)imino) pentane-2-one

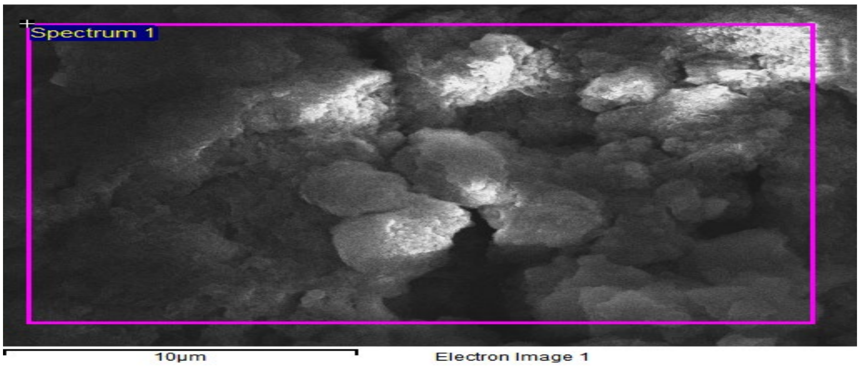


Figure 4: Scanning Electron Microscope image of Cobalt complex of (E)-6-((4-benzoyl-2-((E) (hydroxyl benzylidine) amino)phenyl) imino) tetrahydro-2H-pyran-2-one

There was chemical analysis using EDX of the complex indicated a homogeneous distribution between cobalt and ligand. The peaks of the EDX curves of the cobalt complexes of L_1 and L_2 were shown in Figure 5 and Figure 6, respectively. Research has shown no contamination. In the complex, the elements were consistent with the planned structure, which was related to the perfect combination of elements such as Co, C, N, O, and H constituting the complex, demonstrating the proposed composition.

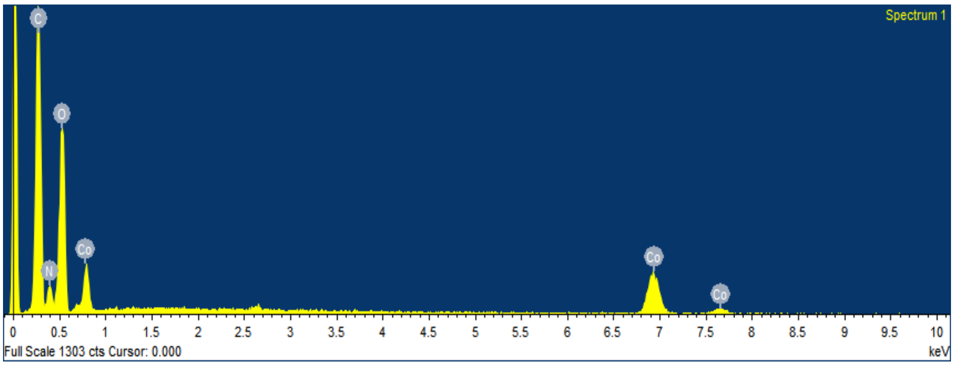


Figure 5: EDX spectrum of Cobalt (II) complex of (E)-4-((5-benzoyl-2-((E)-(2-hydroxybenzylidene)amino)phenyl)imino) pentane-2-one

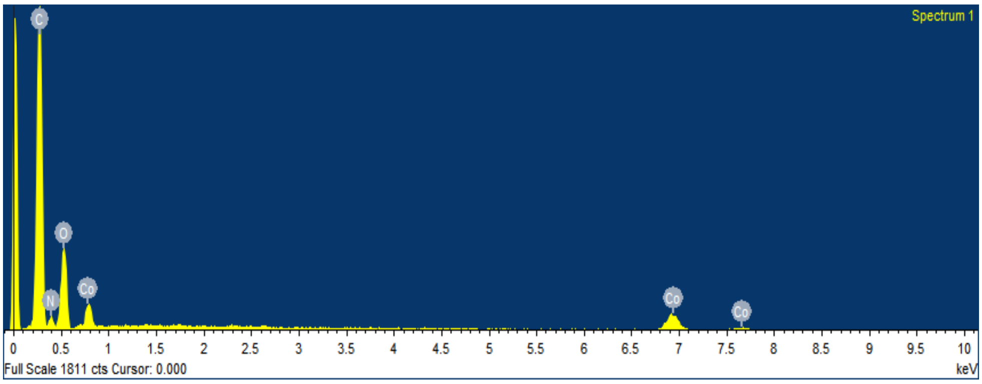


Figure 6: EDX spectrum of Cobalt (II) complex of (E)-6-((4-benzoyl-2-((E) (hydroxybenzylidine) amino)phenyl) imino) tetrahydro-2H-pyran-2-one

4.7. Anticancer behavior

The anticancer activity of the investigation (L_1 and L_2) and their Cobalt (II) complexes were determined against the A549 lung cancer cell line. A 549-cancer cell- line after 24 hours of drug action using crystal violet dye requisite assay. The cells and complex compounds were prepared as per the standard procedure and found the absorbance at 570 nm.

