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Antioxidant, and Anti-inflammatory Studies of Transition Metal Complexes Derived from Dibenzo[a,e]phenazine with DFT and Molecular Docking Investigation

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ABSTRACT

A novel series of Cu(II), Ni(II), Ru(III), VO(IV), and Ce(IV) complexes have been synthesized involving a potentially tetradentate Schiff base ligand, which was obtained by condensation of benzene-1,2-diamine with phenanthrene-9,10-dione. Physicochemical approaches such as UV-Vis, FT-IR, NMR, and Mass spectroscopy were used to determine the geometry of the complexes. DFT calculations at the B3LYP/6-31G(d) level were used to analyze the thermodynamic stability and biological accessibility of the complexes. A molecular docking analysis was also performed on 1BNA receptor. This protein receptor responded favorably to both the Schiff base ligand and metal complexes. All metal complexes have a significant potential to bind to CT-DNA via the intercalation mechanism. All the *in vivo* and *in vitro* screening studies showed that the complexes exhibit higher activities than the free Schiff base.

Keywords: Schiff base, DFT calculation, intercalation, Molecular docking, *in vitro*, *in vivo*.

1. INTRODUCTION

The newly discovered class of macrocyclic molecules has been a stimulating area of research in recent years, because of potential analytical, industrial, and medicinal ramifications. Coordination complexes of macrocyclic ligands have acquired consideration because of its structural resemblance with many other natural systems like cobalamines,

porphyrins etc[1,2]. The synthesis of structurally imine or azomethine (Schiff base) ligands received a lot of attention because they are one of the most common ligand systems in inorganic chemistry. Researchers have devoted considerable thought to designing innovative Schiff bases and metal chelates because to their preparative accessibility and structural flexibility[3]. Metal chelates with Schiff bases as ligands have enormous chemical and biological relevance due to the presence of an azomethine linkage (C = N) incorporated in their skeletons[4.]

Macrocyclic Schiff base ligands results in exceptionally high binding constants for many d- and f-block metals[5]. To detect greater selectivity and sensitivity, Schiff base ligands are also used in optical and electrochemical sensors, as well as in numerous chromatographic techniques. These macrocyclic Schiff base complexes were also employed as dyes, pigments, metallo enzymes magnetic resonance imaging, sensors, catalyst and NMR shift reagents. It also has a wide range of biological applications, including antibacterial, antifungal, anticancer, antiviral, antitumor, and so on. Schiff bases can be utilized to make compounds that are biochemically active[6,7]. The structure of 9,10-phenanthrenequinone is similar to that of phenanthroline compounds, which are capable of intercalating contacts with DNA and causing antiproliferative effects in cells . Unlike other o-quinones, 9,10-phenanthrenequinone is a weaker chelating agent than catecholates, and only a few coordination complexes with transition metal ions have been identified[8,9].

2. EXPERIMENTAL

2.1. Materials and Methods

All the chemicals used were analytical agent supplied from Sigma-Aldrich and metal salts were purchased from E.Merck. All the organic solvents were distilled from appropriate drying agents immediately prior to use

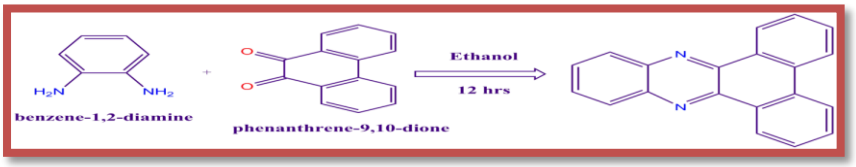
2.2. Physical measurements

Attenuated total internal reflection (ATR) solid state Infrared spectra were performed on a Bruker TENOR 27 spectrometer using a KBr pellet in the range of 400-4000Cm^{-1}. Nuclear Magnetic Resonance was recorded on a JEOL EX270, Bruker DPX 300,DPX 400 or AV 400 spectrometer using TMS ($SiMe_4$) as an internal reference. Absorption spectra were measured JASCO V-530 UV-VIS spectrometer at Room Temperature. Varian E 112 EPR spectrometer was used to record the EPR spectra of complex in DMSO solution both at room temperature (300 K) and liquid nitrogen temperature (77 K) using TCNE (tetracyanoethylene) as the g–marker. Electro spray ionization was (ESI-MS positive) spectra were performed on a MICROMASS Q-TOF mass spectrometer. Plethysmometer was used to measure the anti–inflammation in the paw of albino rats.

