IJPSR (2020), Volume 11, Issue 2 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 24 April 2019; received in revised form, 18 August 2019; accepted, 27 January 2020; published 01 February 2020

SYNTHESIS, CHARACTERIZATION, BIOLOGICAL AND FLUORESCENT BEHAVIOUR OF METAL (II) COMPLEXES WITH PYRAZOLINE DERIVATIVES

T. M. Sharmila

Department of Chemistry, Noorul Islam Centre for Higher Education, Kumaracoil - 629180, Tamil Nadu, India.

Keywords:

Hydroxynapthalene, Binding, Antioxidant, Screening, Fluorescent

Correspondence to Author:
T. M. Sharmila

Department of Chemistry, Noorul Islam Centre for Higher Education, Kumaracoil - 629180, Tamil Nadu, India.

E-mail: josephniche@gmail.com

ABSTRACT: Novel metal complexes of ligands of pyrazoline derivatives were synthesized by the condensation of 1-acetyl-2-hydroxynapthalene and indole-3-carboxaldehyde followed by the condensation of substituted phenylhydrazine. They were characterized by elemental analysis, IR, 1H-NMR, UV-Vis., molar conductance, magnetic susceptibility measurements and electrochemical studies. Based on the magnetic moment and electronic spectral data, square planar geometry has been suggested for metal complexes. The binding behavior of the complexes with calf thymus DNA has been investigated by electronic absorption spectra and cyclic voltammetry techniques. The DNA binding constants reveal that all these complexes interact with DNA through intercalation binding mode. Superoxide dismutase and antioxidant activities of the copper complexes have also been studied. The antioxidant activities of the complexes showed higher activities. Fluorescent studies reveal that the absorption band is shifted towards visible region indicates that the pyrazoline derivatives of metal complexes may exhibit different emission with respect to suitable substituent present in the pyrazoline structural core. Naphthyl group is responsible for the green colour emission due to its conjugation and electronic delocalization within the molecule and leads to longer wavelength.

INTRODUCTION: Metal-containing compounds/ complexes offer many distinct advantages over traditional organic *i.e.*, carbon-based compounds in the development of new medicinal lead molecules due to their capability to coordinate ligands/organic molecules [1-6].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.11(2).947-54

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.11(2).947-54

This synthetic tailor made approach was utilized to organize two or more structural fragments into one molecule with novel mode of drug actions.

Metal-based complexes offer a wealthy environment to build up with a variety of biologically significant molecular structures and provide wide spectrum of coordination numbers and geometries, as well as kinetic properties that are essential for prediction of molecular or drug mechanism [7-9]. The Cu/ Zn-SOD is a vital enzyme in the antioxidant profile which catalyzes the conversion of superoxide ion into hydrogen peroxide and oxygen molecule [10-11].

Till now, the direct usage of Cu/Zn-SOD as therapeutic agent has arrived many problems is due to instability, solubility, digestion *etc*. Therefore, considerable efforts on Cu/Zn-SOD bio-mimics of low molecular weight copper complexes have been synthesized due to the advantages of greater *in-vivo* stability, solubility, membrane penetration and delivery of metal ions to the desired site [12].

The copper (II) complexes of heterocyclic planar ligands containing nitrogen donor atoms have studied as SOD mimic agents due to their redox behaviour, flexible conformation and stability [13]. The planar rigid system of organic molecules in particular heterocyclic molecules was developed as ligands [14]. Pyrazole and pyrazoline moiety have fascinated much more attention due to their wide range of biological activities. Pyrazolines are nitrogen heterocycles have received considerable attention in many years due to their utility as lead molecules and exhibited wide range of bioactivities [15]. Nitrogen heterocycles have studied for their synthetic and biological activities and exciting as drug molecules in market and clinical trials. In the present study has focused on the synthesis, characterization and biological studies of metal complexes of pyrazoline derivatives.

EXPERIMENTAL SECTION: All chemicals and solvents were analaR grade and were purchased from Merck. All supporting electrolyte solutions were prepared using analytical grade reagents. Calf thymus DNA purchased from Genie Biolab, Bangalore, India.

