Original Article

Synthesis and Antioxidant Studies of Co(II), Ni(II) and Zn(II) Metal Complexes of 6-Pyridyl-5, 6-Dihydrobenzo[4,5]-Imidao[1,2-C] Quinazoline (N-N) Derivatives

Chaithra K[1,*], Bheemanna HG[1], Mamatha KS[2], Gayathri V[3]

[1]Department of Chemistry, Vivekananda Institute of Technology, Bangalore, Karnataka, INDIA.
[2]Department of Chemistry, Venkateshwara College of Engineering, Bangalore, Karnataka, INDIA.
[3]Department of Chemistry, Central College Campus, Bangalore University, Bangalore, Karnataka, INDIA.

Submission Date: 13-06-2021; Revision Date: 30-07-2021; Accepted Date: 05-08-2021

ABSTRACT

The major class of organic molecules synthesis involved by the various atoms in their molecules, and they are joined in rings containing at least one atom in any synthesized compound of an element other than that of carbon atom (C). The current study aimed to synthesize the heterocyclic compound as one of the derivative N-heterocycle (I) using various complex materials and to determine their biological property in *in vitro* antioxidant study. Synthesis and antioxidant activities of novel Co(II), Ni(II) and Zn(II) Metal Complexes of 6-Pyridyl-5,6-Dihydrobenzo[4,5]-Imidao[1,2-C] Quinazoline (N-N) derivatives were undertaken employing a convenient and easily accessible procedure. The structures of all the synthesized compounds were confirmed with elemental analysis, IR, C^{13} NMR and H^1NMR to know the probable structure of the molecules by stereochemistry. The synthesized five compounds were screened for *in vitro* antioxidant activity by 2, 2-Diphenyl-1-picrylhydrazyl (DPPH) method. In Antioxidant studies, compound C-2 exhibited maximum inhibition (77%) at 250μg/ml concentration showing satisfactory DPPH free radical scavenging potential with the IC_{50} concentration at 33.61μg/ml compared to the standard drug, ascorbic acid with 6ug/ml used for the study and other compounds were also exhibited minimum antioxidant property.

Key words: Heterocyclic compounds, DPPH, Ascorbic acid, Radical scavenging activity, Stereochemistry.

Correspondence:
Ms. Chaithra K,
Department of Chemistry, Vivekananda Institute of Technology, Bangalore-560074, Karnataka, INDIA.
Phone no: +91-9980776368

Email: chaithra.sudhi@gmail.com

INTRODUCTION

From the last 4 decades, quinazoline and quinazalones skeleton have gained more attention in the class of heterocyclic compounds with due to their remarkable biological and synthetic application. The quinazoline and quinazalones derivatives with complexes are used as drugs in the form of anticancer, antiviral, antibacterial, anti-inflammatory as they exhibit broad range of pharmacological activity.[1-3]

Heterocyclic compounds are of greater value since they are used as key starting materials for synthesis of active pharmaceutical products. Synthesized compounds containing heterocyclic ring systems are of significant both medicinal and industrial applications. As an example, five membered ring heterocycles containing two carbon atoms, two nitrogen atoms and one oxygen atom, known as oxadiazoles, these are having various applications like medicinal, pesticide chemistry, polymer and material science.[4]

In view of wide range of biological activities of Imidao[1,2-C] Quinazoline (N-N) derivatives, a new series of metal complex analogues were synthesized.

SCAN QR CODE TO VIEW ONLINE

www.ajbls.com

DOI: 10.5530/ajbls.2021.10.57

In this context, Imidazo[1,2-c]quinazoline (N-N) derivatives are important five member heterocyclic motifs, which are of great concept of research due to their novel pharmaceutical applications. Extensive use of Imidao[1,2-C] Quinazoline (N-N) derivatives moiety in medicinal chemistry has proved to be an important member of privileged structures.

It shows the integrity of these versatile heterocyclic subunits namely quinolines and imidao into one structural metal complex frame. So that the combination of all these two subunits might exhibit synergetic effect in enhancing the overall bioactivity of newly planned and synthesised structural products. To establish the structure activity relationship, in the present studies, we report herein the synthesis of quinazoline clubbed Imidao[1,2-C] which are subjected to antioxidant properties. Based on the facts mentioned above and our research program on the synthesis of metal complexes cobalt, nitrogen and zinc containing heterocyclic compounds and in continuation of our research program centered on the design and synthesis of potentially bioactive molecules.[5,6] Hence we have planned and designed a new series of potential active compound Co(II), Ni(II) and Zn(II) Metal Complexes of 6-Pyridyl-5,6-Dihydrobenzo[4,5]-Imidao[1,2-C] Quinazoline (N-N). As an applicative objective of synthesized compounds for the biological studies, DPPH free radical scavenging method is employed for the assessment of antiradical properties as it is reliable to determine antioxidant capacity of biological substrates or synthesized compounds. In the current study synthesized five heterocyclic compounds with using different complex materials to design and to know their stability, characterization, stereochemistry, and biological action as *in vitro* antioxidant property.[7-9]