2.3. Ligand and metal complexes synthesis

2.3.1. Synthesis of Ligand

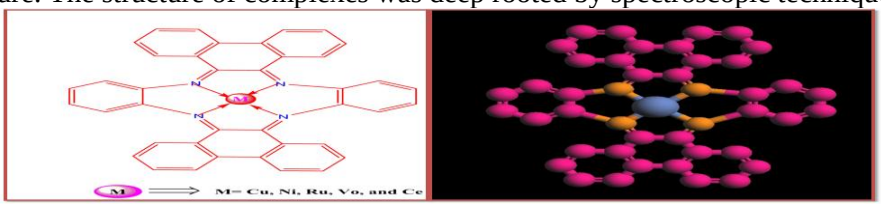
The Schiff base ligand was synthesized by the condensation of benzene-1,2-diamine and phenanthrene-9,10-dione.The ethanolic solution of benzene-1,2-diamine (1mmol) (10mL) was added to a mixture of phenanthrene-9,10-dione (1mmol) (10mL) and then (2-4) drops of glacial CH_3COOH was added. The reaction was refluxed for 12 hrs. The yellow color precipitate was formed. The resulting products was removed from Dean-Stark trap, filtered and washed which is stored in air tight container or cover.



Scheme-1. Synthesis of Schiff base ligand

2.3.2. Synthesis of Metal Complex

About 1:2 proportion of the ethanolic solution of the Hydrated metal salts and the Schiff base ligand was stirred and then refluxed for 9hrs to get a colored precipitate which was collected by filtration, washed with cold ethanol. Finally it was dried at Laboratory temperature. The structure of complexes was deep rooted by spectroscopic techniques.



Scheme-2. Structure of Metal complex and 3D- molecular structure of Metal complex

3. RESULTS AND DISCUSSION

3.1. ^{1}H-NMR and ^{13}C-NMR Studies

Using DMSO-d_6,^{1}H-NMR spectrum of ligand was recorded.The^{1}H-NMR range of ligand does not show a signal equivalent to a primary amine proton, which suggests the condensation of amino group. A peak at 8.04 ppm has been attributed to azomethine proton (-N=CH) of the free ligand.[10,11] The signal moved downfield to 8.45ppm, in the spectra of Ce(IV) complex. This revealed that the ligand containing the azomethine group is participating in coordination to the metal ion. The multiplet observed around 7.47-7.77ppm is due to aromatic protons [Figure-1].

The ^{13}C-NMR spectrum of Schiff base ligand displayed a sharp signal at 162.28 ppm corresponding to imine carbons.[12] This signal migrated upfield to 159.28ppm, in the Ce(IV)

metal complex. Another peak at 129 ppm in the ligand could be attributable to C-N carbons. In metal complex the signal is also shifted upfield to 126ppm after complexation. The signal appeared in 110-128ppm is due to the carbons of the aromatic group [Figure-1].

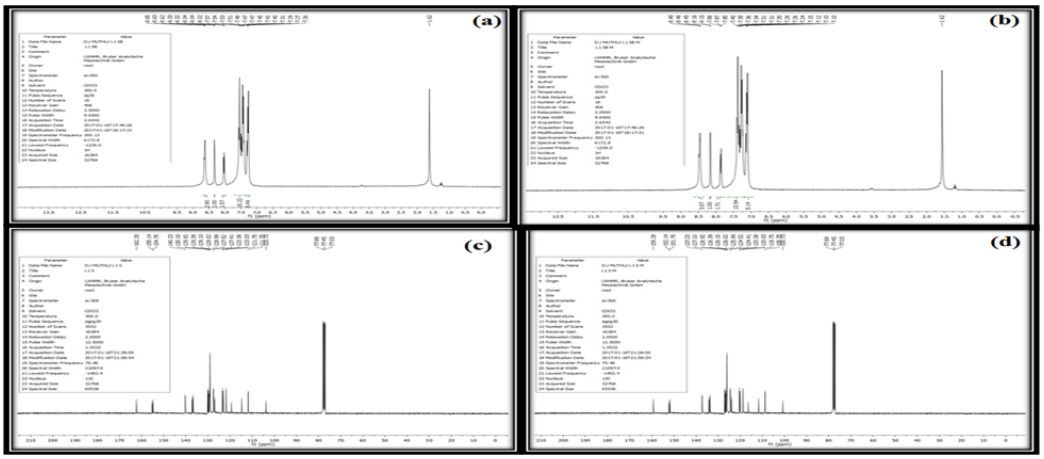


Figure-1 (a) ^{1}H-NMR Spectrum of Schiff base Ligand, (b) ^{1}H-NMR Spectrum of Cerium,(c) ^{13}C-NMR Spectrum of Schiff base Ligand and (d) ^{13}C-NMR Spectrum of Cerium