Figure 7, there indicated that the IC 50 value of Cobalt (II) complex of ligand (L_1) at numerous concentrations like 7.8, 15.6, 31.2, 62.5, 125, 250, 500 1000 µg/ml were observed at 57.67, 50.92, 43.35, 35.22, 29.14, 23.27, 15.49 and 7.87 %. As per ISO 10993-5:2009, the Cobalt complex has 57.67% cell viability at the lower concentration of 7.8 µg/ml. Hence, there was non-toxic. The morphological images of the Cobalt complex have been displayed in Figure. 8.

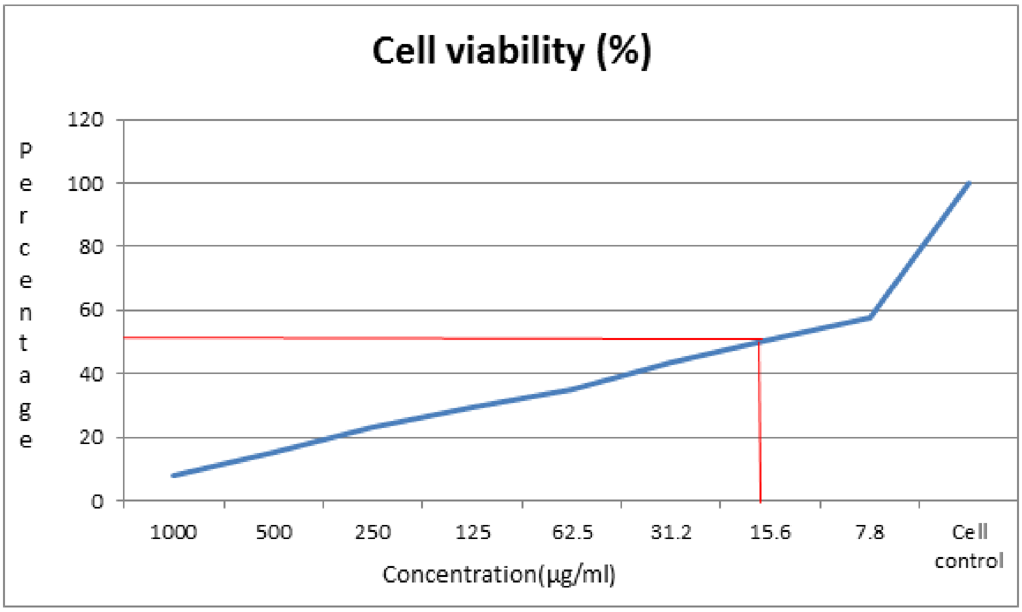
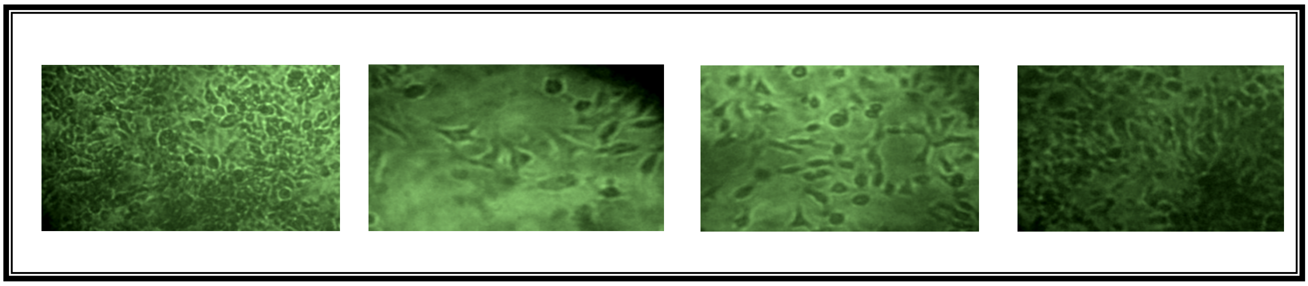