MATERIALS AND METHODS

Experimental

Hydrated metal chlorides and metal bromides were procured from BDH. Metal iodide and hydrated perchlorates were prepared by dissolving metal carbonate in 1:1 or 1:2 aqueous hydroiodic acid and perchloric acid respectively and evaporating the resulting solution to almost dryness under reduced pressure. The N-heterocycle (I) was prepared following the procedure reported for related N- heterocycles.[10]

Measurements

C, H and N analyses of the complexes were carried out on a Heracus Carlo Erba 1108 microanalyzer. Metal content was determined using a Spectra AA-30 spectrophotometer equipped with a Varian DS-15 computer. IR (nujol mull) spectra of the complexes were recorded on Shimadzu IR-435. Magnetic moment measurements at room temperature were made using a Gouy balance with $CuSO_4.5H_2O$ as the calibrant. Conductivity data were obtained using a Systronics –304 conductivity bridge. NMR spectra were recorded in DMSO–d_6 on AMX 400 MHz spectrometer using TMS as the internal standard at SAIF Research centre Indian Institute of Science, Bangalore, India. TGA was carried out on a Mettler TAHE – 20 thermal analyser with a scan rate of 5°C min^{-1} in air.

Preparation of the complexes

$CoCl_2$ (N-N).H_2O

To a solution of hydrated Cobalt (II) Chloride (1mmol) in absolute alcohol/acetone-triethylorthoformate (teof) mixture (10 cm^3), N-N (1mmol) in absolute alcohol/acetone (10 cm^3) was added. The solution was refluxed for 4 hrs when a brown solid separated. The solid was washed with absolute alcohol/acetone and dried in vacuo. Yield: 70-80%.

$[Co(OClO_3)_2(N\text{-}N)]$

To a solution of hydrated Cobalt(II) perchlorate (1mmol) in absolute alcohol-teof mixture (10 cm^3), N-N (2 mmol) in absolute alcohol (10 cm^3) was added. The solution was refluxed for 5 hr when a yellow solid separated. The solid was washed with absolute alcohol and dried in vacuo. Yield: 80%.

$NiX_2L.(H_2O)$ (n = 1, X = Cl; n = 0; X = I)

To a solution of hydrated Nickel(II) halide (1mmol) in absolute alcohol-teof mixture (10 cm^3), N-N (1 mmol) in absolute alcohol-teof mixture (10 cm^3) was added. The solution was refluxed for 5 hr when a yellow solid separated. The solid was washed with absolute alcohol-teof and dried in vacuo. Yield: 80%.

$[Ni (N\text{-}N)_2(OClO_3)_2].H_2O$

To a solution of hydrated Nickel(II) perchlorate (1mmol) in absolute alcohol-teof mixture (10 cm^3), N-N (2 mmol) in absolute alcohol (10 cm^3) was added. The solution was refluxed for 5 hr when a yellow solid separated. The solid was washed with absolute alcohol and dried in vacuo. Yield: 80%.

$[ZnCl_2$ (N-N)]

To a solution of Zinc (II) chloride (1 mmol) in ethanol-teof mixture (10 cm^3) was added slowly with stirring to 10 cm^3 of an ethanolic solution of the N-N (1 mmol) when a white precipitate separated out. The solid was washed with absolute alcohol and dried in vacuo. Yield: 80%.

DPPH free radical scavenging assay

DPPH assay was carried out as described by Blois[11] method. 1.3 mg/ml DPPH was prepared using methanol HPLC grade in that 75 µl of DPPH solution utilized and prepared various concentrations as 15.62, 32.25, 62.5, 125, 250 and 500µg/ml using synthesized compounds solution separately and volume was made upto 3 ml using methanol. All the compounds compared with the standard ascorbic acid and it was considered as reference. The reaction mixture was well mixed and incubated at room temperature for 30 min and the absorbance was recorded at 517 nm wavelength. The control was prepared by adding 2 ml of DPPH solution and 1 ml of methanol[12] and the assay was done in triplicate. The IC_{50} value was determined by using linear regression equation i.e. Y =Mx+C. Here, Y = 50, M and C values were derived from the linear graph trendline.

$$\% \text{ Scavenged [DPPH]} = [(AC - AS)/AC] \times 100$$

Where AC is the absorbance of the control and AS is the absorbance in the presence of the sample of extracts or standard.

