Full Paper

DNA binding behaviour of mixed ligand vanadium(V) complex based on novel tridentate hydrazone and benzhydroxamic acid ligand systems

Poonam Inamdar | Sheela Angappan*

Department of Chemistry, School of Advanced Sciences, VIT University, Vellore, India

Correspondence
Sheela Angappan, Department of Chemistry
School of Advanced Sciences, VIT University, Vellore 632014, TN, India.
Email: asheela@vit.ac.in

Novel tridentate ONO hydrazone ligand (HL) and the corresponding vanadium(V) complex, [VO(HL)(Benz)], based on the ligand and benzhydroxamic acid, were synthesized and characterized using UV–visible, Fourier transform infrared, NMR and mass spectral studies. In order to assess the binding efficacy of the synthesized complex with DNA, UV absorption spectral titrations, fluorescence displacement assays using ethidium bromide and acridine orange dyes, circular dichroism, viscosity and molecular docking studies were carried out. Based on the results obtained, it is evident that the complex shows significant intercalating ability almost comparable to that of the standard intercalator drug cisplatin. The binding affinity values for the [VO(HL)(Benz)] complex and cisplatin were found to be $(3.84 \pm 0.08) \times 10^4 \text{ M}^{-1}$ and $(4.27 \pm 0.012) \times 10^4 \text{ M}^{-1}$. In addition, the cytotoxicity of [VO(HL)(Benz)] was also assessed by MTT assay against the MCF-7 cell line.

KEYWORDS
Cisplatin, DNA binding, hydrazine, Intercalation, UV absorption titration, vanadium

1 | INTRODUCTION

Since the landmark invention of cisplatin in the category of metallodrug therapy, bioinorganic chemists have been exploring metal-based drugs in many ways. Further, the anticancer effects of cisplatin against head, neck and a variety of other tumours opened up new doors for research in metal-based chemotherapeutics,[1] In this context, several structurally modified forms of cisplatin have been explored in addition to other metal-based compounds in order to improve the therapeutic efficacy with no side effects.[2] Thus, transition metal complexes of copper,[3] zinc,[4] ruthenium,[5–7] palladium[8] and vanadium[9] based on various ligand systems have been successfully established as effective cytotoxic agents and are used as alternatives to platinum-based compounds. The biological activity of metal complexes can be tuned based on the ligand system involved in the formation of the complex. In the search for biologically active ligands, hydrazones have been acclaimed widely in research. They are reported for a variety of biological activities such as anticonvulsant, antimicrobial, antitumour and antiplatelet activities.[10,11] In the case of vanadium, hydrazones have been reported to form rare binuclear non-oxidovanadium(V)[12] as well as mixed ligand dioxidovanadium(V) complexes and have shown DNA binding, cytotoxic and antioxidant activities.[13,14]

Mono-oxovanadium(V) complexes based on a combination of ligands such as hydrazones and bidentate ancillary ligands have been explored for the past 10 years. In 2005, Ghosh et al.[15] reported crystal structures of oxovanadium(V) complexes based on ONO hydrazone and 8-hydroxyquinoline for their structural properties. Later, Maurya et al.[16,17] reported oxovanadium(V) complexes having NNO tridentate hydrazone ligand and benzhydroxamic acid as ancillary ligand for anti-amoebic activity. They also reported a similar series of oxovanadium(V) complexes with a variety of NNO tridentate hydrazone and benzhydroxamic acid ligands.[18] Recently, the crystal structure of oxovanadium(V) complex of bromine-substituted NNO hydrazone and benzhydroxamic acid was reported and studied for catalytic epoxidation.[19]
Thus, the mono-oxovanadium(V) complex based on tridentate hydrazone ligand and benzhydroxamic acid is yet to be explored for DNA binding and cytotoxicity studies. Towards achieving the same, in the work reported here, we synthesized, hitherto unreported, ONO hydrazone ligand and its corresponding vanadium(V) complex in the presence of benzhydroxamic acid and assessed its DNA binding ability and cytotoxicity against the MCF-7 cell line.

