Indian Journal of Chemistry
Vol. 55A, November 2016, pp. 1297-1304

Co(II) complex of 2-amino-6-methylbenzothiazole: Synthesis, structure and biological evaluation

S Jone Kirubavathy[a], R Velmurugan[b], R Karvembu[c], N S P Bhuvanesh[d], I V M V Enoch[e], P Mosae Selvakumar[e] & S Chitra[a,*]

[a]Department of Chemistry, PSGR Krishnammal College for Women, Coimbatore 641 004, India
Email: chitrapsgrkc@gmail.com

[b]Department of Chemistry , Kongunadu Arts and Science College, Coimbatore 641029, India

[c]Department of Chemistry, National Institute of Technology, Tiruchirappalli 620015, India

[d]Department of Chemistry, Texas A&M University, College Station, TX 77842, USA

[e]Department of Chemistry, Karunya University, Coimbatore 641114, India

Received 9 September 2016; revised and accepted 26 October 2016

Cobalt(II) complex of 2-amino-6-methylbenzothiazole has been synthesized and characterized by various physico-chemical methods. The ligand 2-amino-6-methylbenzothiazole acts as monodentate, neutral ligand with N as the donor site. The molecular structure of the title complex has been determined by single crystal X-ray diffraction studies. The Co(II) complex shows significant antioxidant activity against DPPH radical. The complex shows cytotoxicity with a IC_{50} value of 14.12 µ*M* against MCF-7 cell line. In addition, the complex shows good antimicrobial and anti-tuberculosis activities against various microbes and mycobacterium tuberculosis respectively. DNA binding of the title complex has been investigated by absorption spectroscopic technique, which reveals that the complex acts as minor groove binder. These results have been validated by molecular docking studies.

Keywords: Co-ordination chemistry, Cobalt, Benzothiazole, Magnetic properties, Antituberculosis activity, Molecular docking

Benzothiazoles are bicyclic ring systems with a thiazole ring fused with benzene. A number of 2-aminobenzothiazoles have been studied as central muscle relaxants and found to interfere with glutamate neurotransmission in biochemical experiments[1]. Benzothiazole derivatives have been studied and found to have various chemical and biological activities like antiviral[2], anticancer[3, 4], antibacterial, antimicrobial and fungicidal[5,6]. Some of the novel benzothiazole sulphonamides act as potent inhibitors of HIV-1-protease[7]. Benzothiazole derivatives are also reported as anti-leishmanial[8], anti-inflammatory[9], anticonvulsant[10], anti-diabetic[11], diuretic[12] and anti-proliferative[13] agents. 2-Aryl substituted benzothiazoles show antitumor activity while condensed pyrimidobenzothiazoles and benzothiazolo quinazolines show antiviral activity. Substituted 6-nitro and 6-aminobenzothiazoles have been reported to possess antimicrobial activity.

El-Shazly*et al.*[14] studied the reactions of 2-mercaptobenzothiazole with Cu(II), Ni(II) and Co(II) and the reaction with Co(II) produced a five coordinated polymeric type compound. Chaurasia *et al.*[15] studied complexes of the type, CoL_2X_2 where L = 6-methyl-2-aminobenzothiazole; X = -I,-NCS and –OAc. Bhagat *et al.*[16] synthesized 4-bromo-2-hydrazino-6-methylbenzothiazole and investigated its chelating tendency towards Fe^{2+}, Co^{2+}, Ni^{2+} at different *p*H. Maji *et al.*[17] synthesized and characterized chlorobis(acetonitrile)triphenylphosphino-2-(2-pyridyl)benzothiazole-N,N-ruthenium(II)chloride where in the ligand acts as N,N-didentate manner and Ru(II) ion is present in an N_4PCl co-ordination environment while PPh_3 and Cl are ***trans*** to each other. Chen *et al.*[18] synthesized and characterized new co-ordination polymers of Cd(II), Zn(II), Ni(II) metal ions with 2-amino-6-methylbenzothiazole and 5-nitroisophthalate as ligands. The structural analysis suggests that 2-amino-6-methylbenzothiazole acted as monodentate ligand and the carboxylate groups in 5-nitroisophthalate as monodentate and chelating bidentate. Abundant hydrogen bond interactions drive the formation of packing structure of the complexes. These complexes also display strong emission peaks from intraligand charge transfer. Joseph *et al.*[19] synthesized and characterized copper complexes of