3.2. Mass spectrum

ESI-MS spectra have been used to investigate at the formation of Schiff base ligand and metal complexes. By correlating the molecular formula weight of these compounds to their m/z values, the hypothesized molecular formulas of these compounds were established[13,14]. The mass spectrum of ligand exhibited a molecular ion peak at m/z 280.10, which supports the proposed formulae (Figure-2). The Schiff base ligand also revealed a sequence of peaks at 217.08, 166.05, 154.05 and 65.04, which corresponded to distinct fragments, such as $[C_{15}H_9N_2]$,$[C_{11}H_5N_2]$,$[C_{10}H_6N_2]$and $[C_5H_5]$. This result correlates to the molecular formula proposed for synthesized compounds. In addition, the mass spectrum of Cu (II) complex displayed the parent molecular ions at m/z 623.17 corresponding to their molecular weight (Figure 11). The m/z of the molecular ion peak confirms that the stoichiometric of the complex. The peak observed at m/z 560.20, 356.13, 281.10, 204.07 and 151.03 assigned to $[C_{40}H_{24}N_4]^+$, $[C_{14}H_8N_2]^+$, $[C_{20}H_{12}N_2]^+$, $[C_{14}H_8N_2]^+$ and $[C_{10}H_6N_2]^+$ respectively.

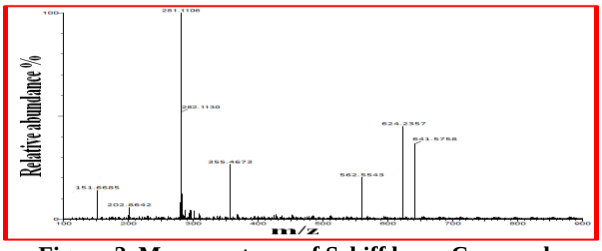


Figure-2. Mass spectrum of Schiff base -Cu complex

3.3. Electronic absorption spectra

The electronic absorption spectra of the ligand and the respective ruthenium and vanadium complexes were recorded in DMSO at room temperature in the range of wavelength of 1100nm to 200nm and the spectral information are recorded in Table-1. The electronic absorption spectrum of Schiff base ligand shows a predominant band at 344nm (29069 cm^{-1}) region, which is assigned as inter ligand charge transfer (INCT) band. These bands move to longer wavelengths during the formation of complexes, indicating that the nitrogen atom of azomethine group is coordinated to the metal ions[15]. The absorption band observed around 518-586nm (19,305-17,3064cm^{-1}) because of d-d transitions of the metal ions. All metal complexes have a square planar geometry, with the exception of the VO(IV) complex, which has a square pyramidal geometry[16]. [Figure-3]

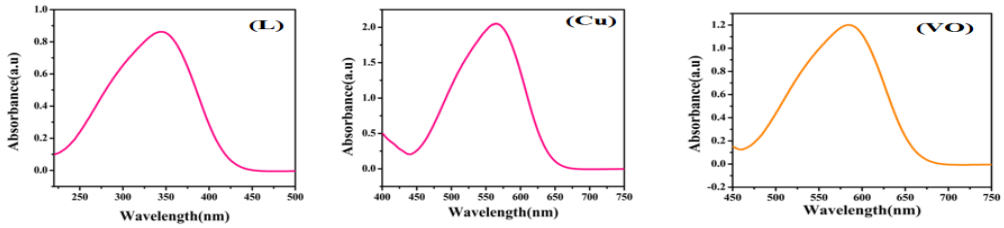


Figure-3. Electronic absorption spectra of Schiff base ligand and Complexes

3.4. FT-IR Spectroscopy

In the integrated Schiff base transition metal complexes, the FT-IR spectra reveals vital information about the type of the functional group linked to the metal ion[17]. The azomethine group of the ligand shows a stretching band at 1625 cm^{-1} which is also shifted to lower frequencies around 1540-1580 cm^{-1}, demonstrating that the azomethine nitrogen atom is coordinated to the metal [Figure-4]. The absence of ν(C=O), and aromatic primary amine bands ν(N-H) expected to exist in free 9,10-phenanthrenequinone and benzene-1,2 diamine individually, supports the formation of the proposed macrocyclic skeleton of the compounds. Moreover, the occurrence of additional bands in their spectra at 450-473 cm^{-1}, ascribed to the ν(M–N) stretching vibrations that are not detected in the spectra of free ligands, further substantiated the complex formation [Table-1]. In expansion, the Vanadyl complex display band at 943 cm^{-1} assignable to V=O mode[18].