2 EXPERIMENTAL

2.1 Materials and measurements

All the chemicals were purchased from commercial sources and used without further purification. 4-Chlorobenzhydrazide, acetic acid, benzhydroxamic acid, 4,4,4-trifluorour-1,3-phenylbutanedione and vanadyl acetylacetone were purchased from Sigma Aldrich. All the solvents such as acetonitrile, methanol, ethanol, diethyl ether, petroleum ether, ethyl acetate and hexane were of AR grade and purchased from SD Fine Chemicals. Calf thymus DNA, leum ether (40:60). Yield 70%; pale yellow solid; m.p. 98°C. Anal. Calcd for C17H12ClF3N2O2 (%): C, 55.37; H, 3.28; N, 7.60. Found (%): C, 55.36; H, 3.26; N, 7.58. UV–visible (MeOH), \( \lambda_{\text{max}} \) nm (\( e, \text{dm}^{-3} \text{mol}^{-1} \text{cm}^{-1} \)): 218 (65 000), 250 (55 700). FT-IR (KBr), \( \nu_{\text{max}} \), cm\(^{-1}\): 1762 (C=O), 1593 (C=N), 3301 (NH). \(^1H\) NMR (400 MHz, CDCl3, \( \delta_{\text{H}}, \text{ppm} \)): 7.972, 7.951, 7.654, 7.635, 7.468, 7.446, 7.425 (Ar H, 9H), 3.548, 3.594, 3.721, 3.761 (CH2 protons, 2H). \(^13C\) NMR (100 MHz, CDCl3, \( \delta_{\text{C}}, \text{ppm} \)): 136.91, 126.91, 128.33, 129.08, 129.88, 131.38, 131.45, 132.02 (Ar C), 138.74 (Ar C=Cl), 153.75 (C=N), 170.05 (C=O). GC–MS: calcd for C17H12ClF3N2O2: 368.05 m/z; found: 368.10 m/z. Chromatogram: \( R_f = 21.77 \) min. Purity: 99.1%.

2.2 Synthesis of tridentate ONO hydrazone ligand: 4-Chloro-N′-(4,4,4-trifluoro-3-oxo-1-phenylbutyldiene) benzohydrazide (HL)

Hot methanolic solutions (20 ml) of 4-chlorobenzhydrazide (500 mg, 2.94 mmol) and 4,4,4-trifluoro-1,3-phenylbutanedione (0.8 ml, 2.94 mmol) and acetic acid were combined and refluxed for 6 h at 60–70°C (Figure. S1). The obtained yellow reaction mixture was evaporated and the pale-yellow coloured crystalline product obtained was washed with diethyl ether and dried. The ligand was column purified using ethyl acetate and petroleum ether (40:60).

Yield 70%; pale yellow solid; m.p. 98°C. Anal. Calcd for C17H12ClF3N2O2 (%): C, 55.37; H, 3.28; N, 7.60. Found (%): C, 55.36; H, 3.26; N, 7.58. UV–visible (MeOH), \( \lambda_{\text{max}} \) nm (\( e, \text{dm}^{-3} \text{mol}^{-1} \text{cm}^{-1} \)): 218 (65 000), 250 (55 700). FT-IR (KBr), \( \nu_{\text{max}} \), cm\(^{-1}\): 1762 (C=O), 1593 (C=N), 3301 (NH). \(^1H\) NMR (400 MHz, CDCl3, \( \delta_{\text{H}}, \text{ppm} \)): 7.972, 7.951, 7.654, 7.635, 7.468, 7.446, 7.425 (Ar H, 9H), 3.548, 3.594, 3.721, 3.761 (CH2 protons, 2H). \(^13C\) NMR (100 MHz, CDCl3, \( \delta_{\text{C}}, \text{ppm} \)): 136.91, 126.91, 128.33, 129.08, 129.88, 131.38, 131.45, 132.02 (Ar C), 138.74 (Ar C=Cl), 153.75 (C=N), 170.05 (C=O). GC–MS: calcd for C17H12ClF3N2O2: 368.05 m/z; found: 368.10 m/z. Chromatogram: \( R_f = 21.77 \) min. Purity: 99.1%.