2-aminobenzothiazole derivatives and studied the antibacterial screening of the ligands and complexes. Studies from the literature have demonstrated that benzothiazoles have various biological activities and the report on the biological activity of transition metal complexes of benzothiazole derivatives is inadequate. In general, the incorporation of metal onto the ligand can alter or enhance the biological activity and also can lead to new therapeutic agents. In this connection, we report the results of our study on Co(II) complex of 2-amino-6-methylbenzothiazole and its various biological activities like antimicrobial, anticancer, antituberculosis and antioxidant. Further, the DNA binding and molecular docking analysis were also carried out.

Materials and Methods

All the reagents were purchased from Sigma Aldrich. Microanalytical data of the compounds were recorded on an ElementarVario EL IIICHN analyzer. Metal was estimated complexometrically by EDTA titration. The FT-IR spectra of the samples were recorded on a Shimadzu spectrophotometer in the range 4000–400 cm^{-1}. The UV-visible spectra were recorded on an Elico SL 159 UV-visible Spectrophotometer. The molar conductance of the complex was measured using a Systronics conductivity bridge at room temperature in DMSO solution. The antimicrobial activity of the ligand and complex was evaluated against the bacterial species ***Pseudomonas aeroginosa, Aeromonas hydrophila, Thiobacillus thidurance, Serratia marcescens, Acinetobater baumauii,*** and the fungal species ***Aspergillus niger*** and ***Candida tropicalis*** by well diffusion method using agar nutrient medium[20]. The ***in vitro*** anticancer activity was studied by MTT assay. The cell inhibition (%) was determined using the formula, Cell inhibition (%) = 100 − Abs (sample)/Abs (control) × 100. Nonlinear regression graph was plotted between % cell inhibition and $\log_{10}$ (concentration) and IC_{50} was determined using graph pad prism software. The minimum inhibitory concentration was determined by serial dilution technique[21]. The ***in vitro*** antituberculosis activity of the complex was checked against ***M. tuberculosis*** using microplate alamar blue assay. The MIC was defined as lowest drug concentration which prevented the color change from blue to pink[22]. Absorption titration experiments of the Co(II) complex in buffer (50 m*M* NaCl + 5 m*M* Tris-HCl, *p*H 7.1) were performed using a fixed complex concentration to which increments of the nucleic acid stock solutions were added. Co(II) complex–nucleic acid solutions were allowed to incubate for 10 minutes before the absorption spectra were recorded. Equal amount of nucleic acid was added to both the complex and reference solutions to eliminate the absorbance of nucleic acid itself.

Synthesis of Co(II) complex

The methanolic solution of 2-amino-6-methyl benzothiazole (2 mmol, 0.328 g) was added to the methanolic solution of cobaltous chloride (1 mmol, 0.236 g). The resulting blue solution was refluxed for 8 h and then cooled to room temperature, which yielded blue color crystals. It was filtered off, washed with methanol and dried. Yield: 74%. M. pt.: 238-242 °C. Anal. (%) Calcd. for $C_{16}H_{16}Cl_2CoN_4S_2$: C, 41.93; H, 3.52; N, 12.23; S, 13.99; Co, 12.86. Found: C, 41.85; H, 3.42; N, 12.26; S, 13.91, Co, 12.78. IR (KBr, cm^{-1}): 3254, 3171, 1603, 1470, 1336, 801, 694. UV-vis (nm): 265, 310. μ: 4.12 BM.

Determination of X-ray crystal structure

A Bruker APEX-2 X-ray (three-circle) diffractometer was employed for crystal screening, unit cell determination and data collection. The X-ray radiation employed was generated from a Mo sealed X-ray tube (K = 0.70173 Å with a potential of 40 kV and a current of 40 mA) fitted with a graphite monochromator in the parallel mode (175 mm collimator with 0.5 mm pinholes). Systematic reflection conditions and statistical tests of the data suggested the space group *P121/c1*. The structure was refined by using SHELXTL (XS)[23]. Hydrogen atoms were placed in idealized positions and were set riding on the respective parent atoms. All non-hydrogen atoms were refined with anisotropic thermal parameters. The structure was refined (weighted least squares refinement on F^2) to convergence[24]. Olex-2 was employed for the final data presentation and structure plots.