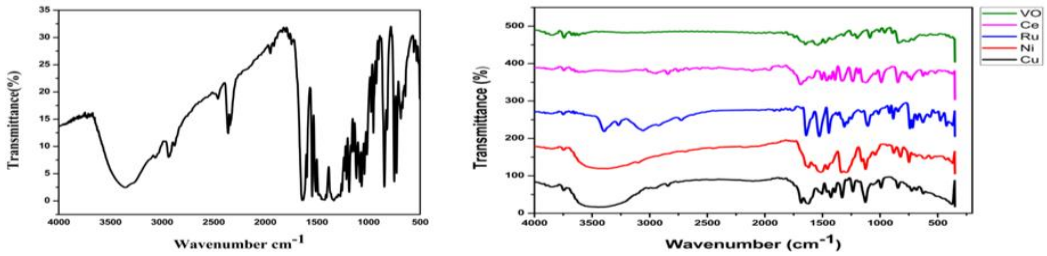


Figure-4. FT-IR spectrum of Ligand and metal complexes

Table-1. Electronic absorption spectral assignments and important IR spectral bands for Schiff base ligand and its complexes

Compounds	λ max (nm)	Absorption (cm^{-1})	Band assignment	Geometry of the complex	*ν*(CH=N) cm^{-1}	*ν*(M-N) cm^{-1}	*ν*(C=C) cm^{-1}
$C_{20}H_{12}N_2$	344	29069	n-π*	-	1625		1450
$C_{40}H_{24}CuN_4$	565	17699	$^2B_{1g}\rightarrow{}^2A_{1g}$	Square planar	1601	445	1445
$C_{40}H_{24}NiN_4$	530	18867	$^1A_{1g}\rightarrow{}^1B_{1g}$	Square planar	1580	486	1467
$C_{40}H_{24}RuN_4$	525	19047	LMCT	Square planar	1569	466	1420
$C_{40}H_{24}VON_{46}$	586	17064	$^2B_2\rightarrow{}^2E$	Square pyramidal	1535	480	1435
$C_{40}H_{24}CeN_{46}$	518	19305	LMCT	Square planar	1540	475	1439

4. *In vitro* BIOLOGICAL STUDIES

4.1. Absorption Spectroscopy

Changes in the absorption spectrum of metal complexes are analyzed with the successive addition of 10^{-3} mM CT-DNA concentrations to explore the distinctive DNA binding modes. The intercalation mode of interaction is defined by a reduction in absorbance (hypochromism) and a red shift in wavelength due to a strong stacking interaction involving the aromatic chromophore and DNA base pairs[19]. The intensity of the hypochromic and bathochromic shifts is used to explain the strength of intercalation. When the complexes intercalated with the base pairs of DNA the π* orbital of intercalated ligand in the complexes could couple with the orbitals of the base pairs of DNA, lowering the π- π* transition energy (energy gap between HOMO and LUMO) and resulting in bathochromism, while hypochromism is caused by non covalent π-π* interaction. Figure-5 shows the absorbance titration curves of complexes in the absence and presence of CT-DNA. The intensity of the π-π* bands diminishes (hypochromism) with a moderate red shift after DNA is added to the complexes[20]. The binding constant K_b was determined and depicted in Table-2. This absorption spectral outcome reveals that the Cu complex has a greater binding affinity than other complexes.