2.3 Synthesis of vanadium metal complex: [VO(HL)] (Benz)

A methanolic solution (15 ml) of [VO(acac)2] (265.16 mg, 1 mmol) was added to a methanolic mixture of hydrazone, HL (368.05 mg, 1 mmol) and benzhydroxamic acid (137 mg, 1 mmol). The brown-coloured mixture was stirred at room temperature for 3 h (Figure. S1). The reaction mixture was evaporated, washed with hexane and the brown powder formed was separated.

Yield 62%; m.p. 198°C; deep brown solid. Anal. Calcd for C24H18ClF3N3O5V: 569.79 m/z; found: 569.93 m/z. Chromatogram: \( R_f = 0.87 \) min. Purity: 99.3%.

2.4 DNA binding studies

2.4.1 UV and fluorescence spectral studies

UV absorption spectral titration was performed in the range 200–600 nm. The concentration of the complex was maintained constant (25 \( \mu \)M) and CT-DNA concentrations were varied from 0 to 140 \( \mu \)M. EtBr and AO fluorescence displacement assays were carried out using EtBr-bound CT-DNA solution (EtBr = 10 \( \mu \)M and DNA = 100 \( \mu \)M) and
AO-bound CT-DNA solution (AO = 10 μM and DNA = 100 μM) as the reference solutions. The excitation wavelengths for EtBr and AO fluorescence displacement assays were 510 and 480 nm, respectively. The emitted fluorescence intensity was observed at 610 nm for EtBr and at 530 nm for AO at room temperature. All the DNA experiments were carried out in 50 mM Tris HCl buffer at pH = 7.2. The UV and fluorescence spectral titrations were also carried out for the standard intercalator drug cisplatin, to compare the binding behaviour of the complex.

2.4.2 Circular dichroism studies

Circular dichroism spectra were recorded with a JASCO J–7 spectropolarimeter using a 0.1 cm quartz cell. The concentration of CT-DNA (100 μM) was kept constant and the experiment was carried out at two different concentrations of the complex. The experiment was done in triplicate to get a final spectrum as an average of successive scans. A blank correction was done for each run.

2.4.3 Viscosity studies

For viscosity measurements, an Ubbelohde viscometer (1 ml capacity) was maintained at 25°C. The efflux time for each sample was measured in triplicate and the average flow time was calculated. The rates of flow for the buffer (10 mM Tris), DNA (100 μM) and DNA in the presence of varying concentrations (20–200 μM) of the vanadium complex were measured and the relative specific viscosity (η) was calculated.

2.4.4 Molecular docking studies

Molecular docking was performed in order to investigate the binding mode of the complex to DNA base pairs and to compare theoretical predictions and experimental observations. The docking was carried out using Autodock vina and MGL tools of the Scripps Research Institute.[20,21] DNA (PDB ID: 2D55) was modified by adding polar hydrogens and by removing water molecules and then kept rigid through the docking process. The docking area was defined by a box. The grid points of 56 × 58 × 56 with 1.0 Å spacing were calculated around the docking area for all the ligand atom types using default optimization parameters. The torsional bonds of the complex were set free by a ligand module in AutoDock Tools-ADT. A PyMOL molecular viewer and MGL tools were used to analyse the docking results of the chosen lowest energy conformer.[22]

