Original Article

Synthesis, Structural Characterization Of Benzothiazole Schiff Base Metal (II) Complexes And Their Interaction With DNA

Patil Pratiba[1], Virupaxappa S. Betageri[2]*, M. S. Latha[3], Shridhar A H[4]

[1]Department of Chemistry, GM Institute of Technology, Davangere-577001, Karnataka, India, Affiliated to Visveswaraya Technological University, Belagavi-590018, India;

*[2]Department of Chemistry, GM Institute of Technology, Davangere-577001, Karnataka, India, Affiliated to Visveswaraya Technological University, Belagavi-590018, India;

[3]Department of Chemistry, K.L.E Society's RLS Institute Belagavi-590001, Karnataka, India; Affiliated to Rani Channamma University Belagavi-591156, India

[4]Department of UG studies in chemistry, SVM Arts, Science and Commerce College Ilkal-587125, Affiliated to Rani Channamma University Belagavi-591156, India.

***Correspondent Author:-**Virupaxappa S. Betageri

*[2]Department of Chemistry, GM Institute of Technology, Davangere-577001 Affiliated to Visvesvaraya Technological University, Belagavi-590018,E-mail:virupaxb@gmail.com
Doi: 10.47750/pnr.2022.13.S05.75

Abstract

A potential metal-based chemotherapeutic product based on a benzothiazole Schiff base and first-row transition metals was synthesized and illustrated analytically and spectrally to investigate the biochemical priority of transition-metal drugs for molecular target DNA. As a result of the magnetic susceptibility data, it was shown that Co (II), Ni (II) and Cu (II) complexes are paramagnetic and have an octahedral geometry at ambient temperatures. Molar conductivity experiments showed that almost all of the complexes in dimethyl formamide were non-electrolytes. This study examined the interactions between CT-DNA and metal (II) complexes. Therefore, the copper(II) complex significantly improves DNA binding compared to the other complexes. Additionally, this finding was supported by gel electrophoresis, thermal denaturation, and viscosity methods.

1. INTRODUCTION

In order to better understand how natural biomolecules operate in biological systems, researchers have been interested in creating tiny model molecules that resemble natural biomolecules, as metal complexes interact with DNA. Inorganic chemistry and biology have been collaborating to create stable, non-toxic, inert metal complexes with spectroscopically active metal centers.**[1-2]** Most metal-based cancer therapies work by interacting with DNA, like cisplatin and its derivatives. As a result of their side effects, overall toxicity, and built-up drug resistance their use is limited. Due to these constraints, inorganic chemists are motivated to develop anticancer medications that are more effective, less expensive, less poisonous, and, preferably, non-covalently bound. In this undertaking, examining compounds containing transition metal ions other than platinum represents a novel approach. **[3]** The transition metals like cobalt, nickel, and copper, belong to the first row of transition metals and are physiologically important because they are associated with a variety of proteins that function in vital physiological processes. **[4]**

Schiff bases are also the most thoroughly studied compounds in medicinal chemistry because of their diverse range of pharmacological activities, including their antioxidant, anti-inflammatory, antituberculosis, antimicrobial, antihelmintic anticonvulsant, and anticancer, properties. As polymer stabilisers, catalysts, dyes, and organic synthesis intermediates, Schiff bases are widely used.**[5]** Further, benzothiazoles are a well-known bioactive chemical found in heterocyclics, with a variety of biological effects, including those that are anti-inflammatory, anti-malarial, anti-microbial, anti-tumor, anti-HIV, and anti-tubercular. In addition, Schiff base, which is synthesized from benzothiazole, has a wide range of applications in analytical, biological, inorganic, medical, and pharmaceutical fields. **[6]**

There are a number of unique properties associated with benzothiazole Schiff bases that have been discovered in pharmacological research. These properties include antioxidant properties, antifungal properties, anti-inflammatory properties, antibacterial properties, anticancer properties, and cytotoxic properties. As a result of their distinctive characteristics, significant physicochemical properties, and potential for use as novel therapeutics. A considerable amount of attention has been drawn to the construction of metal complexes based on hydrazine/hydrazone ligands.**[7-9]**

The extra donor sites provided by benzothiazole anchored hydrazones—nitrogen and sulfur atoms—make them a highly intriguing class of ligands. Additionally, benzothiazole's biological properties are closely associated with metal ion coordination, which enhances its synthetic selectivity, sensitivity, and flexibility toward transition metal ions. When compared with a free ligand, metal ions enhance the overall activity of the complex. **[10-12]**