Table-2. Electronic absorption spectral data for the interaction of CT-DNA synthesized metal complexes

S. No	Compound	λ max		Δ λ	H%	$Kb\times10^4\,(M^{-1})$
		Free	**Bound**			
1.	$C_{40}H_{24}CuN_4$	397	391	6	1.51	3.78
2.	$C_{40}H_{24}NiN_4$	388	381	7	1.80	3.11
3.	$C_{40}H_{24}RuN_4$	374	369	5	1.33	2.83
4.	$C_{40}H_{24}VON_4$	379	374	5	1.31	2.31
5.	$C_{40}H_{24}CeN_4$	381	374	7	1.83	1.78

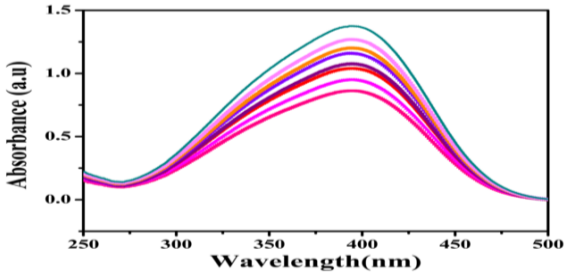


Figure-5. The absorption spectra of the Cu complex in buffer (pH =7.2) at 25°C in presence of increasing amount of CT-DNA.

4.2. Antioxidant activity

The stable DPPH radical scavenging model is widely used to investigate antioxidant activity in less time than other approaches. The interaction of the compounds with the free stable radical 1,1-diphenyl-2-picryl-hydrazyl (DPPH) at various concentrations was used to determine their reducing abilities with vitamin C as a standard. The Schiff base metal complexes were shown to significantly lower the concentration of the initial DPPH radical in solution.[21,22]. The graphical representation for the antioxidant activity of the ligand and metal complexes is shown in Figure-6. The corresponding ligand of all metal complexes has potent antioxidant action. Complex [$C_{40}H_{24}CuN_4$] has a greater antioxidant activity than other complexes. This is because metal ion chelation inhibits enzymes in the same manner as detoxifying enzymes function (superoxide dismutase). This brings the oxidation process to a stop (by reduction alkoxyl and phenylradicals).

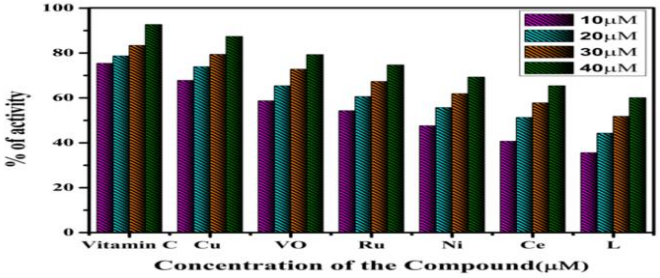


Figure-6. Antioxidant activity of ligand and metal complexes

5. *In-silico* STUDIES

5.1. Density Functional Theory studies:

DFT calculations and the B3LYP/6-31G(d) approach were used to optimize the geometry of the Schiff base ligand and its metal complexes[23]. Frontier molecular Orbital, HOMO and LUMO properties depicts the electrons in stable compounds. During the

chemical reactivity and optical characteristics analysis, HOMO and LUMO values are merely important. The ground state HOMO and LUMO energies of the synthesized compounds were determined and are shown in Figure-7&7a. Furthermore, the energy gap between E_{HOMO} and the E_{LUMO} becomes apparent in terms of molecular stability and activity, which may also be used to define the hardness or softness of compounds. A hard molecule with a large E_g band gap has limited reactivity, whereas a soft molecule with a smaller E_g band gap has a higher polarizable capacity and better adsorption tendency[24]. The E_{HOMO} for the free Schiff base ligand was -0.2297eV, and it was found on one of the imidazoline moiety, while the E_{LUMO} (-0.0830eV) was establish on both the azomethine group. The chemical hardness showed that Ni(II), Ru(III) and Ce(IV) are the most stable and less reactive complexes. Surprisingly, Cu(II) and VO(IV) had the lowest values, reflecting the softness and the hindrance capacity of the molecule. All coordination processes are unconstrained and stable, as demonstrated by the negative heat of formation value of all complexes. This is also confirmed experimentally by *in vitro* and *in vivo* studies.