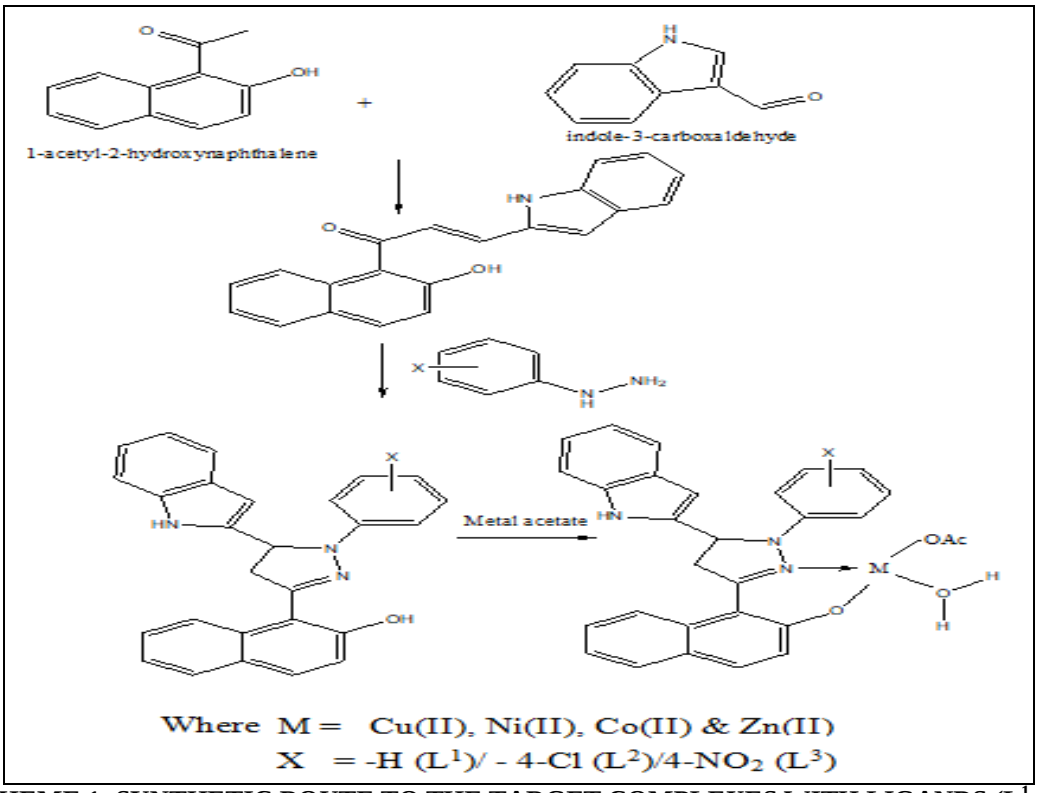
Instrumentation: The amount of metal content present in the metal complexes was estimated using ammonium oxalate method. Elemental analysis of ligands and their metal complexes were carried out using Elementar Vario EL III. Molar conductance of the complexes was measured using a coronation digital conductivity meter. The ^{1}H-NMR spectra of the ligands were recorded using TMS as internal standard. Chemical shifts are expressed in units of parts per million relative to TMS. The IR spectra of the ligands and their metal complexes were recorded on a Perkin-Elmer 783 spectrophotometer in 4000-200 cm^{-1} range using KBr disc. Electronic spectra were recorded in a Systronics 2201 Double beam UV-Vis., spectrophotometer within the range of 200-800 nm regions. Magnetic moments were measured by Guoy method and corrected for diamagnetism of the component using Pascal's constants. Cyclic voltammetry was performed on a CHI 604D electrochemical analyzer with three electrode system of glassy carbon as the working electrode, a platinum wire as auxiliary electrode and Ag/AgCl as the reference electrode. Tetrabutylammonium perchlorate (TBAP) was used as the supporting electrolyte. Solutions were deoxygenated by eradication with N_2 previous to measurements. The interactions between metal complexes and DNA were studied using electrochemical and electronic absorption techniques. The pyrazoline derivatives bearing indole and naphthyl moieties were synthesized in two stages. In the first stage, the ethanolic solution of 1-acetyl-2-hydroxynapthalene and indole-3-carboxaldehyde was mixed together in the presence of sodium hydroxide and continuous stirring for 4 h. The precipitate (chalcone) was observed in the reaction vessel and washed with cold water. Then, it was recrystallized from ethanol. In the second stage, the hot ethanolic solution of chalcone (0.01 M) and phenylhydrazine (0.01 M) L^1/- 4-chloro L^2/- 4-NO_2 L^3 with NaOH was refluxed for 6 h. The resulting solution was poured into cold water. The observed precipitate was filtered, dried and recrystallized from methanol. The synthetic route to the target compounds is outlined in **Scheme 1**.