As various efforts have been made to develop new structural prototypes for DNA-targeted guest molecules, benzothiazoles continue to be among the most adaptable classes of chemicals and are thus excellent substructures for further molecular research. Because of their diverse biological actions, such as those that are anti-malarial, anti-helmintic, anti-diabetic anti-convulsant, anti-tubercular, anti-analgesic, and anti-inflammtory, benzothiazole derivatives have received ongoing study.**[13-15]**

The current work was initiated in an effort to investigate the structural relationship between the first row transition metal ions and benzothiazole-derived hydrazone, as well as to investigate the mechanism of interaction of these metal complexes with DNA. The benzothiazole-derived ligand and its transition metal complexes are synthesised and characterised in this work. Agar gel electrophoresis, viscosity, and electronic absorption spectroscopy were also used to examine the binding and cleavage behavior of the synthesized metal complexes. **[16-17]**

2. EXPERIMENTAL DETAILS

Spectroscopic analysis viz., FT IR, UV-Vis., NMR, ESI-mass, TGA, magnetic susceptibility, physical experiments like, molar conductance, DNA binding, cleavage and antimicrobial screening, molecular docking procedures *etc*.

2.1 Synthesis of (E)-N'-((6-hydroxybenzo[d]thiazol-5yl) methylene) isonicotino hydrazide (H_2L^3)

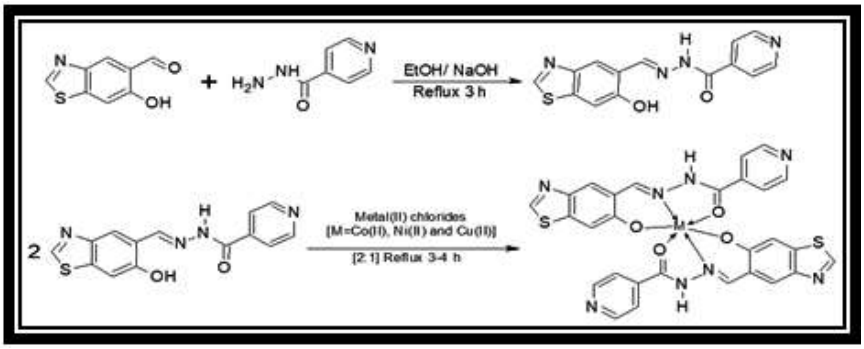
Schiff base ligand, (*E*)-*N*'-((6-hydroxybenzothiazol-5yl)methylene) isonicotinohydrazide (**H_2L^3**) was prepared by dissolving 2 mmol of 6-hydroxy-1,3-benzothiazole-5-carbaldehyde in 20 mL of ethanol and 2 mmol of isoniazid in 20 mL of ethanol, then added the catalytic amount of the NaOH. The mixture of these two reactants was refluxed for 3 h. The resulting yellow solid was filtered and recrystallized from ethanol, and then dried in vacuum at room temperature.
M.P. 187 °C; yield 84%; FT-IR (KBr, ν cm^{-1}): 3385 phenolic (OH), 3175 amine (N–H), 3044 aromatic (C–H), 2952-2862 aliphatic (C–H), 1643(C=N). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 10.1 (bs, 1H, -NH, hydrazide), 9.3 (s, 1H, -CH=N), 8.3(s, 1H, benzothiazole S–CH=N), 7.95 (d, 2H, pyridine Ar-H), 7.80-7.77 (q, 2H, Ar-H), 7.65 (s, 1H, Ar-H), 7.02 (s, 1H, Ar-H), 5.2 (bs, 1H, Ar-OH). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 98.1, 115.3, 121.3, 121.7, 122.4, 134.2, 140.8, 146.2, 149.2, 149.8, 153.5, 154.2, 158.6, 163.2. ESI-MS (m/z): 299 $(M+H)^+$

2.2 General procedure for the preparation of complexes

To prepare metal (II) complexes, the Schiff base ligand (**L=** (*E*)-*N*'-((6-hydroxybenzothiazol-5yl) methylene) isonicotinohydrazide) (0.566 g, 2 mmol) and the metal chloride salt ($CuCl_2.4H_2O$) (0.170 g, 1 mmol) were dissolved in ethanol in a 2:1 ratio (50 mL). Then, for 3 h, the above mixture was allowed to stir and reflux (**Scheme 4**). The resulting product was ethanol washed, filtered, and then recrystallized. The solid product obtained was dried in a vacuum over anhydrous $CaCl_2$. The same methodology was adopted to synthesis Ni (II) and Co (II) complexes by employing an ethanolic solution of various metal salt such as Nickel (II) chloride ($NiCl_2.6H_2O$), and Cobalt (II) chloride ($CoCl_2.6H_2O$), respectively.