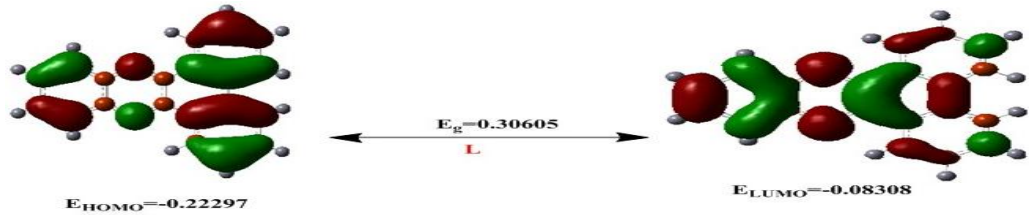


Figure-7. Illustrative presentation of frontier molecular orbital of Schiff base obtained using B3LYP/6-31G (d)basis set

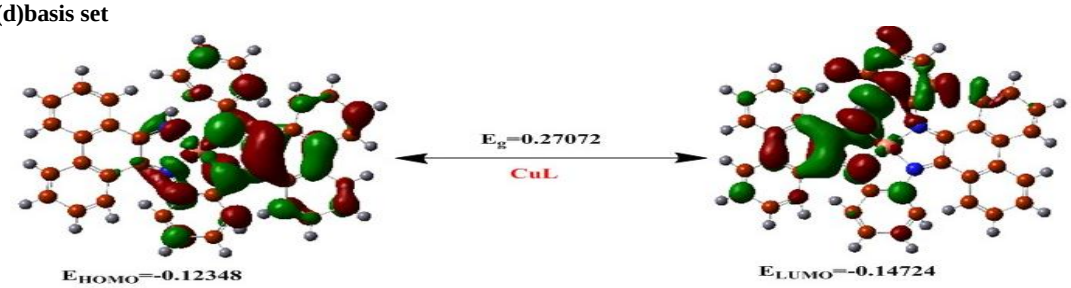


Figure-7a. Illustrative presentation of frontier molecular orbital of Cu(II) complexes obtained using B3LYP/6-31G (d)basis set

5.2. Molecular Docking

The molecular docking methodology has recently become the preferred method for the creation of innovative drug design. The purpose of molecular docking is to better understand the interaction between drugs and nucleic acids, as well as to confirm the drug molecule's binding location on the target DNA[25]. The synthesized compounds were docked with the DNA duplex of sequence d(CGCGAATTCGCG)2 dodecamer (PDB ID: 1BNA) during molecular docking study. The docking results revealed the proper binding location and underlined the orientation of compounds inside the DNA [26]. Lower binding energy

emphasizes the molecule's (Schiff base and its metal complexes) greater potency of binding affinity towards the receptor (DNA). The docking study produced useful results, as shown in Figure-8, which depicts the most likely docked poses of the chemicals investigated. The interaction between the chemicals and DNA can be extrapolated from the image as intercalation with the oxygen atom of the phosphate backbone. Intercalation is achieved by enhancing van der Waals and hydrophobic interaction with the DNA functional group, resulting in stability. -231.15 (L), -340.61 (Cu), -271.57 (Ni),-315 (Ru), -309.34 (Ce) and -330.32 (VO) kJ/ mol were discovered to be the binding energies of docked ligand and metal complexes, respectively. The higher binding affinities of the complexes suggest that they bind to DNA more effectively than the ligand, according to the data. This can also be deduced from the fact that the lower the relative binding energy, the more complexes bind to DNA. The results match the DNA binding affinity found in vitro DNA binding experiments. As a result, it is possible to conclude that the spectroscopic techniques and the molecular docked model have a reciprocal complement that can justify the spectroscopic results. This further gives solid proof of intercalation mode.

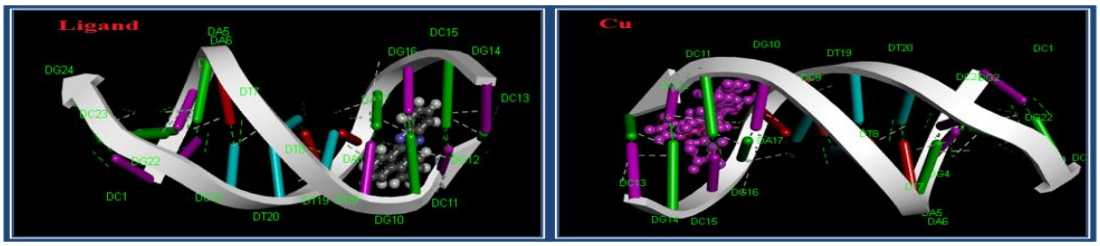


Figure-8.Three dimension(3D) binding interaction of Ligand and metal complexes with DNA (PDB ID:1BNA)