DNA Binding Studies: The binding interactions between metal complexes and DNA were studied using electrochemical and electronic absorption methods by using different concentrations of CT-DNA. Calf thymus DNA was stored at 4 °C. The DNA stock solutions were prepared with buffer solution (50 mM Tris-HCl at pH 7.2). The stock solutions of the complexes were prepared by dissolving copper complexes in DMSO and diluting with the corresponding buffer to the required concentration for all experiments. This resulted in a series of solutions with varying concentrations of DNA but with a constant concentration of the complex. The absorbance (A) of the most red-shifted band of complex was recorded after each successive additions of CT DNA. The intrinsic binding constant, K_b, was determined from the plot of [DNA]/(ε_a- ε_f) *vs.* [DNA], where [DNA] is the concentration of DNA in base pairs, ε_a, the apparent extinction coefficient

which is obtained by calculating A_{obs}/[complex] and ε_f corresponds to the extinction coefficient of the complex in its free form. The data were fitted to the following equation where ε_b refers to the extinction coefficient of the complex in the fully bound form.

$$[DNA]/(\varepsilon_a - \varepsilon_f) = [DNA]/(\varepsilon_b - \varepsilon_f) + 1/K_b(\varepsilon_b - \varepsilon_f) \quad \text{---------- (1)}$$

Each set of data, when fitted to the above equation, gave a straight line with a slope of $1/(\varepsilon_b - \varepsilon_f)$ and a y-intercept of $1/K_b(\varepsilon_b - \varepsilon_f)$. K_b was determined from the ratio of the slope to intercept.



SCHEME 1: SYNTHETIC ROUTE TO THE TARGET COMPLEXES WITH LIGANDS (L^1-L^3)

Antioxidant Assay:

Superoxide Dismutase Activity (SOD): The superoxide dismutase activity (SOD) of the copper complexes were evaluated using alkaline DMSO as source of superoxide radicals ($O_2^{\bullet-}$) generating system in association with nitro blue tetrazolium chloride (NBT) as a scavenger of superoxide. Add 2.1 ml of 0.2 M potassium phosphate buffer (pH 8.6) and 1 ml of 56 µl of NBT solutions to the different concentration of copper complex solution. The mixtures were kept in ice for 15 min and then 1.5 ml of alkaline DMSO solution was added while stirring. The absorbance was monitored at 540 nm against a sample prepared under similar condition except NaOH was absent in DMSO.

Hydrogen Peroxide Assay: A solution of hydrogen peroxide (2.0 mM) was prepared in phosphate buffer (0.2 M, 7.4 pH) and its concentration was determined spectrophoto-metrically from absorption at 230 nm.

The complexes of different concentration and vitamin C (100µg/ml) were added to 3.4 ml of phosphate buffer together with hydrogen peroxide solution (0.6 mL). An identical reaction mixture without the sample was taken as negative control. The absorbance of hydrogen peroxide at 230 nm was determined after 10 min against the blank (phosphate buffer).

Antimicrobial Activities: The *in-vitro* antimicrobial activities of the investigated compounds were tested against the bacterial species. Sterile Muller Hinton Agar plates were prepared poured and overnight cultures of bacterial pathogens were swabbed on it. The discs were prepared by using Whatman no. 1 filter paper. The disc size of about 6 mm diameter was made using disc paper puncher. The filter discs were sterilized and stored in its dried form. About 100 µl of copper complexes were poured over the sterile filter paper disc and kept for drying in hot air oven at 45 ºC for

2 h. Muller Hinton Agar plates were prepared and overnight bacterial pathogens broth culture was swabbed on the surface of the agar media. The culture filtrate loaded discs were placed aseptically on the surface of the agar using a disc dispenser or a sterile forceps. The plates were incubated at 37 ºC for 24 h. The inhibitions around the antibiotic discs were measured after incubation.

RESULTS AND DISCUSSION: The preparation of pyrazoline derivatives (L^{1-3}) and their metal complexes are given in **Scheme 1**. The chalcone(s) were formed by the condensation reaction of hot ethanolic solution of 1-acetyl-2-hydroxy-naphathalene and indole-3-carboxaldehyde with sodium hydroxide. The obtained chalcone was reacted with substituted phenylhydrazine undergoes cyclization in the presence of base leads to the formation of pyrazoline derivatives. It was transferred into a crushed ice, the coloured solid was formed and isolated by filtration process. It was purified by column chromatographic technique. They are crystalline solids and soluble in DMSO. The formation of product was confirmed by single spot in the TLC. This confirms the product formation from the condensation reaction followed by cyclization. The prepared compounds and complexes were stable at room temperature (as evidenced from TG measurements). They are in good agreement with theoretical values within the experimental error. The structural compositions and spectral features were arrived on the basis of elemental analyses, spectroscopic and thermo gravimetric analysis.