3. RESULT AND DISCUSSION

In this study, novel divalent metal complexes were prepared by using the Schiff base ligand (H_2L^3) in an ethanolic medium with the corresponding metal chlorides in a 1:2 ratio (**Scheme 5.1**). The ligand and its metal complex can be dissolved in widely used organic solvents such as DMF and DMSO without any restrictions. Complexes and ligands are both stable at room temperature.



Scheme 5.1: Synthetic Route Of Schiff Base Ligand (H_2L^3) And Its Metal (II) Complexes

3.1 Elemental analysis and molar conductance measurements

The Schiff base ligand (H_2L^3) was used to generate the novel metal complexes in a 2:1 ethanolic solution with the appropriate metal chloride (M= Co (II), Ni (II), and Cu (II), and their elemental compositions are shown in **Scheme 5.1**.

Its metal (II) complexes were soluble in DMSO and DMF, and the ligand is soluble in a wide range of organic solvents. The conductivity values of these complexes (13-22 Ω^{-1} mol^{-1} cm^2) indicate that they are non-electrolytic in nature and analytical and spectral data on these complexes provide good results to predict the geometry of the complexes. Both the ligand and the metal complexes are stable at room temperature. In this case study, single crystal X-ray analysis was unsuccessful.

Table 5.1: Analytical Data And Physical Properties Of The Metal Complexes

Complexes	Color	Molecular Weight (Yield%)	M.p. (°C)	Λ_m (Ω^{-1} mol^{-1} cm^2)	% of Found (Calculated)			
					M	C	H	N
$[Co(HL^3)_2]$	Brown	654 (63)	>300	13	9.08 (9.02)	51.65 (51.46)	2.78 (2.78)	17.49 (17.19)
$[Ni(HL^3)_2]$	Dark green	653 (62)	>300	18	9.04 (8.98)	51.57 (51.48)	2.88 (2.78)	17.29 (17.15)
$[Cu(HL^3)_2]$	Dark brown	658 (59)	>300	22	9.69 (9.65)	51.19 (51.10)	2.78 (2.76)	17.11 (17.03)

3.2 ^{1}H NMR spectra

The ^{1}H NMR spectra of the Schiff base ligand (H_2L^3) in DMSO were recorded with TMS as an internal standard and are shown in **Fig. 5.1**. After comparison with the values from the standard literature, the value of chemical shifts was assigned to different protons. The -NH proton of the hydrazide group was assigned to the signal in the ^{1}H NMR spectrum of the ligand at 10.1 ppm and the singlet signal of the -CH=N proton in the Schiff base was detected at 9.3 ppm. The multiplet in the signal spectrum between 8.89 and 6.97 ppm was assigned to the aromatic ring proton of the ligand. The aromatic ligand OH is represented by the signal at 5.2 ppm.

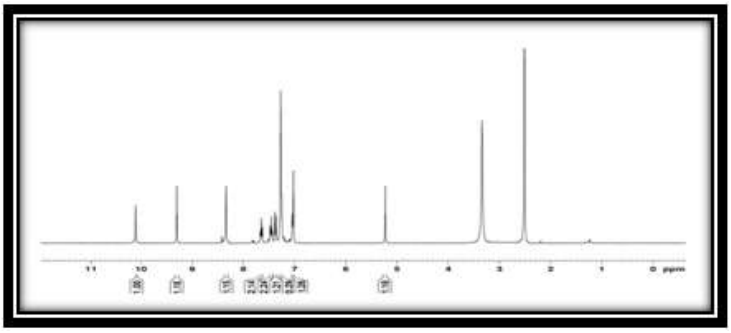


Figure 5.1: ^{1}H NMR Spectra Of Schiff Base Ligand (H_2L^3)

3.3 Mass spectroscopy

The ESI-mass spectrum was performed on the Schiff base ligand to determine its molecular mass (**Fig. 5.2)**. The molecular ion peak in the spectrum confirms the predicted structure of the synthesized compounds.

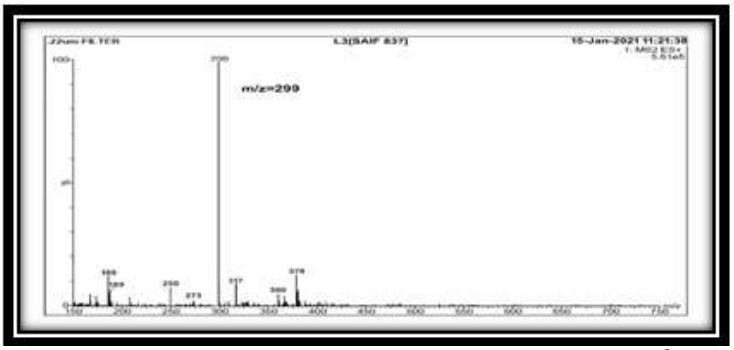


Figure 5.2: ESI-MS Spectra Of Schiff Base Ligand (H_2L^3)