2.5 Cytotoxicity Studies

3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was performed against the MCF-7 cell line following the method described by Carmichael et al.[23] and the percentage cell viability was measured by spectrophotometric determination of accumulated formazan derivative in treated cells at 570 nm. Test compound (0–200 μM) was added as 2× concentration to the cells in 10 μl volume. The plates were further incubated for 48 h in a CO₂ incubator. The assay solution consisted of MTT at a concentration of 5 mg ml⁻¹ in phosphate buffered saline (1.5 mM KH₂PO₄, 6.5 mM Na₂HPO₄, 137 mM NaCl, 2.7 mM KCl; pH = 7.4). From this solution, 50 μl was pipetted into each well to achieve a final concentration of 1 mg ml⁻¹. The plate was further incubated for 4 h in an incubator and the medium was carefully decanted. The formazan crystals were air-dried in the dark and then dissolved in 100 μl of dimethylsulfoxide and the plates were mildly shaken at room temperature and the optical density was measured using a Synergy H4 (BioTek) microplate reader at 570 nm. IC₅₀ value for the complex was calculated from the growth curve.

3 RESULTS AND DISCUSSION

3.1 Synthesis and characterization

Ligand HL was prepared as shown in Figure. S1 and was characterized using UV, FT-IR and NMR spectroscopies, GC–MS and elemental analysis. The ligand was found to be soluble in methanol and ethanol. The vanadium complex [VO(HL)(Benz)] was synthesized and was characterized using elemental analysis and UV–visible, FT-IR and ESI-MS techniques. The complex was found to be air-stable at room temperature and was soluble in methanol, dimethylsulfoxide and acetonitrile. Attempts to obtain a single crystal of the complex suitable for X-ray determination were unsuccessful.

Elemental analysis data of the ligand HL and complex are in agreement with the calculated data. The UV–visible spectrum of [VO(HL)(Benz)] was recorded in methanol and was compared to that of the ligand (Figure. S2). Intraligand transitions for the complex were observed at 220 and 277 nm, for the ligand at 216 and 243 nm and for benzhydromycin acid at 238 nm. The strong intraligand transitions can be attributed to the imine functionality of the hydrazone moiety. These transitions are shifted to higher wavelength in the case of the complex due to complexion of the imine functionality of the hydrazone with the metal. Benzhydromycin ligands induce a marked charge transfer to the metal centre.[16] Thus, the complex exhibits ligand-to-metal charge transfer at 455 nm arising from transfer from phenolate oxygen (of benzhydromycin acid) to an empty d orbital of vanadium (V) centre of the complex.[24] As the vanadium(V) complex is a d⁰ system, it does not show any d–d transition.[25]

Vibrational spectroscopy helps in determining the coordination mode of the ligand with the metal ion. In the case of ligand HL, the intense peak at 1672 cm⁻¹ corresponds to –C=O (carbonyl) functionality and the peak at 1593 cm⁻¹ corresponds to –C=N (imine) functionality (Figure. S3). The peaks for the C=O and C=N functionalities in the complex show reduced intensity and a shift towards lower wavenumber at 1666 and 1591 cm⁻¹, respectively (Figure. S3). Thus, the
imine and carbonyl functionalities are involved in coordination with the vanadium metal. Coordination of imine group to the vanadium metal can also be supported by the presence of a strong peak at 460 cm$^{-1}$ due to the formation of V=N bond.

Coordination of C=O group of the ligand to the metal through enolization (Figure. S3) can be supported by the appearance of a new, weak band at 1535 cm$^{-1}$ due to intramolecular C=N formation and also by the presence of C=O enolate stretching band in the range 1250–1305 cm$^{-1}$ in the spectrum of the complex. The FT-IR spectrum of benzhydroxamic acid shows a strong peak at 3287 cm$^{-1}$ due to the phenolic OH group (Figure. S4). The phenolic OH peak in the spectrum of the complex has completely disappeared proving its coordination to the metal centre through the deprotonation of the phenolic OH group. This coordination can be supported by the presence of the V=Ophenolate peak in the complex spectrum at 1342 cm$^{-1}$. The stretching band at 923 cm$^{-1}$ suggests the presence of a hexacoordinated environment around the metal centre.