Statistical analysis

All the experiments were carried out in triplicates and the results were expressed as mean ± standard error of the mean. The data were statistically analyzed using Microsoft Office Excel 2007.

RESULTS

The solid-state IR spectra of the complexes are comparable with those of the uncoordinated N-heterocycle barring minor shifts in the positions of the peaks. The spectra of the complexes displayed peaks around 1535 and 1616 cm^{-1} due to $\nu_{C=C}$ and $\nu_{C=N}$ respectively and a peak at 3100 cm^{-1} due to the ν_{NH} vibration.

The electronic spectra of the complexes have been recorded in nujol mull. The spectra of Cobalt (II) complexes exhibited three multiple absorption bands around 4000, 8000 and 16000 cm^{-1}. The positions of the bands and their intensities suggest a tetrahedral geometry for the complexes. The bands are assigned to the transitions ${}^4A_2 \rightarrow {}^4T_2(F)(\nu_1)$, ${}^4T_1(F)(\nu_2)$ and ${}^4T_1(P)(\nu_3)$ respectively. The electronic spectrum of $[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$ has displayed bands of low intensity at 8291, 11737 and 28571 cm^{-1} and the bands are assigned respectively to the transitions ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}$, ${}^3T_{1g}$, ${}^3T_{1g}(P)$. The bands are split and the nature of splitting indicates that the tetrahedral structure is distorted. The ligand field (10 Dq), the Racah (B', interelectronic repulsion) and nephelauxetic (β) parameters have been calculated for the complexes. The 10 Dq values for the halo complexes follow the known spectrochemical series order I < Br < Cl. The magnitude of B' in the complexes is considerably reduced relative to the free ion value (971 cm^{-1}) indicating appreciable covalent character for the metal–ligand bonds. Thermogravimetric analyses of the chloro complexes of cobalt, nickel and $[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$ revealed the presence of lattice water molecule.

The ${}^1H$ NMR spectra of the N-heterocycle N-N, $[ZnCl_2(N\text{-}N)]$ has revealed that the proton resonances of quinazoline ring unit have undergone –ve coordination induced shifts (c.i.s $=\delta_{complex} - \delta_{ligand}$) (upfield shift) on complexation while benzimidazole and pyridine ring units have undergone +vec.i.s on complexation. The resonance due to NH of quinazoline unit is around 5.42 δ. On deuteration, this peak disappears confirming it is due to the proton of NH in the quinazoline unit.

N-N– [H – 7(7.64d), H – 8,9 (7.24m), H – 10 (7.32d), CH (7.72s), NH (5.4s), H-2' (7.16d), H-3' (7.06t), H – 4'(6.80t) H – 5'(6.83d), H – 3" (7.94d), H-4"(7.74t), H-5"(7.30t), H-6"(8.4d)]

[ZnCl$_2$ (N-N)]–[H –7(7.66d), H – 8,9 (7.22m), H – 10 (7.35d), CH (7.75s), NH (7.69s), H-2' (7.16d), H-3' (7.10t), H – 4'(6.80t) H – 5'(6.88d), H – 3" (7.94d), H-4"(7.77t), H-5"(7.30t), H-6"(8.45d)]

The ${}^{13}C$ NMR spectrum of the N-heterocycle exhibits ten signals in the range of δ 110.0 – 158.4 and peak due to CH is at δ 68.50. The assignments of the signals are made with the aid of off-resonance decoupled spectrum of the heterocycle and literature reports. The resonances due to carbon atoms in the coordinated heterocycle are shifted up field. The coordination induced shifts, (c.i.s = δcomplex - δligand). The negative c.i.s may be attributed to greater metal-to-ligand π-back donation, where as positive c.i.s to ligand–to–metal σ -donation.

N-N–[C-2 (158.4), C-3(112.1), C-4(133.0), C-7(123.9), C-8(122.0), C-9 (122.2), C-10(124.6), CH(68.5), C-2'(110.4), C-3'(114.7), C-4'(118.1), C-5'(118.6), C-6'(142.9), C-7'(143.8), C-2"(146.9), C-3"(137.4), C-4"(120.2) C-5"(131.5), C-6"(149.64)]

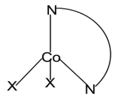
[ZnCl$_2$ (N-N)]---[C-2 (158.32), C-3(112.0), C-4(132.99), C-7(123.94), C-8(122.1), C-9 (122.2), C-10(124.7), CH(68.43), C-2'(110.4), C-3'(114.74), C-4'(118.07), C-5'(118.56), C-6'(143.0), C-7'(143.7), C-2"(146.9), C-3"(137.4), C-4"(120.22) C-5"(131.59), C-6"(149.44)]

Stereochemistry

The analytical data, IR, NMR and electronic spectral results have indicated that the N-heterocycle is coordinated to the metal ion. The N-heterocycle is planar and can serve as chelating or bridging bidentate ligand. The complexes are proposed to have a tetrahedral geometry in which the N-heterocycle acts as a chelating bidentate ligand. The $[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$ complex is proposed to have octahedral geometry.