3.4 FT-IR spectra

The spectrum of the complexes and the free ligand is compared in **Fig. 5.3**. The infrared spectroscopy results are summarized in **Table 5.2**. The infrared spectrum of the unbound Schiff base ligand has a wide bandwidth of about 3405 cm^{-1}. This explains why the intramolecular hydrogen bond between the phenolic hydrogen, the phenolic segment, and the azomethine nitrogen atoms [C-H=N] perturbs the low frequency of an aromatic hydroxyl exchange. However, the presence of a stronger OH group in the metal complex spectrum between 3346 and 3325 cm^{-1} suggests that the hydroxyl oxygen is still covalently bound to the M (II) ion without proton displacement.

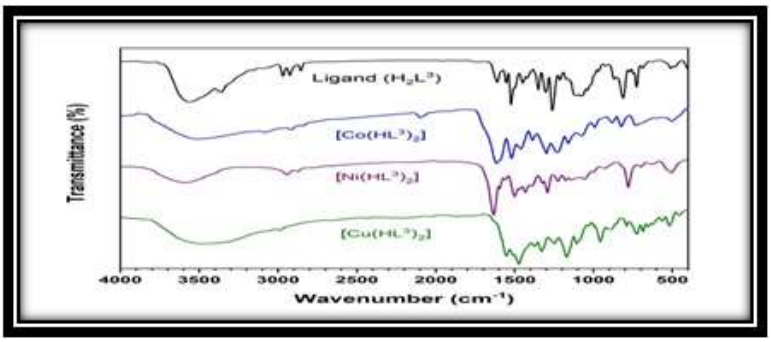


Figure 5.3: IR Spectra Of Schiff Base Ligand (H_2L^3) And Its Metal (II) Complexes

The (C=N) complexes are found in the 1610-1605 cm^{-1} region, but the ligands in the 1653 cm^{-1} region show a typical (C=N) group. The rate of extension of the (C=N) bonds decreased, suggesting that the ordered structure of the bonds improved as a result of the coordination of the metals with the amine nitrogen lone pair. Metal complexes showed the phenolic vibration of the ligands C-O at 1282 cm^{-1}, indicating that phenolic oxygen is aligned with a low frequency range. **[18, 19]**. Bands at 563-546 cm^{-1} and 454-446 cm^{-1} compatible with (M-O) and (M-N) stretching, respectively, were seen in far-IR spectroscopy of the metal complexes. **[20, 21]**.

Table 5.2: Infrared Spectral Data Of The Ligand And Its Metal Complexes

Complexes	υ(OH)	υ(-C=N)	υ(COO)	υ(C-O) phenolic	υ (M-O)	υ (M-N)
$C_{14}H_{10}N_4O_2S$ (H_2L^3)	3385	1653	1608	1282	-	-
$[Ni(HL^3)_2]$	3346	1605	1568	1242	558	454
$[Co(HL^3)_2]$	3338	1607	1564	1264	546	446
$[Cu(HL^3)_2]$	3325	1609	1563	1235	551	451

3.5 Electronic spectra and magnetic moment data

The electronic spectral bands and magnetic moment of metal complexes are summarized in **Table 5.3** and **Fig. 5.4.** The electronic spectra of the $[Ni(HL^3)_2]$ complex in aqueous medium show three absorption bands at 463 nm, 547 nm and 604 nm, corresponding to the transitions $^3A_{2g}(F)\rightarrow{}^3T_{1g}(P)$, $^3A_{2g}(F)\rightarrow{}^3T_{1g}(F)$ and $^3A_{2g}(F)\rightarrow{}^3T_{2g}(F)$. The Ni (II) ion has an octahedral structure as evidenced by the magnetic moment of two unpaired electrons measured on a scale of 3.24 BM (Table 5.3), which was within range in a high-spin configuration. [**20, 21**]

According to the six-coordinate octahedral Co (II) ion, the electronic spectrum of the [Co $(HL^3)_2$] complex (**Table 5.3**) shows two bands at 507 and 422 nm corresponding to $^4T_{1g}(F)\rightarrow{}^4A_{2g}(F)$ and $^4T_{1g}(F)\rightarrow{}^4T_{1g}(P)$ transitions. An octahedral cobalt (II) ion in a high-spin state may have contributed to the orbital contribution of the reported magnetic moment, which is larger (4.02 BM). **[22-24]**