Figure 7. IC50 Values of the Cobalt (II) complex of ligand (L_1) against A549 cell line



Normal A549 Cell line **Toxicity – 1000µg/ml** **Toxicity – 15.6 µg/ml** **Toxicity – 7.8µg/ml**

Figure 8. Morphological images of anticancer effect of Cobalt (II) complex of ligand (L_1) on *A549 cell* line

4.8. Cytotoxicity

The cytotoxicity of the Cobalt (II) complex of ligand (L_1) was appraised in the Vero cell line with the MTT assay. For the Cobalt complex, the IC50 value was illustrated in Figure 9. Based on the MTT assay, cell viability was found to be 98.88, 93.48, and 87.79% at the listed complex concentrations of 7.8 µg/ml, 15.6 µg/ml, and 31.2 µg/ml. The concentrations were considered non-toxic compositions, as increasing concentrations indicated a tendency towards moderate cytotoxicity [24-25]. Figure 10 has showed the morphologic images of the cytotoxicity effect of the Cobalt complex of ligand (L_1).

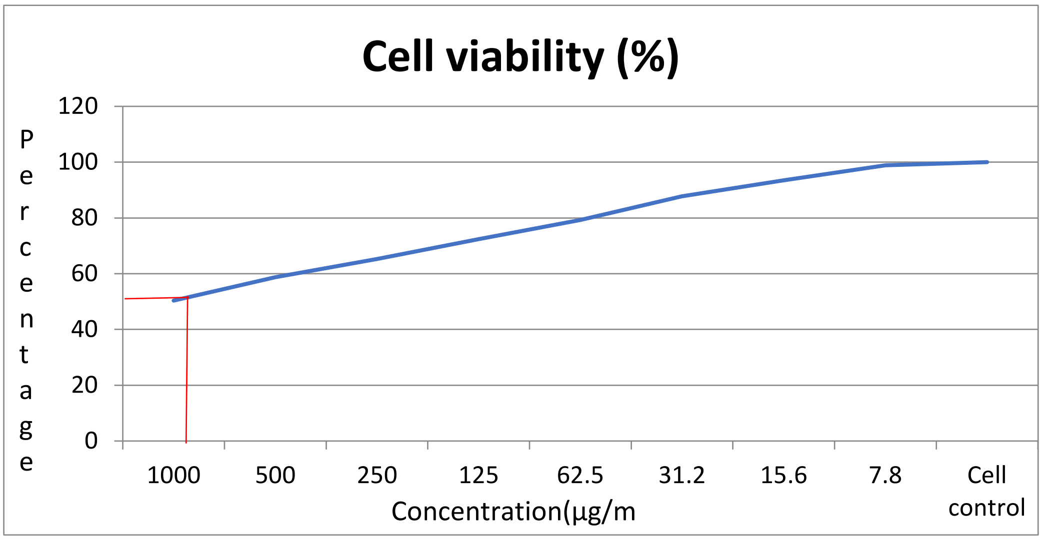
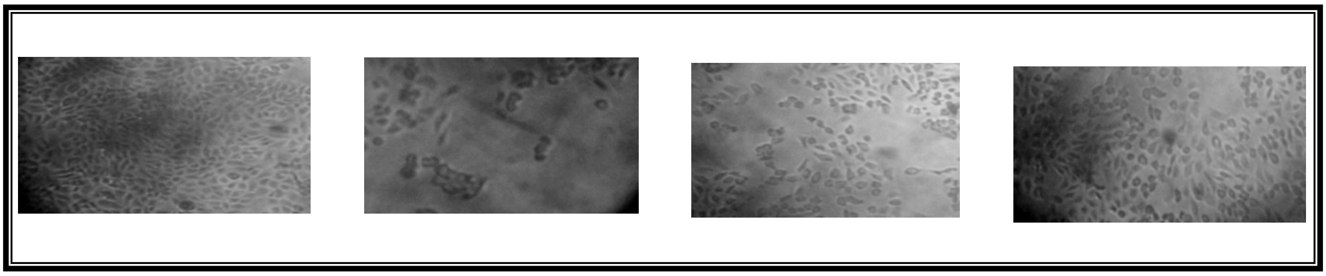


Figure 9. IC50 Values of the Cobalt (II) complex of ligand (L_1) on Vero cell line



Normal Vero Cell line **Toxicity – 1000µg/ml** **Toxicity – 62.5 µg/ml** **Toxicity – 7.8µg/ml**

Figure 10: Morphological images of Cytotoxicity effect of Cobalt (II) complex of ligand (L_1) on *Vero cell* line

5. Conclusions

The research highlights compounds that were environmentally friendly, simple, have short reaction times, was thermally stable, and have high product yields. The current research was divided into physical research and spectroscopic research. Analytical evidence confirmed the presence of only one cobalt (II) ion in L_1 and L_2. Electronic and magnetic studies reveal the octahedral geometry of Co (II) complexes. These cobalt complexes were found to be non-electrolytic. The cobalt (II) complex of the ligand (L_1) was non-toxic based on cell viability.