DPPH free radical scavenging activity

The synthesized compounds exhibited a significant dose dependent inhibition of DPPH scavenging activity. A concentration-dependent assay was carried out with the compound and the results were presented in Graph 1 to 6. Among five graded concentrations were used in the study along with blank, cell control and standard control.

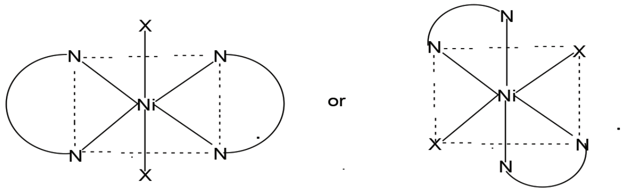


II

M = Co; X = Cl or ClO_4

M = Ni; X = Cl or I

M = Zn; X = Cl



V

X = ClO_4

In compound C-1 showed scavenging activity as 7.238%, 20.571%, 26.666%, 41.904%, 62.666% and 88% inhibition at 15.62, 31.25, 62.50, 125.00, 250.00 and 500µg/ml concentrations respectively. On the other hand, standard ascorbic acid showed 44% inhibition. The inhibitory concentration (IC_{50}) value of the compound C-1 showed 220.7µg/ml against the DPPH (Table 1 and Graph 1).

In compound C-2 showed scavenging activity as 43.047%, 48.761%, 51.809%, 66.095%, 77.333% and 96% inhibition at 15.62, 31.25, 62.50, 125.00, 250.00 and 500µg/ml concentrations respectively. On the other hand, standard ascorbic acid showed 44% inhibition. The inhibitory concentration (IC_{50}) value of the compound C-2 showed 33.61µg/ml against the DPPH (Table 1 and Graph 2).

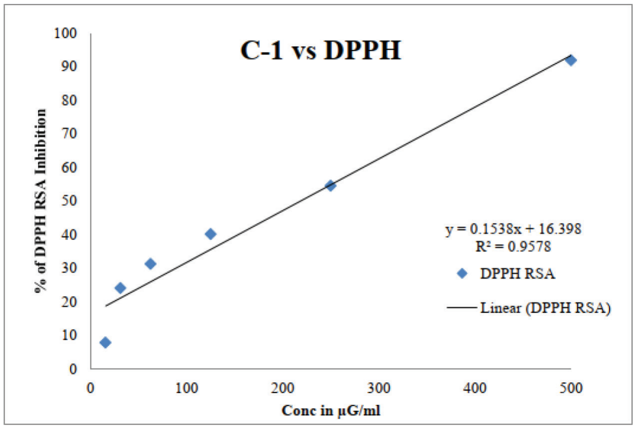
In compound C-3 showed scavenging activity as 41.714%, 49.904%, 53.333%, 60%, 72% and 95.809% inhibition at 15.62, 31.25, 62.50, 125.00, 250.00 and 500µg/ml concentrations respectively. On the other hand, standard ascorbic acid showed 44% inhibition. The inhibitory concentration (IC_{50}) value of the compound C-3 showed 47.28µg/ml against the DPPH (Table 1 and Graph 3).

In compound C-4 showed scavenging activity as 20.761%, 29.142%, 38.476%, 46.476%, 64% and 88.571% inhibition at 15.62, 31.25, 62.50, 125.00, 250.00 and 500µg/ml concentrations respectively. On the other hand, standard ascorbic acid showed 44% inhibition. The inhibitory concentration (IC_{50}) value of the compound C-4 showed 180.68µg/ml against the DPPH (Table 1 and Graph 4).

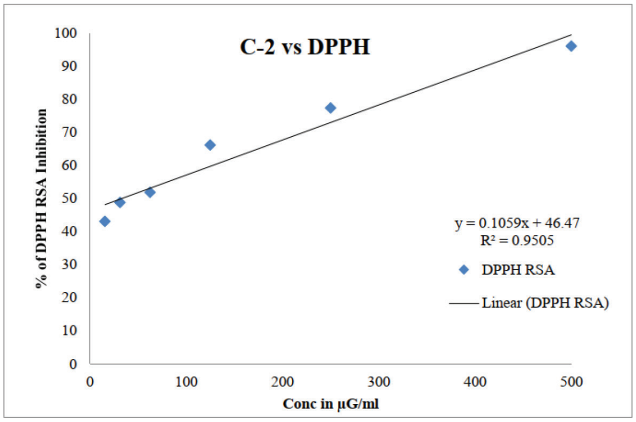
In compound C-10 showed scavenging activity as 7.863%, 24.102%, 31.282%, 40.170%, 54.529% and 91.794% inhibition at 15.62, 31.25, 62.50, 125.00,

Table 1: Table showing the % of inhibition and IC_{50} value of test compounds concentrations.