In the $^1$H NMR spectrum (Figure. S5) of ligand HL, signals of aromatic proton present in the chlorine-substituted phenyl ring are observed at 7.97 and 7.95 ppm with the expected integration value as they have similar magnetic environment. This confirmed the presence of four aromatic protons from chlorophenyl ring. The signals of remaining aromatic protons from diketone moiety were found to be present at 7.46, 7.44, 7.42 ppm and 7.65, 7.63 ppm. Geminal coupling was observed for $=\text{CH}_2$ protons at 3.54–3.76 ppm. NH proton was observed at 6.62 ppm. The $^{13}$C NMR spectrum of the ligand (Figure. S6) shows the presence of aromatic carbon atoms having similar magnetic environment observed at 126.91–132.02 ppm, whereas the signal of the carbon atom attached to chlorine was observed to be shifted downfield at 138.74 ppm. The presence of carbonyl carbon was confirmed from the peak at 170.05 ppm and imine carbon at 155.75 ppm.

The mass spectrum of ligand HL was recorded using GC–MS in methanol solvent and molecular weight was confirmed. The molecular ion peak (Figure. S7) was found to be at 368.10 m/z. Pure ligand was separated at $R_T = 21.77$ min as shown in the chromatogram. MS analysis for the complex (Figure. S8) was carried out using the ESI-MS technique in acetonitrile and M$^+$ peak was observed at 569.94 m/z. The (M + 2) peak was also observed at 571.95 m/z which may be due to the presence of chlorine (halogen) substitution in the structure.

### 3.2 DNA binding studies

UV absorption spectral titration and EtBr and AO fluorescent displacement assays were used to determine the mode of binding of the complexes with DNA. This is further supported by circular dichroism and molecular docking studies. The stability of the complex was monitored by observing the UV spectrum of the complex recorded in Tris HCl buffer for 2 h (Figure. S9).

#### 3.2.1 UV absorption spectral titration

UV absorption spectral titration was carried out by monitoring electronic spectra of the [VO(HL)(Benz)] complex at constant concentration of 25 μM. On binding to the complex, DNA perturbs the ligand-centred bands in the UV region. UV absorption titration for cisplatin at the same concentration as that of the complex was also carried out in order to compare the binding affinity of the complex with DNA.

A hypochromic effect with slight red shift was observed as successive additions of DNA were carried out from 20 to 100 μM in the case of the complex (Figure. 1). Hypochromism suggests the intercalative mode of interaction of the complex with DNA. In the case of this complex, two aromatic moieties from hydrazone and benzhydroxamic.
acid may have imparted the desired planarity to show intercalative behaviour. These planar rings of the complex may have inserted between the DNA base pairs forming a $\pi-\pi$ stacking interaction thereby leading to the changes in the absorption spectra of the complex after the addition of DNA.

The DNA binding efficacy of the [VO(HL)(Benz)] complex was compared with that of the standard intercalator, the anticancer drug cisplatin (Figure 2). The binding affinity is the measure of the binding interaction of the complex with DNA. Thus, the binding affinity of the complex and cisplatin was compared in terms of binding constants. $K_b$ was calculated using the formula

$$\frac{[\text{DNA}]}{[\text{DNA}] + \frac{1}{K_b (\varepsilon_a - \varepsilon_f)}} = \frac{[\text{DNA}]}{e_a - e_f}$$

where $\varepsilon_a$, $\varepsilon_f$ and $\varepsilon_b$ correspond to $A_{obsd}/\text{[vanadium(V)]}$, the extinction coefficients for free vanadium complex and that of vanadium complex in fully bound form, respectively. $[\text{DNA}] / \left(\varepsilon_a - \varepsilon_f\right)$ versus $[\text{DNA}]$ values were plotted and $K_b$ was obtained from the ratio of the slope to the intercept. $K_b$