6. *In vivo* EXAMINATION OF ANTI-INFLAMMATORY OF *albino* RATS

The anti-inflammatory activity of the Schiff base ligand and metal complexes *in vivo* was tested using Carragenan-induced mouse paw edoema hindrance[27]. This anti-inflammatory action was dose-dependent, with the most noteworthy fixation, 200 mg/kg, being statistically significant. Investigation of Figure-9 reveals that all of the complexes effectively reduce inflammation. The anti-inflammatory activity of all the complexes at 1h, 2h, 3h and 4h was compared with the reference drug ibuprofen and parent drug felbinac. The anti-inflammatory activity of the consolidated ligand and its metal complexes was excellent. When contrasting the anti-inflammatory effectiveness of metal chelates to that of standard ibuprofen, the free ligand was shown to be significantly less effective. The expanded action of the metal chelates can be clarified in light of the chelation theory[28]. Copper and vanadyl complexes have the most activity among metal complexes. It is possible to conclude that the findings of this study support the use of this complex in the treatment of several inflammatory and painful disorders, confirming the existence of heterocyclic moieties in the ligand system.

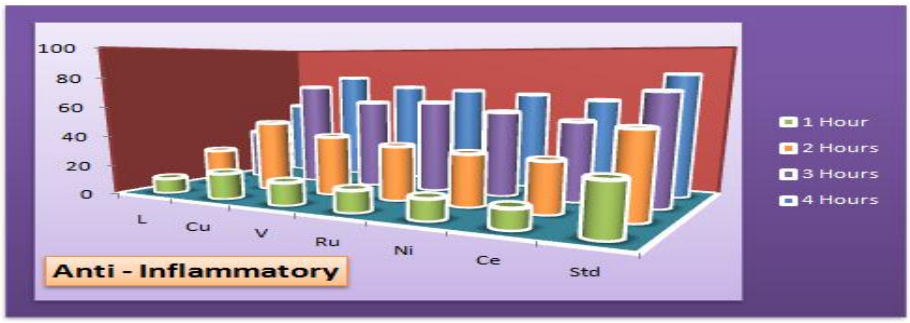


Figure-9. Anti-inflammatory activity of ligand and metal complexes

7. CONCLUSION

In the current research work, biologically active Schiff base ligand and their metal complexes are synthesized and characterized. Physical and spectral data were confirmed the square planar geometry of the metal complexes. DFT calculation also confirms the square planar geometry and the stability of the metal complexes. Electronic absorption assays confirmed the intercalative binding mode between the synthesized complexes and CT-DNA. Molecular Docking studies against the 1 BNA receptors corroborated the higher biological efficiency of the metal complexes. Pharmaceutical examinations like antioxidant, and anti inflammatory properties are higher for copper complexes than the other compounds.

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REFERENCES

1. Kun Zhang,Chao Jin, Yuchen Sun, Feifan Chang and Wei Huang, *Inorganic Chemistry Communication*, 53, 7803 (2014). x.doi.org/10.1021/ic5008846
2. A.A. A. Aziz and S. H. Seda, *Journal of Fluorescence*, 27, 1051 (2017). DOI 10.1007/s10895-017-2039-9
3. E. V. Shchegolkov, I. V. Shchur, Y. V. Burgart, P.l A. Slepukhin, N. P. Evstigneeva, N. A. Gerasimova, N. V. Zilberberg, N. V. Kungurov,V.I. Saloutin and O. N. Chupakhin, Polyhedron, 194, (15) , 114900 (2021) https://doi.org/10.1016/j.poly.2020.114900
4. S. H. Sumrra, M. Ibrahim, S. Ambreen, M. Imran, M. Danish, and F. S. Rehmani, *Bioinorganic Chemistry and Applications*, 2014 (2014). http://dx.doi.org/10.1155/2014/812924