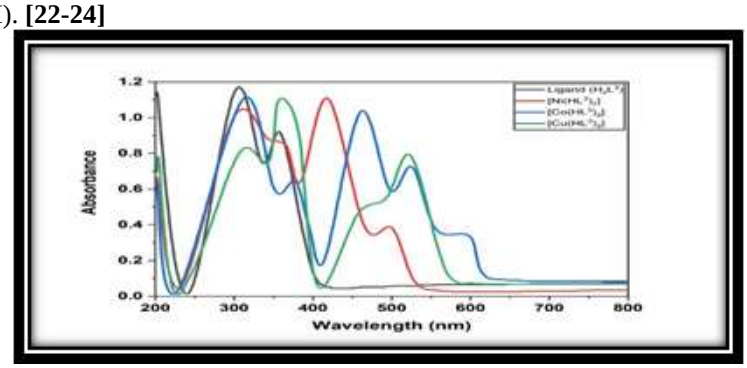


Figure 5.4: Electronic Spectra Of Ligand, [Ni $(HL^3)_2$], $[Co(HL^3)_2]$ And $[Cu(HL^3)_2]$

Table 5.3: Electronic Spectral Data, Their Assignment, And μ_{Eff} (B.M)

Compound	μ_{eff} (BM)	Band Position (nm)	Assignment
$[Co(HL^3)_2]$	4.02	507 422	$^4T_{1g}(F)\rightarrow{}^4A_{2g}(F)$ $^4T_{1g}(F)\rightarrow{}^4T_{1g}(P)$
$[Ni(HL^3)_2]$	3.24	604 547 463	$^3A_{2g}(F)\rightarrow{}^3T_{2g}(F)$ $^3A_{2g}(F)\rightarrow{}^3T_{1g}(F)$ $^3A_{2g}(F)\rightarrow{}^3T_{1g}(P)$
$[Cu(HL^3)_2]$	1.61	442	$^2E_g\rightarrow{}^2T_{2g}$

In the copper (II) complex scenario (**Table 5.3**), a broad and strong region conducive to $^2E_g\rightarrow{}^2T_{2g}$ Cu(II) ion transition in a distorted octahedral structure was observed [**25**]. The observed values of the magnetic moment (1.73 BM) of the copper

(II) complex are consistent with an orbitally non-degenerate ground state [**26**].

3.6 DNA binding studies (UV-visible spectroscopic studies)

Absorption spectroscopy is the most useful technique to determine how synthetic drugs interact with DNA helices. An increase or decrease in the absorbance hypsochromically recognized for the intercalation of the molecule with DNA results from the active, strong interaction between the chromophore of the molecule and the DNA. The strength of intercalative interactions and hypochromia are inversely associated.[**27**] The electronic absorption range for a Schiff base metal complex with CT-DNA (Tris buffer pH=7.2) is presented in **Fig 5.5.**

This is shown in **Fig. 5.5,** that the significant hypochromism (H%) was observed in the absorption spectrum of the metal complexes associated with CT-DNA, which is attributed to atomic interactions between molecules and the DNA [28]. The visible absorption spectra of all compounds show distinct and larger MLCT transitions. Bands below 350 nm are attributed to intra-ligand (IL) to $\pi \rightarrow \pi^*$ transitions

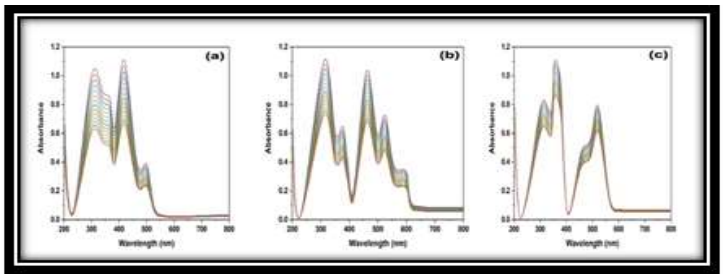


Figure 5.5: The absorption spectra of (a) = Co (II), (b) = Ni (II) and (c) = Cu (II) in Tris–HCl buffer upon addition of DNA.

To estimate the intrinsic binding constants K_b of complexes with CT–DNA, the absorbance at 507, 604 and 442 nm was measured. Intrinsic binding constants (K_b) were 0.91×10^4 M^{-1}, 1.74×10^4 M^{-1} and 3.08×10^4 M^{-1}, respectively for the complexes. Thus, the order of binding with CT-DNA was **Cu (II)** > **Ni (II)** > **Co (II)**. The continuity of the interaction of complexes with CT-DNA is determined by the planarity of the intercalating molecule. This suggests that the difference in K_b between the three complexes is determined by the co-ordination of the primary compound.