Molar Conductance Measurements: The metal (II) complexes were dissolved in DMSO and the molar conductivities of 10^{-3} M of their solution at room temperature were measured. The lower molar conductivity values of metal complexes were found in the range of (8-14) ohm^{-1} cm^2 mol^{-1}. From the observed values, the complexes are non-electrolyte nature [15] indicated that no counter ions present outside the coordination sphere. The pyrazoline derivatives (ligands) showed conductivity values due to the presence of hydroxyl group in the naphthyl moiety whereas in the case of metal complexes, the conductivity values are decreased due to the deprotonation of OH group (in the naphthyl moiety) in the pyrazoline core. It is concluded that the free ligand contain phenolic oxygen atom as coordinating site and essential for complexation or chelation. The analytical data are in a good agreement with the proposed stoichiometry $[ML(OAc)_2]$ of all the complexes.

FT-IR: A strong vibrational band was observed in the region 1662-1654 cm^{-1} which is assignable to the ν(C=N) stretch frequency of pyrazoline derivatives. This band was shifted to lower vibrational frequencies due to the involvement of azomethine nitrogen in coordination with the metal complexes. In the ligands, the indole moiety contains –NH group was observed at 3312–3430 cm^{-1}. The phenolic C–O vibration was observed at 1356-1348 cm^{-1} in the ligands whereas there is a positive shift indicates that phenolic oxygen atom undergoes chelation with metal ions. Therefore, the azomethine nitrogen and phenolic oxygen atoms are donor sites present in the ligands to coordinate with metal ion through bidentate manner. The two absorption bands at 420-434 cm^{-1} and 496-520 cm^{-1} corresponds to ν(M-O) and ν(M-N) vibrations were observed in the complexes. Further, the ν(asym) and ν(sym) vibrational frequencies were appeared at 1534 cm^{-1} and 1420 cm^{-1} and the difference is ~106 cm^{-1} which indicates that acetate ion coordinate to metal ion as monodentate. The new vibrational frequency was appeared in the region 3300-3500 cm^{-1} indicates that the water molecule bound or coordinated to metal ion. In addition, the frequency at 860 cm^{-1} was assigned to coordinated water molecule in the metal complexes [16, 17].

Electronic Spectral Features: The electronic absorption band of the ligand, L^3 showed two bands at 260 nm and 332 nm indicates that π–π*and n-π* transition of the chromophore present in the pyrazoline derivative. These bands were shifted in the electronic absorption spectrum of the complexes to 254 nm and 324 nm due to coordination behavior [18]. The Cu(II) complex showed a broad absorption band around 496 nm may be assigned to $^2B_{1g} \rightarrow {}^2A_{1g}$ transition. This indicates that the square planar geometry around the Cu(II) ion [19]. The zinc complex exhibited a band at 360 nm and may be assigned to intraligand transitions within the ligand molecules. This spectral behaviour is due to its d^{10} electron configuration with completely filled d orbital. The electronic spectrum of nickel complex of (L^3)

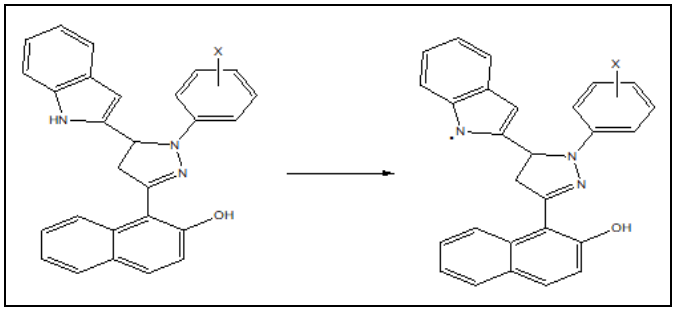
showed a band appeared at 568 nm which is attributed to $^1A_{1g} \rightarrow {}^1A_{2g}$ transition [20]. These transitions, as well as the measured value of the magnetic moment ($\mu_{eff} = 0$) suggested that a square planar geometry of the complexes. In the case of Co(II) complex of (L^3), square planar Co(II) complexes exhibited two bands around 632 nm and 546 nm which corresponds to the transitions $^2A_{2g} \rightarrow {}^2B_{1g}$ and $^2A_{1g} \rightarrow {}^2E_g$, respectively [21]. Similarly, all the other complexes showed spectral features.