Supplementary File: It is available online at www.iikii.com/afm

Author Contributions: The author, Dr.A.P. Arumugam has contributed to the synthetic aspects of the present investigation. Dr.G Elango, who had been the key source of arrangement of laboratory, chemicals, and synthetic ideas in the capacity of research guide of Dr.A.P.Arumugam. The corrections carried out and uploading editing of the entire work have been done by Dr.S. Guhanathan in the capacity of a doctoral member of Dr.A.P.Arumugam.

Funding: “This research did not receive external funding”.

Acknowledgment: The authors are thankful to Government Arts College, Tiruvannamalai for providing lab facilities to carry out the experiments. The authors also thank the various research institutes for spectral and other instrumental studies.

Conflicts of Interest: Certify that no conflict of interest.

References

1. Arumugam A.P, Guhanathan S and Elango, Co (II), Ni (II) and Cu (II) Complexes with Schiff Base Ligand: Syntheses, Characterization, Antimicrobial Studies and Molecular Docking Studies, *SOJ Materials Science & Engineering* **2017,** 5(2): 1–12, (DOI: http://dx.doi.org/10.15226 /sojmse.2017.00149)
2. Airley, R., Cancer Chemotherapy: Basic Science to the Clinic. Wiley-VCH 2009; pp 342–343.
3. Davis, K.J.; Richardson, C.J.; Beck, L.; Knowles, B.M.; Guédin, A.; Synthesis, and characterization of nickel Schiff base complexes containing the meso-1,2-diphenylethylenediamine moiety: selective interactions with a tetramolecular DNA quadruple. *Dalton Trans*. **2015,** *44*: 3136–3137.
4. Finney, L.A.; O'halloran, T.V., Transition metal speciation in the cell: insights from the chemistry of metal ion receptors. *Science* **2003,** *300*: 931–936.
5. Yang, P.; Kong, X.; Cheng, C.; Li, C.; Yang, X., Synthesis and biological evaluation of 8-substituted and deglucuronidated scutellarin and baicalin analogues as antioxidant responsive element activators. *Science China Chemistry*, **2011,** *54*: 1565.
6. Patil, S.S.; Thakur, G.A.; Shaikh, M.M., Synthesis, characterization, and antibacterial studies of mixed ligand dioxouranium complexes with 8-hydroxyquinoline and some amino acids. ISRN Pharm. **2011**; 2011:168539. doi: 10.5402/2011/168539. Epub 2011 Sep 27. PMID: 22389843; PMCID: PMC3263721.
7. El-Sherif, A.A.; Shehata, M.R.; Shoukry, M.M.; Barakat, M.H., Thermodynamic investigation and mixed ligand complex formation of 1, 4-Bis-(3-aminopropyl)- piperazine and biorelevant ligands. *Bioinorganic Chemistry and Applications*, **2012**. pp 1-10
8. Ahmed, K.; Yasmin, F.; Hussain, N., Green synthesis of nickel nanoparticles by using plant leaf extract as reducing agent. *Science International,* **2016,** *28*: 2511.
9. Chang, E.L.; Simmers, C.; Knight, D.A., Cobalt complexes as antiviral and antibacterial agents. *Pharmaceuticals* **2010**, *3*: pp1711-1728.
10. Xiao, Y.; Yuen, J., The biological application of cobalt. In: Cobalt: Characterizatics, Compounds and Applications. Nova Science Publishers, **2011,** pp: 307-317
11. Rayees, A.S.; Ismail, A.R.; Maqsood, A.M.; Norhayati, L.; Sam'an, M.M.; Shaeel, A. Al-T., Transition Metal Complexes with Mixed Nitrogen-Sulphur (NS) Donor Macrocyclic Schiff Base Ligand: Synthesis, Spectral,Electrochemical and Antimicrobial Studies, *Int. J. Electrochem. Sci*., **2013**, *8*; pp 6972–6987.