![FIGURE 2 UV absorption spectral titration of cisplatin in the presence of increasing concentrations of DNA](image)

![FIGURE 3 EtBr fluorescence displacement assay of (a) [VO(HL)(Benz)] complex and (b) cisplatin](image)
values for the [VO(HL)(Benz)] complex and cisplatin were found to be \((3.84 \pm 0.08) \times 10^4 \text{ M}^{-1}\) and \((4.27 \pm 0.012) \times 10^4 \text{ M}^{-1}\), respectively.\(^{[32]}\) The red shift in the absorption maxima of the complex was measured and \(\Delta \lambda\) was found to be 0.7 nm, whereas in the case of cisplatin the shifts in the wavelengths were negligible. The hypochromicity for the complex and cisplatin was 42 and 46%, respectively.

3.2.2 | Fluorescence-based EtBr and AO displacement assays

Absorption spectral studies have suggested the intercalative behaviour of the [VO(HL)(Benz)] complex. Thus, to confirm the stacking nature of the complex, EtBr and AO displacement assays were carried out. EtBr is a classic DNA intercalator and AO is an AT-specific intercalator. Planar phenanthridine ring of EtBr and acridine ring of AO impart the intercalating nature to those respective molecules. Therefore, other intercalating moieties can lead to the quenching of fluorescence intensity of these dyes and can displace them from DNA base pairs. The displacement of dye may be due to the acceptance of excited-state electron of dye through photoelectron transfer mechanism.\(^{[33]}\)

The fluorescence spectra of EtBr- and AO-bound DNA in the presence of increasing concentrations of the metal complex are shown in Figures 3(a) and 4(a). A decrease in the intensity of EtBr–DNA and AO–DNA fluorescence was observed as the concentration of the complex was increased from 10 to 100 \(\mu\text{M}\) substantially indicating the competitive binding. A similar quenching experiment was carried out for cisplatin as standard intercalator drug (Figures 3(b) and 4(b)). The extent and propensity of the binding is measured by calculating \(K_{SV}\) (Stern–Volmer constant), using the Stern–Volmer equation:

\[
\frac{F_0}{F} = 1 + K_{SV} [Q]
\]

where \(F_0\) and \(F\) indicate the fluorescence intensities in the absence and presence of quencher (complex), respectively, \(K_{SV}\) is the linear Stern–Volmer quenching constant and \([Q]\) is the concentration of the quencher.

\(K_{SV}\) values for EtBr displacement assay for the complex and cisplatin were found to be \(2.05 \times 10^3\) and \(1.50 \times 10^3 \text{ M}^{-1}\), respectively. The quenching for EtBr displacement assay for the complex and cisplatin was found to be 26.31 and 20.01%, respectively. \(K_{SV}\) values for AO displacement assay for the complex and cisplatin were found to be \(2.62 \times 10^3\) and \(1.15 \times 10^3 \text{ M}^{-1}\), respectively. The quenching for the complex and cisplatin was found to be 50 and 45%, respectively. Thus, the extent of quenching and the \(K_{SV}\) values of the complex for both of the displacement assays suggest its intercalative mode of binding.

3.2.3 | Circular dichroism studies

Interaction of the metal complex perturbs the structure of the DNA helix. To correlate the spectral findings of the intercalating ability of the complex, circular dichroism studies were carried out. Circular dichroism spectra of DNA were recorded in the presence and absence of the complex. Right-handed B-DNA shows a characteristic positive band at 277 nm due to base stacking and a negative band at 246 nm due to helicity.\(^{[34]}\) Stacking of the intercalators between the DNA base pairs leads to an increase in the DNA chain length perturbing its distinctive helicity. Intercalators have been reported to lead to an increase in the intensities and shifting in the bands of the DNA. Thus, the red shift observed (Figure. S10) in both of the bands of DNA in the presence of different concentrations of the complex implies its intercalating nature.