The intrinsic binding constants K_b of complexes containing CT-DNA were estimated by measuring absorbance at 507, 604 and 442 nm. The intrinsic binding constants (K_b) for the complexes were 0.91×10^4 M^{-1}, 1.74×10^4 M^{-1} and 3.08×10^4 M^{-1}, respectively. In this case, Cu (II) was found to bind with CT-DNA more strongly than Ni (II) and Co (II). As a result of the planarity of the intercalating molecule, continuous complexes bind to CT-DNA more efficiently. This implies that the coordination of the main component determines the difference in K_b between the three complexes.

3.7 Viscosity measurement

Viscosity measurements were used to identify new DNA binding properties. This is the most important and least significant approach to detecting DNA binding in solution. [**29**] A test was conducted at room temperature to measure the viscosity. A partial and non-classical intercalation chemical is used to reduce the length and viscosity of the DNA. This measurement provides more support for intercalative binding and is a useful way to identify changes in DNA length and learn more about how metal complexes bind to DNA. Intercalative bonding in DNA has been shown to result in an increase in viscosity because the strong separation of DNA base pairs causes the DNA molecule to stretch due to intercalative bonding. As a powerful intercalating agent, ethidium bromide is commonly used in DNA binding investigations because of its capacity to accept ligand between DNA base pairs. Using viscosity measurements, **Fig. 5.6** depict the binding of complexes to DNA. Enhanced viscosity measurements have shown that metal complexes such as Cu (II) and Ni (II) have higher binding efficiencies with DNA, while molecules such as Co (II) have a significantly lower viscosity. Amplified viscosity may be attributable to the complex's intercalative affinity: EB > Cu (II) > Ni (II) > Co (II).

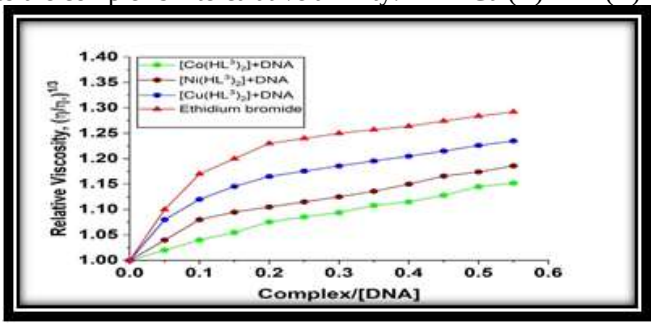


Figure 5.6: Effects Of Increasing Amount Of 4(A-D) Compounds On The Relative Viscosity Of CT-DNA At 25 ±0.1 °C.

3.8 DNA photocleavage studies

The photoinduced DNA cleavage activity of Schiff base ligands and their metal (II) complexes at 50 M was investigated after irradiation with UV light at 365 nm for 1 h. (**Fig. 5.7**). Upon irradiation, ligand and complexes cleave DNA by producing singlet oxygen or hydroxyl radicals. There are a number of essential properties these molecules possess, including the ability to interact with double-stranded DNA and to intercalate between DNA base pairs. The pUC 19 DNA is available in three distinct configurations: supercoiled, nicked, and linear. Electrophoresis allows these different types of proteins to be distinguished based on their different migration speeds. It has been observed that super-coiled DNA migrates at the fastest rate, nicked DNA migrates at the slowest rate, and linear DNA migrates between the two. As shown in Figure 5.7, pUC19 DNA was separated by gel electrophoresis after complex incubation and 365 nm illumination. There was no DNA cleavage in the control (lane 1) in the absence of chemicals. As the complex concentration grows, the amount of DNA in form I gradually decline while the amount of DNA in form II increases.[**30**] All the complexes shows DNA cleavage at greater doses. The photocleavage activities of these compounds is caused by the presence of free HC=N links in the imine compound and the presence of additional heterocyclic atoms via photoexcitation of ligand π-π* and n-π* transitions.

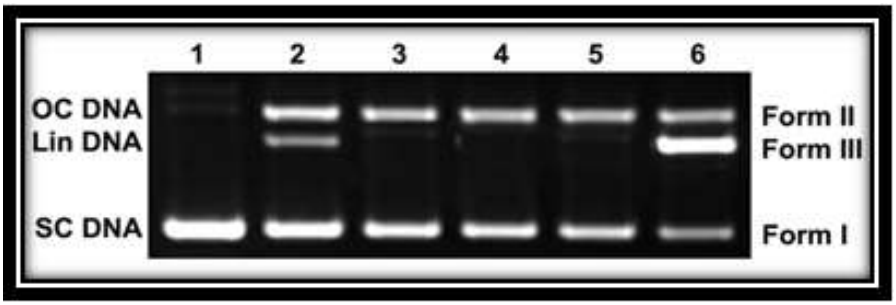


Figure 5.7: Effects Of Ligand/Co/Ni/Cu Complexes At Same Concentrations (50 µmol/L) On The Puc 19 Supercoiled DNA Against OH Generated By Photolysis At 360 Nm For 30 Min. Lane 1, Untreated DNA (Control); Lane 2, DNA + H_2O_2; Lane 3, DNA + Schiff Base Ligand (50 µmol/L); Lane 4, DNA + Co(II) Complex (50 µmol/L); Lane 5, DNA + Ni(II) Complex (50 µmol/L); Lane 6, DNA + Cu(II) Complex (50 µmol/L).