12. Mozaffar Asadi, Hajar Sepehrpour and Khosro Mohammadi., J. Serb. Chem. Soc. **2011,** 76 (1) pp 63–74
13. Nagajothi, A.; Kiruthika, A.; Chitra, S.; Parameswari, K.; "Synthesis and characterization of tetradendate Co(II) Schiff base complexes – imicrobial and DNA cleavage studies" *Int. J. of Research in Pharmaceutical and Biomedical Sciences*, **2012**, *3*(4), pp.1768–1778. (https://www.yumpu.com/en/document/read/28384857/schiff-base-complexes-international-journal-of-research-in-)
14. Anwar, Z.M.; Sung, Y.K. Synthesis and solution properties of La(III)-N-ethylmorpholine complex. *Chem. Soc*. **2011**; *76*: pp. 249–261.
15. Gulcan, M.; Sonmez, M.; Berber, I., Synthesis, Characterization and antimicrobial activity of a new pyrimidine Schiff base and its Cu(II), Ni(II), Co(II), Pt(II) and Pd(II) complexes. *Turk J. Chem*. **2012**; *36*: pp.189–200.
16. K. Sathish Kumar, Vijay Kumar Chityala, N. J. P. Subhashini, Y. Prashanthi, undefined Shivaraj, "Synthesis, Characterization, and Biological and Cytotoxic Studies of Copper(II), Nickel(II), and Zinc(II) Binary Complexes of 3-Amino-5-methyl Isoxazole Schiff Base", *International Scholarly Research Notices*, *2013*, Article ID 562082, 7 pages, **2013**. https://doi.org/10.1155/2013/562082.
17. Bhagat, T.M.; Swamy, D.K.; Deshpande, M.N., *J. Chem and pharm Research*, **2012,** *4*, pp. 100–104,
18. Nakamoto. K, Infrared spectra of Inorganic and Coordination Compounds, Wiley Intern science, New York, **1970** pp. 90.
19. Azza A. A. Abou – Hussein, Wolfgang, L., Synthesis, spectroscopic, coordination and biological activities of some organometallic complexes derived from thio-Schiff base ligands, Spectrochimica Acta (A), 2012, 95, pp. 596–609.
20. Usharani, M.; Akila, E.; Jayaseelan, P.; Rajavel, R., Structural Elucidation of Newly Synthesized Potentially Active Binuclear Schiff Base Cu(II), Ni(II), Co(II) and Mn(II) Complexes using Physicochemical Methods, *International journal of scientific & Engineering Research*, **2013,** *4*, pp. 1055–1064
21. Mozaffar, A.; Hajar, S.; Khosro, M., Tetradentate Schiff base ligands of 3,4-diaminobenzophenone: Synthesis, characterization and thermodynamics of complex formation with Ni(II), Cu(II) and Zn(II) metal ions. J. Serb. Chem. Soc,**2011,** *76* (1), 63–74
22. Seema. I Habib, S.; Shah N. N.; Mohammed, A.B.; Praffullkumar, A.K., Synthesis and Characterization of Cobalt (II), Nickel (II), and Copper (II) Complexes of Some 2'- Hydroxychalcones *J. Chem. Pharm. Res*., **2011**, *3*(1): 788–792.
23. Vinay Kumar, B.; Bhojya Naik, H.S.; Girija, D.; Sharath, N.; Pradeepa, S.M.; Joy Hoskeri, H.; Prabhakar, M.C. Synthesis, DNA-binding, DNA-photonuclease profiling and antimicrobial activity of novel tetra-aza macrocyclic Ni(II), Co(II) and Cu(II) complexes constrained by thiadiazole, *Spectrochimica Acta*, **2012,** A 94 pp. 192–199.
24. Selvaraj, V.; Bodapati, S.; Murray, E.; Rice, K.M.; Winston, N.; Shokuhfar, T.; Zhao, Y.; Blough, E., Cytotoxicity and genotoxicity caused by yttrium oxide nanoparticles in HEK293 cells, *International Journal of Nanomedicine*, **2014,** *9*, pp. 1379–91

25. Kodisundaram, P.; Duraikannu, A.; Balasankar, T.; Pravin, S.A.; Roy, K., Cytotoxic and Antioxidant Activity of a Set of Hetero Bicylic Methylthiadiazole Hydrazones: A Structure-Activity Study, *Int J Mol Cell Med*. **2015** *4*(2): pp.128–137.

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