DNA Binding Experiments:

Cyclic Voltammetric Studies: Cyclic voltammetry is a versatile protocol in the study of electron transfer properties. The DNA binding of metal complex was confirmed by the changes in electrode potential and current and biologically accessible oxidation states formed during electrolysis. In general, when a metal complex binds with DNA through intercalation, the positive potential shift with decrease in current was observed whereas in the case of electrostatic interaction, there is a negative potential shift. If positive and negative shift of electrode potential was observed, the molecule may bind to DNA through both intercalation and electrostatic binding interactions [22]. The cyclic voltammogram of the Cu(II) complex of (L^3) in the absence and presence of DNA in a Tris/HCl buffer solution in the range +1.0 to -1.2 V with a scan rate of 100 mV/s. In the absence of DNA, it shows a quasi-reversible one electron redox process involving the Cu^{2+} /Cu^{+} couple [Epc at -0.246 V and Epa at +0.104 V]. The $E_{1/2}$ was taken as the average of Epc and Epa is +0.146 V in the absence of DNA. In the presence of DNA, the cathodic peak potential (Epc) appears at -0.214 V and the anodic peak potential (Epa) at +0.096 V. The $E_{1/2}$ is +0.132 V in the presence of DNA. The incremental addition of DNA to the complex, the redox couple causes a significant shift in $E_{1/2}$ of 0.16 mV. The ipa/ipc values also decreases in the presence of DNA. The decrease of the anodic and cathodic peak currents of the complex in the presence of DNA is due to decrease in the apparent diffusion coefficient of the Cu(II) complexes upon complexation with the DNA macromolecules.

Absorption Spectral Titrations: The binding properties of complexes to the CT-DNA helix have been determined by electronic absorption spectral methods. The magnitude of hypochromism and red shift depends upon the strength of interaction between metal complexes and CT-DNA. As the DNA concentration is increased, the following changes to be observed in the absorbance and shift in wavelength of ligand as well as metal complexes. On the addition of CT-DNA, there is a decrease in molar absorptivity (hypsochromism) blue shift of 4-9 nm in the $[CuL^1(OAc)_2]$ complex. These data suggested that metal complex clearly bind to partial intercalative binding mode. The same binding features were observed for the $[CuL^2(OAc)_2]$ and $[CuL^3(OAc)_2]$ complexes. The d-d transition for complexes at 464 nm indicates that the copper complexes interacts with N(7) of guanine of CT-DNA. All these data were then fitted to Eq. (1) to obtain the intrinsic binding constant (K_b) values and resulted that $[CuL^1(OAc)_2]$ complexes bind with DNA by partial intercalation mode [23.] The Intrinsic binding constants (K_b) for copper complexes were in the range of 3.22×10^5 M^{-1} - 3.32×10^5 M^{-1} are less when compared with the reported few intercalating complexes $[Ru(bpy)_2(dppz)]^{2+}$ (4.90×10^6 M^{-1}) [33] and $[Ru(bpy)_2(HBT)]^{2+}$ (5.71×10^6 M^{-1}) [34]. Binding energy is the measure of stability of complexes.

Antioxidant Activity: The antioxidant activity of pyrazoline derivatives, metal complexes and the standard ascorbic acid were evaluated using DPPH (1,1-diphenyl-2-picryl hydrazyl) and hydrogen peroxide scavenging methods [24]. After the successful investigations of DPPH and hydrogen peroxide assay methods, the comparision of the antioxidant activity of the pyrazoline derivative (L3) (IC_{50} value is 94 µg/mL) with that of the metal complexes (IC_{50} values of Cu(II), Ni(II), Co(II) and Zn(II) complexes are 48, 68, 72 and 60 µg/ mL, respectively). In the case of hydrogen peroxide assay method, the p-chloro substituted pyrazoline derivative and its Cu(II), Co(II), Ni(II) & Zn(II) complexes showed IC_{50} values are 74, 46, 68, 54 and 60 µg/ mL, respectively. It is indicated that the Cu(II) complex possesses higher scavenging activity towards hydroxyl radical than the parent ligand and other metal complexes, respectively. The observed values are found to be very close to the standard ascorbic acid (IC_{50} value is 22 µg/mL). All other ligands and their metal complexes showed similar behavior.



SCHEME 2: PROPOSED MECHANISM FOR ANTI-OXIDANT (FREE RADICAL SCAVENGING) ACTIVITY OF PYRAZOLINE DERIVATIVES

Antimicrobial Activity: The *in-vitro* antimicrobial activities of the investigated compounds were tested against the five bacterial species, *Staphylococcus aureus, Escherichia coli, Klebsiella pneumaniae, Proteus vulgaris*, and *Pseudomonas aeruginosa* by disc diffusion method [25]. The comparative study (MIC) of ligands with their metal complexes indicated that the complexes have higher activities than the synthesized ligands. In general, the synthesized metal complexes have higher biological activities compared to the free ligands. The increased inhibition activity of the metal complexes can be explained on the basis of Tweedy's chelation theory [26]. In metal complexes, on chelation the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π- electrons over the whole chelate ring.