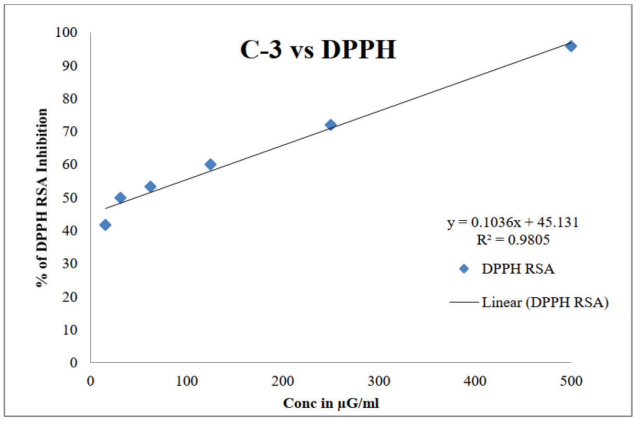
Sl. No.	Concentration (uG)	Compounds % of Inhibition				
		C-1	C-2	C-3	C-4	C-10
1	Blank					
2	Cell Control	0	0	0	0	0
3	Std Control	44	44	44	44	44
4	15.62	7.238	43.047	41.714	20.761	7.863
5	31.25	20.571	48.761	49.904	29.142	24.102
6	62.5	26.666	51.809	53.333	38.476	31.282
7	125	41.904	66.095	60	46.476	40.170
8	250	62.666	77.333	72	64	54.529
9	500	88	96	95.809	88.571	91.794
	IC_{50} (µg/ml)	**220.70**	**33.61**	**47.28**	**180.68**	**219.67**



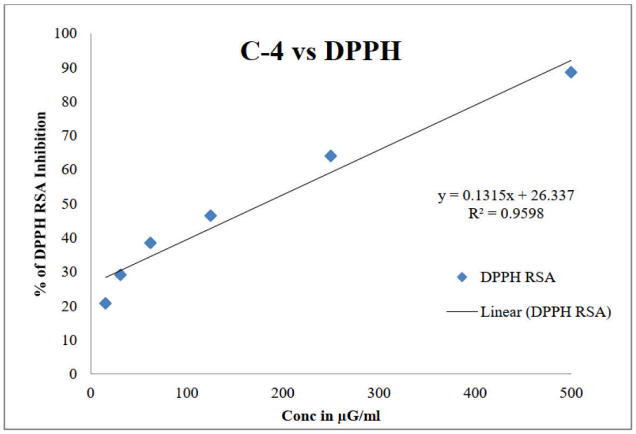
Graph 1: Scatter graph showing the % of inhibition of sample C-1 against the DPPH and the inhibitory concentration (IC_{50} value) observed is 220.7µg/ml.



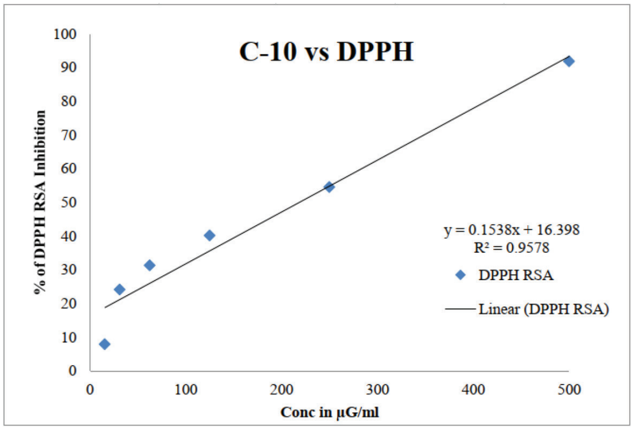
Graph 2: Scatter graph showing the % of inhibition of sample C-2 against the DPPH and the inhibitory concentration (IC_{50}value) observed is 33.61µg/ml



Graph 3: Scatter graph showing the % of inhibition of sample C-3 against the DPPH and the inhibitory concentration (IC_{50}value) observed is 47.28µg/ml



Graph 4: Scatter graph showing the % of inhibition of sample C-4 against the DPPH and the inhibitory concentration (IC_{50} value) observed is 180.68µg/ml