4 CONCLUSION

In this chapter, we discuss the synthesis of benzothiazole based Schiff base ligand and its metal (II) complexes and their characterization using various analytical and spectroscopic techniques. A study of the interaction between compounds and DNA was conducted using UV–VIS spectroscopy and viscometer measurements. In summary, the findings confirm that the complexes bind to double-stranded DNA with binding constants, and reveal that intercalation is the mode of binding through intercalation. An increase in concentration of the compounds resulted in a greater viscosity of DNA bound to the compounds. In the synthesized complexes, Cu (II) complex appear to produce good result, as revealed by DNA cleavage results.

REFERENCES

1. S. S. David, E. Meggers, Inorganic chemical biology: from small metal complexes in biological systems to metalloproteins, Current Opinion in Chemical Biology, 12, **2008**, 194-196.
2. S.P. Fricker, Metal based drugs: from serendipity to design, Dalton Trans. 43, **2007**, 4903–4917.
3. M. Selvaganapathy, N. Raman, Pharmacological Activity of a Few Transition Metal Complexes: A Short Review. J Chem Biol Ther 2: **2016**, 108.
4. P. Jayaseelan, E. Akila, M. Usha Rani, R. Rajavel, Synthesis, spectral characterization, electrochemical, anti-microbial, DNA binding and cleavage studies of new binuclear Schiffbase metal(II) complexes derived from o-hydroxyacetophenone, J. Saudi Chem. Soc. 20(6), **2016**, 625–634.
5. M.P. Sathisha, S. Budagumpi, N.V. Kulkarni, G.S. Kurdekar, V.K. Revankar, 615 K.S.R. Pai, Eur. J. Med. Chem. 45, **2010**, 106-113.
6. M. Sirajuddin, S. Ali, A. Badshah, Drug-DNA interactions and their study by UV–visible, fluorescence spectroscopies and cyclic voltametry, J. Photochem. Photobiol. B Biol. 124, **2013,** 1–19.
7. Kellett, Z. Molly, C. Slator, V. McKee, N.P. Farrell, Molecular methods for assessment of non-covalent metallodrug-DNA interactions, Chem. Soc. Rev. 48(4), **2019,** 971–988.
8. J. Lion, C.S. Matthews, G. Wells, T.D. Bradshaw, M.F.G. Stevens, A.D.621 Westwell, Bioorg. Med. Chem. Lett. 16, **2006,** 5005-5008.
9. R.D. Chakole, N.D. Amnerkar, P.B. Khedekar, K.P. Bhusari, Indian J. 627 Heterocycl. Chem. 15, **2005**, 27-30.
10. M.S. Kasare, P.P. Dhavan, B.L. Jadhav, S.D. Pawar, In-vitro antibacterial activity of Ni(II), Cu(II), and Zn(II) complexes incorporating new azo-azomethine ligand possessing excellent antioxidant, anti-inflammatory activity and protective effect of free radicals against plasmid DNA, Synth. Commun. 49(23), **2019**, 3311–3323.
11. Chimirri, S. Grasso, P. Monforte, A. Rao, M. Zappalà, A.M. Monforte, C. Pannecouque, M. Witvrouw, J. Balzarini, E.D. Clercq, Synthesis and biological activity of novel 1H,3H-thiazolo[3,4-a]benzimidazoles: Non-nucleoside human immunodeficiency virus type 1 reverse transcriptase inhibitors, Antivir. Chem. Chemother. 10(4), **1999**, 211–217.
12. M.A. Malik, O.A. Dar, P. Gull, M.Y. Wani, A.A. Hashmi, Heterocyclic Schiffbase transition metal complexes in antimicrobial and anticancer chemother- apy, Med Chem Comm 9(3), **2018**, 409–436.
13. H. Hiyoshi, N. Goto, M. Tsuchiya, K. Iida, Y. Nakajima1, N. Hirata, Y. Kanda, K. Nagasawa, J. Yanagisawal, 2-(4-Hydroxy-3-methoxyphenyl)-benzothiazole suppresses tumor progression and metastatic potential of breast cancer cells by inducing ubiquitin ligase CHIP, Sci. Rep. 4, **2014,** 1–10.
14. N.A. Al-Masoudi, N.N.A. Jafar, L.J. Abbas, Baqir S.J, C. Pannecouque, Synthesis and anti-HIV activity of new benzimidazole, benzothiazole and car- bohyrazide derivatives of the anti-inflammatory drug indomethacin, Z. Naturforsch –Sect. B J. Chem. Sci. 66(9), **2011,** 953–960.
15. K. Shanthalakshmi, M. Bhat, S.L. Belagali. Synthesis of Benzothiazole Schiff's bases and screening for the anti-oxidant activity. 6(3), **2017,** 610-616.
16. S. Sarkar. Design, synthesis, and evaluation of antitubercular activity of a novel benzothiazole-containing an azetidinone ring. 48(2), **2018**, 28-31.