Fluorescent Behavior: Photochromism defines that in the presence of light, the molecules exhibit different absorption spectra with different colors [27–32]. This phenomenon attributes different sensing applications [33-36]. The fused aromatic heterocyclic molecules constitute an interesting class of photochromic compounds**.** The exposure of UV light to the solution of copper complex of (L^2) & (L^3) induces a colour change from colourless to green. This colour change may also occur in DCM solution.

On increasing the irradiation time, the absorption band is shifted towards visible region indicates that the pyrazoline derivatives of metal complexes may exhibit different emission with respect to suitable substituent present in the pyrazoline structural core. The colour emission depends on the structural core surrounded on copper centre. The structural core conjugation with heterocyclic molecule contains electron releasing or electron withdrawing groups which impart colour emission. Naphthyl and indole moieties are responsible for the green colour emission due to its conjugation and electronic delocalization within the molecule and leads to longer wavelength. The electron withdrawing substituent is also responsible for the above colour emission. The good thermal stability (was confirmed from TGA technique) of metal complexes may be used in high temperature optoelectronic applications.

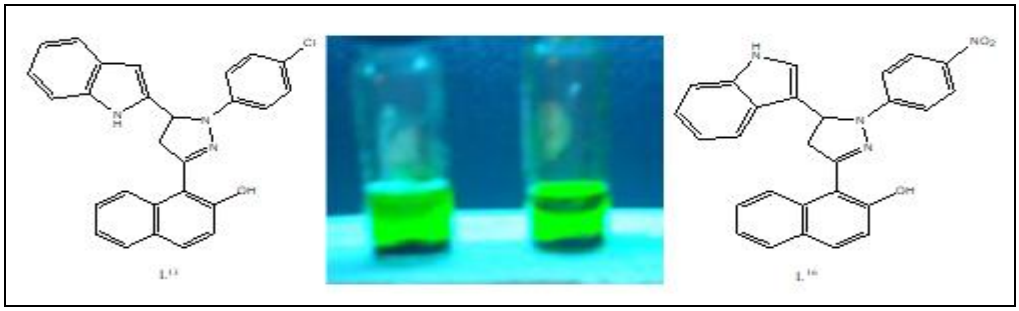


FIG. 1: GREEN FLUORESCENCE EMISSION UPON UV IRRADIATION OF COPPER COMPLEXES OF LIGANDS, L^2 AND L^3

CONCLUSION: In the present investigations, bioactive pyrazoline derivatives and their metal complexes were synthesized and characterized. On the basis of spectral and analytical techniques, a square planar geometry was assigned for the metal complexes. Further, the biological studies of metal complexes were performed and obtained significant results. Naphthyl and indole moieties are responsible for the green colour emission due to its conjugation and electronic delocalization within the molecule and leads to longer wavelength. The electron withdrawing substituent is also responsible for the above colour emission. Therefore, the copper complexes of pyrazoline derivatives have higher biological activity and high temperature optoelectronic applications.

ACKNOWLEDGEMENT: We express our sincere thanks to the Chancellor, Noorul Islam Centre for Higher Education, Kumaracoil for providing research facilities.

CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Raman N and Selvaganapathy M: Pyrazolone incorporating amino acid metallointercalators as effective DNA targets: Synthesis and *in-vitro* biocidal evaluation, Inorganic Chemistry Communications 2013; 37: 114-20.
2. Tabti S, Benmahmoud M, Djedouani A, Semmari L and Hamimid A: Synthesis, characterization and electrochemical behavior of new transition metal complexesderivatives of 4-hydroxy-6-methyl-3-[(2E)-3-(4-(dimethylamino) phenyl) prop-2-enoyl]-2H-pyran-2-one, J Mater Environ Sci 2018; 9(9): 2624-30.
3. Liu Y, Yang L, Yin D, Dang Y, Yang L, Zou Q, Li J and Sun J: Solvent-free synthesis, characterization, biological activity of schiff bases and their metal (II) complexes derived from ferrocenyl chalcone, Journal of Organometallic Chemistry 2019; 120903.
4. Devika BG, Doreswamy BH, Mallikarjuna NM and Tandon HC: Synthesis, characterisation and molecular structure study of metal complexes of antipyrine based ligand, Journal of Molecular Structure 2019; 1185: 69-77.
5. Kumar M, Sodhi KK, Singh P, Agrawal PK and Singh DK: Synthesis and characterization of antibiotic-metal complexes $[FeCl_3(L1)2H_2O$ and $Ni(NO_3)_2(L2)2H_2O]$ and enhanced antibacterial activity. Environmental Nanotechnology, Monitoring & Management 2019; 11: 100209.
6. Ali AE, Elasala GS and Ibrahim RS: Synthesis, characterization, spectral, thermal analysis and biological activity studies of metronidazole complexes, Journal of Molecular Structure 2019; 1176: 673-84.
7. Gacki M, Kafarska K, Pietrzak A, Korona-Glowniak I and Wolf WM: Synthesis, characterisation, crystal structure and biological activity of metal(II) complexes with theophylline. Journal of Saudi Chemical Society 2019, 23: 346-54.
8. Yıldırım T, Köse DA, Avcı E, Özer D and Şahin O: Novel mixed ligand complexes of acesulfame / nicotinamide with some transition metals. Synthesis, crystal structural characterization, and biological properties, Journal of Molecular Structure 2019; 1176: 576-82.
9. Huseynova M, Taslimi P, Medjidov A, Farzaliyev V and Gulçin I: Synthesis, characterization, crystal structure, electrochemical studies and biological evaluation of metal complexes with thiosemicarbazone of glyoxylic acid. Polyhedron 2018; 155: 25-33.
10. Delgado F, Nicova E, Agotegaray M, Pardo VG and Dennehy M: Ni-thiosaccharinate complexes: Synthesis, characterization and DFT studies. Biological properties as superoxide dismutase mimetics and as anti-carcinogenic agents. Inorganica Chimica Acta 2019; 494: 55-64.
11. He J, Ma L, Wei Z, Zhu J, Peng F, Shao M, Lei L, He L, Tang M, He L, Wu Y and Chen L: Synthesis and biological evaluation of novel pyrazoline derivatives as potent anti-inflammatory agents. Bioorganic & Medicinal Chemistry Letters 2015; 25: 2429-33.
12. Ahmad K, Naseem HA, Parveen S, Shah H and Ashfaq M: Synthesis and spectroscopic characterization of medicinal azo derivatives and metal complexes of Indandion. Journal of Molecular Structure 2019; 1198: 126885.
13. De A, Ray HP, Jain P, Kaur H and Singh N: Synthesis, characterization, molecular docking and DNA cleavage study of transition metal complexes of o-vanillin and glycine derived schiff base ligand. Journal of Molecular Structure, In press, journal pre-proof 2019; 126901.
14. Venkatachalam TK, Bernhardt PV, Noble CJ, Fletcher N and Reutens DC: Synthesis, characterization and biological activities of semicarbazones and their copper complexes. J of Inorganic Biochem 2016; 162: 295-08.
15. Masoud MS, Ali AE, Elasala GS and Kolkaila SA: Synthesis, spectroscopic, biological activity and thermal characterization of ceftazidime with transition metals, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2018; 193: 458-66.
16. Abdel-Rahman LH, Abu-Dief AM, Ismael M, Mohamed MAA and Hashem NA: Synthesis, structure elucidation, biological screening, molecular modeling and DNA binding of some Cu(II) chelates incorporating imines derived from amino acids, Journal of Molecular Structure 2016; 1103: 232-44.
17. Sathiyaraj S, Sampath K, Butcher RJ, Pallepoguc R and Jayabalakrishnan C: Designing, structural elucidation, comparison of DNA binding, cleavage, radical scavenging activity and anticancer activity of copper(I) complex with 5-dimethyl-2-phenyl-4-[(pyridin-2-ylmethylene)-amino]-1,2-dihydro-pyrazol-3-one Schiff base ligand. European Journal of Medicinal Chemistry 2013; 64: 81-89.
18. Nair MS, Arish D and Johnson J: Synthesis, characterization and biological studies on some metal complexes with Schiff base ligand containing pyrazolone moiety. J of Saudi Chemical Society 2016; 20: s591-s598.
19. Chu YC, Wang TT, Wang LJ, Luo QY and Zhu HL: Synthesis, characterization, and biological evaluation of a novel Zn(II)-Naproxen complex. Polyhedron 2019; 163: 71-76.
20. Daravath S, Vamsikrishna N, Ganji N, Venkateswarlu K and Shivaraj: Synthesis, characterization, DNA binding ability, nuclease efficacy and biological evaluation studies of Co(II), Ni(II) and Cu(II) complexes with benzothiazole Schiff base. Chemical Data Col 2018, 17-18: 159-68.
21. Venugopal N, Krishnamurthy G, Bhojyanaik HS and Krishna PM: Synthesis, spectral characterization and biological studies of Cu (II), Co (II) and Ni (II) complexes of azo dye ligand containing 4–amino antipyrine moiety. Journal of Molecular Structure 2019; 1183: 37-51.
22. Kareem A, Khan MS, Nami SAA, Bhat SA and Nishat N: Curcumin derived Schiff base ligand and their transition metal complexes: Synthesis, spectral characterization, catalytic potential and biological activity. Journal of Molecular Structure 2018; 1167: 261-73.
23. Hernández-Ayala LF, Flores-Álamo M, Escalante-Tovar S, Galindo-Murillo R and Ruiz-Azuara L: Synthesis, characterization, theoretical studies and biological activity of coordination compounds with essential metals containing N4-donor ligand 2,9-di(ethylaminomethyl)-1,10-phenanthroline. Inorganica Chimica Acta 2018; 470: 187-96.
24. Mandal S, Das M, Das P, Samanta A and Saha NC: Synthesis, characterization, DFT and antimicrobial studies of transition metal ion complexes of a new schiff base ligand, 5-methylpyrazole-3yl-N-(2́-hydroxyphenylamine) methyleneimine, (MPzOAP). Journal of Molecular Structure 2019; 1178: 100-11.
25. Iftikhar B, Javed K, Khan MSU, Akhter Z and Mckee V: Synthesis, characterization and biological assay of