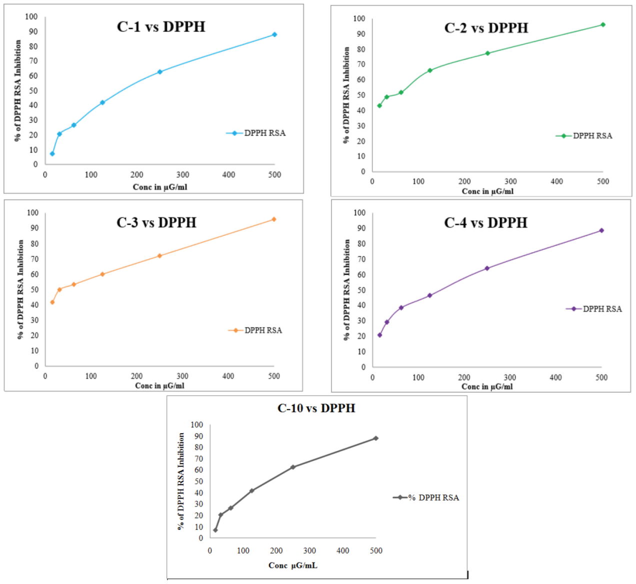
Graph 5: Scatter graph showing the % of inhibition of sample C-10 against the DPPH and the inhibitory concentration (IC_{50} value) observed is 219.67µg/ml

250.00 and 500µg/ml concentrations respectively. On the other hand, standard ascorbic acid showed 44% inhibition. The inhibitory concentration (IC_{50}) value of the compound C-10 showed 219.67µg/ml against the DPPH (Table 1 and Graph 5).

DISCUSSION

The perchlorate complexes, in addition to the heterocycle peaks, showed additional peaks due to the perchlorate group. The perchlorate complexes of cobalt 1095 and 622 cm^{-1} which are characteristic of coordinated perchlorate group.[13]

The spectra of the complexes have revealed the no resonances around 5.4 ppm indicated the disappearance of NH group in quinazoline unit. The resonance signal for the CH-proton of quinazoline group is around 7.72 ppm. According to Orellana *et al*.[14] the



Graph 6: Comparative DPPH free radical scavenging activity of compound C-1, C-2, C-3, C-4 and C-10 of % inhibition.

c.i.s arise due to electron donation from the ligand to the metal via the σ bond, metal electron π-back donation to the ligands, Vander Waals interaction and magnetic anisotropy of ring currents.

The room temperature magnetic moments of the complexes indicate the paramagnetic nature of the metal ions. The magnetic moments of the Chloro, and perchlorate complexes of Co(II) are in the range 4.0 – 4.4 BM. The values are typical of tetrahedral geometry for the complexes. The μ_{eff} values of nickel (II) halo complexes are in the range 3.0 - 3.4 BM. The values are in the range expected for tetrahedral/square pyramidal geometry.[15-17]

Antioxidant property of synthetic compounds are related to their electron or hydrogen atom donating ability to DPPH radical, so that they become stable diamagnetic scaffolds. The interaction of synthesized compounds with stable DPPH free radical indicates their free radical scavenging ability. The reduction ability of DPPH radicals was determined by decline in their absorbance at 517 nm enthused by antioxidants.

The effect of synthesized compounds on free radical scavenging was studied using DPPH assay and found better and higher radical scavenging activity than the controls. The increased scavenging activity is concentration dependent of the extract and it is may be due to its potent hydrogen donating ability of the compounds.[18-20] The compound C-2 and C-3 exhibited significant IC_{50} value 33.61 and 47.28µg/ml respectively and indicated its high free radical scavenging activity compare to other three compounds, indeed it's an indication of good antioxidant activity (Graph 6). Such scavenging activity resembles the findings inversely proportionate to the IC_{50} value.[21-24] These findings are lower IC_{50} value exhibited in the studies was due to the purified nature of the synthesized compounds and reacting as antioxidant potential.

CONCLUSION

Most of the major classes of pharmaceutically synthetic agents which are in current clinical use containing a number of coordination compounds. Due to wide range of biological applications of heterocyclic compounds with metal complexes, recent research mainly focuses on the synthesis of metal complexes using heavy metals. Therefore the present work involves the modification of functional group of the drug 6-Pyridyl-5,6-dihydrobenzo[4,5]-Imidao[1,2-C] Quinazoline (N-N) to obtain heterocyclic ligands. From this ligand four novel complexes i.e., Co(II), Ni(II) and Zn(II) were synthesized 5 compounds. Characterization of compounds by spectroscopic data such as IR, NMR, UV and Mass reveals that the metal to ligand ratio is 1:2 and the synthesized $[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$ complex is proposed to have octahedral geometry. As a biological action, it is exhibited antioxidant potential and it can be noted that metal complexes showed good property than the heterocyclic ligands.