17. H.M. Diaz, R.V. Molina, R.O. Andrade, D.D. Coutino, L.M. Franco, S.P. Webster, M. Binnie, S.E. Soto, M.I. Barajas, I.L. Rivera, G.N. Vazquez, Bioorg. Med. Chem. Lett. 18, **2008**, 2871-2877.
18. J. Devi, S. Kumar, D. Kumar. Synthesis, characterization, in vitro antimicrobial and cytotoxic evaluation of Co(II), Ni(II), Cu(II) and Zn(II) complexes derived from bidentate hydrazones. Res Chem Intermed 48, **2022**, 423–455.
19. Y. Deswal, S. Asija, D. Kumar. Transition metal complexes of triazole-based bioactive ligands: synthesis, spectral characterization, antimicrobial, anticancer and molecular docking studies. Res Chem Intermed 48, **2022**, 703–729.
20. Z. Abbas, H.S. Tuli, , M. Varol. Organotin (IV) complexes derived from Schiff base 1,3-bis[(1E)-1-(2-hydroxyphenyl)ethylidene] thiourea: synthesis, spectral investigation and biological study to molecular docking. J Iran Chem Soc 19, **2022**, 1923–1935.
21. J. Devi, S. Sharma, S. Kumar. Transition metal (II) complexes of hydrazones derived from tetralone: synthesis, spectral characterization, in vitro antimicrobial and cytotoxic studies. Res Chem Intermed 47, **2021**, 2433–2467.
22. S. Chandra, L. K. Gupta. Mass. EPR, IR and electronic spectroscopic studies on newly synthesized macrocyclic ligand and its transition metal complexes. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 62, 4–5, **2005**, 1125-1130.
23. O.G. Shakirova, N.V. Kuratieva, L.G. Lavrenova, A.N. Protsenko, I.A. Tkachenko, S.K. Petkevich, V.I. Potkin. Syntheses, structures and properties of magnetically active copper(II) compounds with 3-amino-5-(4-methylphenyl)isoxazole, Polyhedron, 146, **2018**, 121-128.
24. S.G. Shankarwar, B.B. Nagolkar, V.A. Shelke, T.K. Chondhekar. Synthesis, spectral, thermal and antimicrobial studies of transition metal complexes of 14-membered tetraaza [N_4] macrocyclic ligand, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 145, **2015**, 188-193.
25. Kareem, H. Zafar, A. Sherwani, O. Mohammad, T.A. Khan, Synthesis, characterization and in vitro anticancer activity of 18-membered octaazamacrocyclic complexes of Co(II), Ni(II), Cd(II) and Sn(II), Journal of Molecular Structure, 1075, **2014**, 17-25.
26. R. Kumar, S. Obrai, A. Sharma, A. K. Jassal, M. S. Hundal, J. Mitra, Synthesis, structural, spectral characterization, DFT analysis and antimicrobial studies of aquabis(L-ornithine)copper(II) picrate, Journal of Molecular Structure, 1075, 2014, 43-48,
27. Gubendran, J. Rajesh, K. Anitha, P. Athappan. Synthesis, characterization, DNA-binding and cleavage studies of polypyridyl copper(II) complexes, Journal of Molecular Structure, 1075, **2014**, 419-429.
28. H. Wu, T. Sun, K. Li, B. Liu, F. Kou, F. Jia, J. Yuan, Y. Bai, Synthesis, Crystal Structure, and DNA-Binding Studies of a Nickel(II) Complex with the Bis(2-benzimidazolymethyl)amine Ligand. Bioinorganic Chemistry and Applications, vol. 2012, Article ID 609796, **2012**, 7 pages.
29. L. Arno, B. Jessica L. Viscosity Measurements of DNA Solutions with and Without Condensing Agents. Biorheology, 51, **2014**, 15-28.
30. N. Shahabadi, M. Falsafi, N. H. Moghadam, DNA interaction studies of a novel Cu(II) complex as an intercalator containing curcumin and bathophenanthroline ligands, Journal of Photochemistry and Photobiology B: Biology, 122, **2013**, 45-51.