Salicylaldehyde Schiff base Cu(II) complexes and their precursors. Journal of Molecular Structure 2018; 1155: 337-48.
26. Jayamani A, Bellam R, Gopu G, Ojwach SO and Sengottuvelan N: Copper(II) complexes of bidentate mixed ligands as artificial nucleases: Synthesis, crystal structure, characterization and evaluation of biological properties. Polyhedron 2018; 156: 138-49.
27. Jailani NMAK, Xavier A and Ramu A: Synthesis, spectroscopic characterization, DNA binding ability and biological activities of transition metal complexes containing tridentate schiff base. Materials Today: Proceedings 2018; 5: 22200-14.
28. Benhassine A, Boulebd H, Anak B, Ali MK and Belfaitah A: Co(II) complexes derived from (1-methyl-1H-imidazol-2-yl)methanol: Synthesis, characterization, spectroscopic study, DFT/TD-DFT calculations and biological evaluation. Inorganica Chimica Acta, In press, journal pre-proof, Available online 13 August 2019.
29. Manimohan M, Pugalmani S and Sithique MA: Biologically active novel N, N, O donor tridentate water soluble hydrazide based O-carboxymethyl chitosan Schiff base Cu (II) metal complexes: Synthesis and characterization. International Journal of Biological Macromolecules 2019; 136: 738-54.
30. Bougherra H, Berradj O, Adkhis A and Amrouche T: Synthesis, characterization, electrochemical and biological activities of mixed ligand copper(II) complexes with dimethylglyoxime and amino acids. Journal of Molecular Structure 2018; 1173: 280-90.
31. Manjuraj T, Krishnamurthy G, Bodke YD, Naik HSB and Kumar HSA: Synthesis, XRD, thermal, spectroscopic studies and biological evaluation of Co(II), Ni(II) Cu(II) metal complexes derived from 2-benzimidazole. Journal of Molecular Structure 2018; 1171: 481-87.
32. Ikeda NEA, Novak EM, Maria DA, Velosa AS and Pereira RMS: Synthesis, characterization and biological evaluation of Rutin–zinc(II) flavonoid -metal complex. Chemico-Biological Interactions 2015; 239: 184-91.
33. Syed Ali Fathima S, Paulpandiyan R and Nagarajan ER: Expatiating biological excellence of aminoantipyrine derived novel metal complexes: Combined DNA interaction, antimicrobial, free radical scavenging studies and molecular docking simulations. Journal of Molecular Structure 2019; 1178: 179-91.
34. Medina JJM, Naso LG, Pérez AL, Rizzi A and Williams PAM: Synthesis, characterization, theoretical studies and biological (antioxidant, anticancer, toxicity and neuroprotective) determinations of a copper(II) complex with 5-hydroxytryptophan. Biomedicine & Pharmaco-therapy 2019; 111: 414-26.
35. Zordok WA and Sadeek SA: Synthesis, spectroscopic characterization, biological studies and DFT calculations on some transition metal complexes of NO donor ligand. Journal of Molecular Structure 2018; 1158: 205-20.
36. Kavitha B, Sravanthi M and Reddy PS: DNA interaction, docking, molecular modelling and biological studies of o-Vanillin derived Schiff base metal complexes. Journal of Molecular Structure 2019; 1185: 153-67.

How to cite this article:
Sharmila TM: Synthesis, characterization, biological and fluorescent behaviour of metal (II) complexes with pyrazoline derivatives. Int J Pharm Sci & Res 2020; 11(2): 947-54. doi: 10.13040/IJPSR.0975-8232.11(2).947-54.