ACKNOWLEDGEMENT

Authors are thankful to Vivekananda Institute of Technology, Bangalore, India for the instrumental facility and other necessary help.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ABBREVIATIONS

^{13}C NMR: Carbon-13 Nuclear Magnetic Resonance; **BDH:** British Drug House; **CH:** Methine; **cm^3:** cubic centimetre; **Co(II):** Cobalt II; **Co(OClO$_3$:** Cobalt(II) perchlorate; **CoCl$_2$:** Cobalt(II) chloride; **CuSO$_4$.5H$_2$O:** Copper(II) sulfate pentahydrate; **DMSO:** Dimethyl sulfoxide; **DPPH:** 2, 2-Diphenyl-1-picrylhydrazyl; **H^{1}NMR:** Proton Nuclear Magnetic Resonance; **H$_2$O:** Water; **HPLC:** High Pressure Liquid Chromatography; hr: hour; **IC$_{50}$:** Inhibitory Concentration; **IR:** Infra Red Spectroscopy; **mg:** mili gram; **MHz:** Meter Hertz; **ml:** mili litre; **mm:** mili molar; **mmol:** mili moles; **NH:** Amine; **Ni (N-N)2(OClO$_3$)2:** Nickel(II) perchlorate;

Ni(II): Nickel II; **NiX_2L:** Nickel(II) halide; **nm:** nano meter; **SAIF:** Sophisticated Analytical Instrument facility; **TGA:** Thermogravimetric Analysis; **TMS:** Tetramethylsilane; **UV:** Ultra violet; **Zn(II):** Zinc II; **$ZnCl_2$:** Zinc (II) chloride; **μeff:** Effective Magnetic Moment; **μg:** micro gram.