5. E. Pelit and Z. Turgut , *Arabian Journal of Chemistry*, 9, 421 (2016). http://dx.doi.org/10.1016/j.arabjc.2014.02.017
6. S. S. Jawoor, S. A. Patil and S. S. Toragalmath, *Journal of Coordination Chemistry*, 71 (2), 271 (2018) https://doi.org/10.1080/00958972.2017.1421951
7. I. H. Ibrahim, and H. A. Hasan, *Systematic Reviews in Pharmacy*, 12, (1), 306 (2021).
8. A. J. Antony and M. J. Kala, Der Pharmacia Lettre, 8 (1), 310 (2016)
9. A. Anjum, S. Paswan, M. kumar, H.Ali and R. K. Dubey, *Asian Journal of Chemistry*; 31, (4), 943 (2019) https://doi.org/10.14233/ajchem.2019.21861
10. E.Yousif, A. Majeed, K. Al-Sammarrae, N. Salih ,J. Salimon and B.Abdullah, *Arabian Journal of Chemistry*, 10, S1639 (2017) http://dx.doi.org/10.1016/j.arabjc.2013.06.006
11. A. J. Abdulghani and A. M. N. Khaleel, *Bioinorganic Chemistry and Applications*, (2013) http://dx.doi.org/10.1155/2013/219356
12. M. Shakira, A. Abbasia, M.Azama and A. U. Khan, *Spectrochimica Acta Part A*, 79, 1866 (2011) https://doi.org/10.1016/j.saa.2011.05.077
13. M.Padmaja, J.Pragathi, B. Anupama, and C. Gyana Kumari, *European Journal of Chemistry*, 9(4), 2145(2012,)
14. A.K. Surabhi, and K. Pradeepkumar, *Journal of Applied Chemistry*, 9 (11), 11 (2016).
15. A.A. Ahmed, S. A. BenGuzzi and O. M. Ahshad, *Rasayan Journal of Chemistry*, 2, (4), 781, (2009), https://www.researchgate.net/publication/319723486
16. B. E. Klamm, C. J. Windorff, M. L. Marsh, D. S. Meeker, and T. E. A. Schmitt, *Royal Society of Chemistry*, 00, 1-3, (2018) DOI: 10.1039/C8CC03571G
17. J. M. Mir, R.C. Maurya, P.K. Vishwakarma, D.K. Rajak, B.A. Malik, P.S. Jaget and P. Bohre, *Journal of Theoretical & Computational Science*, 4, (1) (2017) DOI: 10.4172/2376-130X.1000152
18. A. A. S. Al-Hamdani a,A.M. Balkhi, A. Falah and S. A. Shaker, Journal of Saudi Chemical Society, 20 (5), 487 (2016) http://dx.doi.org/10.1016/j.jscs.2012.08.001
19. E. S. Aazam and M. Zaki, *Inorganic Chemistry*, 5, 610 (2020) DOI: 10.1002/slct.201903583
20. S. Zehra, T. Roisnel, and F. Arjmand, *ACS Omega*, 4, 7691 (2019), DOI: 10.1021/acsomega.9b00131
21. M.Sirajuddin, N. Uddin , S. Ali, and M. N. Tahir, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 116, 111 (2013). http://dx.doi.org/10.1016/j.saa.2013.06.096
22. M. Sirajuddin, S. Ali, F. A. Shah, M. Ahmad and M. N. Tahir, *Journal of Iranian Chemical Society*, 11, 297 (21013), DOI 10.1007/s13738-013-0301-x
23. I. Warad, H. Suboh, N.Al-Zaqri, A. Alsalme, F.A. Alharthi, M. M. Aljohanie and A. Zarrouk, *Royal Society of Chemistry*, 10, 21806 (2020) DOI: 10.1039/d0ra04323k
24. N. Uddina, F. Rashidb, S. Alia, S. A. Tirmizia, I.Ahmad, S. Zaibb, M. Zubira, P L. Diaconescud, M. N. Tahire, J.Iqbal and A. Haider, *Journal of Biomolecular Structure and Dynamics*, 38 (11) 3246 (2020) https://doi.org/10.1080/07391102.2019.1654924

25. A. Paul, S.Anbu, G. Sharma, M. L. Kuznetsov, B. Koch, M. Fátima C. Guedes da Silva and A. J. L. Pombeiro, *Dalton Transition*, 44, 19983, (2015) DOI: 10.1039/c5dt02880a
26. M. Musthafa, K.N. Aneesrahman, B. Perumalsamy, T. Ramasamy, R. Ganguly, and A. Sreekanth, *Journal of Molecular Structure*, 1180 (15) 585 (2019), https://doi.org/10.1016/j.molstruc.2018.12.019.
27. B.H.M. Jayakumarswamy, F. Rahaman, V.K. Revankar, K.Vasantakumar Pai, *International Journal of PharmTech Research*, 3 (3) 1864 (2011).
28. K. Abhishek, F. Jennifer. and K. Pankaj, *International Journal of Drug Development & Research Abbreviation*, 6 (2): 165, (2014).