3.2.4 | Viscosity studies

Interaction of a metal complex with DNA leads to changes in the length of the DNA. Hydrodynamic parameters which are
sensitive to perturbations in length can be monitored using viscosity studies. In order to confirm the intercalative mode of binding, viscosity studies were carried out with solutions of DNA incubated along with the complex. A comparison of the flow rates of buffer, DNA (100 μM) and DNA incubated with the complex at various concentrations (20–200 μM) was carried out. The relative specific viscosity was calculated, using the equation \((t - t_0)/t_0\), where \(t_0\) is the flow time of buffer and \(t\) the flow time for DNA in the presence and absence of the complex. Plot of \((\eta/\eta_0)^{1/3}\) versus \(1/R\) (where \(R = [\text{complex}]/[\text{DNA}]\)) is presented in Figure. S11, where \(\eta\) is the viscosity of DNA in the presence of varying concentrations of the complex and \(\eta_0\) is the viscosity of the DNA alone. The complex, with increasing concentrations, caused significant changes in the viscosity of DNA thus supporting its DNA intercalative binding mode. Ideal intercalators like EtBr after insertion into DNA base pairs lengthen the DNA strand leading to an increase in the relative viscosity. Intercalation results in bending of DNA helix that leads to a decrease in specific viscosity.

3.2.5 | Molecular docking studies

Autodock Vina generates the minimum energy conformers of the complex depending on the nature of rotatable bonds present in the structure. The best conformer was selected based on the minimum energy and thus was used for the docking studies with DNA (PDB ID: 2D55). It has been inferred that the complex shows intercalative behaviour but through the sides of two different base pairs (Figure. 5), DC13 (deoxycytosine) and DG12 (deoxyguanine). The side-on intercalation behaviour has been reported for isomeric ruthenium complexes\(^{[35]}\) based on dppz and phenanthroline ligand system with DNA. In the case of the present complex, phenyl ring of benzhydroxamic acid gets easily inserted between the base pairs. The complex shows two hydrogen bond interactions with binding energy of \(-9.7\) kcal mol\(^{-1}\). Hydrogen atom from amino group of the benzhydroxamic acid interacts through a hydrogen bond with oxygen atom (O2) of the DC13 at a distance of 3.58 a.u. Another hydrogen bond interaction was observed between oxygen atom of the carbonyl group of the acid functionality of benzhydroxamic acid with hydrogen atom of NH group of DG12 at a distance of 3.22 a.u.

3.3 | Cytotoxicity

The viability of cell line MCF-7 decreases on treatment with the complex as a function of concentration indicating a dose-dependent growth (Figure. S12) inhibitory effect. The IC\(_{50}\) value for the vanadium(V) complex was found to be 6.0 μM which was calculated using growth response curve (Figure. S12). Further, the cytotoxic activity of the complex is significant as compared to the reported value of cisplatin (IC\(_{50} = 22.8\) μM) for the same cell line.\(^{[36]}\)
Novel tridentate hydrazone ONO ligand and the corresponding mixed ligand vanadium(V) complex using benzhydroxamic acid as the co-ligand were synthesized and characterized. Based on the results of DNA binding studies using UV absorption titration and fluorescence assays, it has been observed that the complex has intercalating ability comparable to that of cisplatin indicated by the obtained binding constant values. In addition, the displacement efficacy of the complex was found to be more effective than cisplatin as indicated by the quenching values. This is further supported by circular dichroism, viscosity and molecular docking studies. The cytotoxicity of the complex assessed by the obtained IC50 values. This is further indicative of more effective anticancer potential than cisplatin indicated by the obtained IC50 values. Further investigations and thorough studies are required in order to prove the greater effectiveness of the complex over cisplatin and are underway.

REFERENCES


SUPPORTING INFORMATION

Additional supporting information can be found in the online version of this article at the publisher's website.