REFERENCES

1. Tiwary BK, Pradhan K, Nanda AK, Chakraborty R. Implication of quinazoline-4(3H)-ones in medicinal chemistry: A brief review. J Chem Biol Ther. 2015;1:104.
2. Amareshwar V, Goudgaon N, Patil S. Synthesis, *in vitro* and *in vivo* antifungal activity of 5-phenylthio-2,4-bisbenzyloxypyrimidine: A novel nucleobase. Ind J Pharm Sci. 2010;72(6):778-81. doi: 10.4103/0250-474X.84593.
3. Nandeshwarappa BP, Sandeep C, Sadashiv SO, Patil SJ, Onkarappa HS. Nitrogen and selenium containing heterocycles. Chem Data Collect. 2021;2:Synthesis and antimicrobial activities of novel S-5-(2-oxo-2H-selenopyrano [2,3-b]quinolin-3-yl)-1,3,4-oxadiazol-2-yl-2-cyanoethanethioates:33. PMID 100716.
4. Pace A, Pierro P. The new era of 1,2,4-oxadiazoles. Org Biomol Chem. 2009;7(21):4337-48. doi: 10.1039/b908937c, PMID 19830279.
5. Nandeshwarappa BP, Sandeep C, Prakash GK. Nitrogen and selenium containing heterocycles. Chem Data Collect. 2020;1: Synthesis of some new substituted 3-(5-(2-oxopropylthio)-1,3,4-oxadiazol-2-yl)-2H-selenopyrano[2,3-b]quinolin-2-ones:29. PMID 100534.
6. Nandeshwarappa BP, Chandrashekharappa S, Prakash GK, Prasannakumar JK. Efficient synthesis and characterization of novel 2H-[1, 4] oxaselenepino [5, 6-b] quinolin-3 (5H)-ones derivatives. Chem Data Collect. 2020;28. doi: 10.1016/j.cdc.2020.100446, PMID 100446.
7. Haleshappa R, Patil SJ, Usha T, Murthy SM. Phytochemicals, antioxidant profile and GCMS analysis of ethanol extract of *Simarouba glauca* seeds. ASI J Biol Life Sci. 2020;9(3):379-85.
8. Haleshappa R, Patil SJ, SiddalingMurthy KR. Phytochemical analysis, *in vitro* evaluation of antioxidant and free radical scavenging activity of *Simarouba glauca* seeds. Advances in Pharmacology and Pharmacy. 2021;9(1):1-8. doi: 10.13189/app.2021.090101.
9. Kolgi RR, Haleshappa R, Sajeeda N, Keshamma E, Karigar CS, Patil SJ. Antioxidant studies, *in vitro* cytotoxic and cell viability assay of flavonoids and alkaloids of *Leucas aspera* (Wild.) Linn leaves. ASI J Biol Life Sci. 2021;10(1):165-71.
10. Saif MJ, Flower KR. A general method for the preparation of n-heterocyclic carbene–silver(I) complexes in water. Transit Met Chem. 2013;38(1):113-8. doi: 10.1007/s11243-012-9667-3.
11. Blois MS. Antioxidant determinations by the use of a stable free radical. Nature. 1958;181(4617):1199-200. doi: 10.1038/1811199a0.
12. Haleshappa R, Keshamma E, Girija CR, Thanmayi M, Nagesh CG, Fahmeen GHL, Lavanya M, Patil SJ. Phytochemical study and antioxidant aroperties of ethanolic extracts of *Euphorbia milii*. Asian J of Biolog Sci. 2019;13(1):77-82. doi: 10.3923/ajbs.2020.77.82.
13. El-Mekabaty A. Synthesis and antioxidant activity of some new heterocycles incorporating the pyrazolo-[3,4-D]pyrimidin-4-one moiety. Chem Heterocycl Compd. 2015;50(12):1698-706. doi: 10.1007/s10593-015-1640-6.
14. Orellana G, Alvarez Ibarra C, Santoro J. Hydrogen-1 and carbon-13 NMR coordination-induced shifts in a series of tris(.alpha.-diimine)ruthenium(II) complexes containing pyridine, pyrazine, and thiazole moieties. Inorg Chem. 1988;27(6):1025-30. doi: 10.1021/ic00279a018.
15. Prasad S, Agarwal RK. Synthesis, Antibacterial and Antifungal Activities of Some Cobalt(II) and Nickel(II) Complexes of Thiosemicarbazones. J Korean Chem Soc. 2011;55(2):189-98. doi: 10.5012/jkcs.2011.55.2.189.
16. Johnson RC, Basolo F. Coordination chemistry. In: The chemistry of metal complexes, Benjamin WA. Inc. 1964. p. 40-4.
17. Litzow MR, Power LF, Tait AM. Complexes of 8-amino-2-methylquinoline with nickel(II). J Chem Soc A. 1970:275-9. doi: 10.1039/j19700000275.
18. Iranshahi M, Askari M, Sahebkar A, Adjipavlou-Litina D. Evaluation of antioxidant, anti-inflammatory and lipoxygenase inhibitory activities of the prenylated coumarin umbelliprenin. DARU J Phar:m Sci. 2009;17:99-103.
19. Barbuceanu SF, Ilies DC, Saramet G, Uivarosi V, Draghici C, Radulescu V. Synthesis and antioxidant activity evaluation of new compounds from hydrazine carbothioamide and 1,2,4-triazole class containing diarylsulfone and 2,4-difluorophenyl moieties. Int J Mol Sci. 2014;15(6):10908-25. doi: 10.3390/ijms150610908, PMID 24941252.
20. Ghareeb M. Antioxidant activity of heterocyclic compounds derived from 4-(4-acetamidophenyl)-4-oxobut-2- enoic acid. Int J Sci Res. 2014;3:1274-82.
21. Ezzatzadeh E, Hossaini Z. A novel one-pot three-component synthesis of benzofuran derivatives via Strecker reaction: study of antioxidant activity. Nat Prod Res. 2020;34(7):923-9. doi: 10.1080/14786419.2018.1542389, PMID 30587038.
22. Soliman AM, Karam HM, Mekkawy MH, Ghorab MM. Antioxidant activity of novel quinazolinones bearing sulfonamide: potential radiomodulatory effects on liver tissues via NF-κB/ PON1 pathway. Eur J Med Chem. 2020;197:112333. doi: 10.1016/j.ejmech.2020.112333.
23. Shyamlal BRK, Yadav L, Tiwari MK, Mathur M, Prikhodko JI, Mashevskaya IV, Yadav DK, Chaudhary S. Synthesis, bioevaluation, structure–activity relationship and docking studies of natural product inspired (z)-3-benzylideneisobenzofuran-1(3h)-ones as highly potent antioxidants and antiplatelet agents. Sci Rep. 2020;10(1):2307. doi: 10.1038/s41598-020-59218-6.
24. Meeran MN, Hussain AZ. Synthesis, characterization and dpph scavenging assay of isatin related spiroheterocyclic compounds. Ind J Pharm Sci. 2017;79(4):641-5. doi: 10.4172/pharmaceutical-sciences.1000273.

Cite this article: Chaithra K, Bheemanna HG, Mamatha KS, Gayathri V. Synthesis and Antioxidant Studies of Co(II), Ni(II) and Zn(II) Metal Complexes of 6-Pyridyl-5,6-Dihydrobenzo[4,5]-Imidao[1,2-C] Quinazoline (N-N) Derivatives. Asian J Biol Life Sci. 2021;10(2):427-33.