Antioxidant activity

The 2, 2-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity of the compounds was measured according to the method of Elizabeth. The DPPH radical is a stable free radical having a λ_{max} at 517 nm. A fixed concentration of the experimental compound (100 μL) was added to a solution of DPPH in methanol (0.3 m*M*, 1 mL) and the final volume was made up to 4 mL with doubly distilled water. DPPH

solution with methanol was used as a positive control and methanol alone acted as a blank. The solution was incubated at 37 °C for 30 min in dark. The decrease in absorbance of DPPH was measured at 517 nm. The tests were run in triplicate, and various concentrations (20-100 µg/mL) of the compounds showed 50% of the activity. In addition, the percentage of activity was calculated using the formula, Suppression ratio (%) = $[(A_o\text{-}A_c)/A_o]\times100$ where A_o and A_c are the absorbance in the absence and presence of the tested compounds respectively. The 50% activity (IC_{50}) was calculated using the percentage of activity[25].

Molecular docking analysis

The structure of the complex was further considered for molecular docking analysis using HEX 6.3, an interactive protein docking and molecular superposition program that is mainly used for feasible docking of various ligands with proteins, enzymes, DNA, and also in protein-protein docking. Docking parameters were set to include complex-DNA interactions and various parameters for non-covalent interactions were used as implemented in the program. The duplex DNA D(*CP*GP*CP*GP*AP*AP*TP*TP*CP*GP*CP*G)-3') dodecamer was taken from the Protein Data Bank (PDB ID: 1BNA) and used in docking studies. All possible docking poses were considered and the docking was performed[26].

Results and Discussion

Crystal structure of Co(II) complex

The Co(II) complex crystallizes in the monoclinic system with the space group *P121/c1* with unit cell dimensions *a*=11.549(3) Å, *b*=13.395 Å, *c*=11.682 Å and β=97.414(3)°. The bond lengths of Co(1)–Cl(1) and Co(1)–Cl(2) are almost same, i.e., 2.2677(14) and 2.2471(13) Å respectively. The coordinate bonds Co(1)–N(1) and Co(1)–N(3) are also almost similar [2.021(4) and 2.034(4) Å]. The crystal data and the structure refinement parameters are given in Table 1. The chlorine atoms form hydrogen bonding with the amine nitrogens (Table 2). The *trans* orientation of Cl and N atoms around cobalt is revealed from the bond angles of Cl(2)–Co(1)–Cl(2) and N(1)–Co(1)–N(3). The bond angles N(3)–Co(1)–Cl(1) [108.75(10)°] and N(3)–Co(1)–Cl(2) [108.23(10)°] show distorted tetrahedral structure. The other important bond angles and bond lengths are shown in Table 3. The crystal structure of the complex is given in Fig. 1.

Table 1—Crystal data and structure refinement parameters of Co(II) complex

Emp. formula	$C_{16}H_{16}Cl_2CoN_4S_2$
Formula wt	458.28
Temp. (K)	110.15
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	*P 1*
Unit cell dimensions	
a (Å)	11.549(3)
b (Å)	13.395(4)
c (Å)	11.682(3)
(°)	97.414(3)
Vol. ($Å^3$)	1792.0(9)
Z	4
D_{calc} (mg/m^3)	1.699
Abs. coeff. (mm^{-1})	1.496
F(000)	932
Θ range for data collection	1.778 to 27.526°
Reflect. collected	14638
Ind. Reflect. /R_{int}	4077 / 0.0810
Data/ restraints/ parameters	4077/ 0/ 228
Goodness-of-fit on F^2	1.088
Final R indices [I>2σ(I)]	R1 = 0.0628, wR2 = 0.0885
R indices (all data)	R1 = 0.1113, wR2 = 0.1040
Extinction coeff.	n/a
Largest diff. peak/hole (e $Å^{-3}$)	0.709/-0.684

Table 2—Hydrogen bonding parameters for the Co(II) complex

D-H...A	*d*(D-H) (Å)	*d*(H...A) (Å)	*d*(D...A) (Å)	<(DHA) (°)
N(2)-H(2A)...Cl(2)	0.86	2.42	3.237(4)	157.7
N(2)-H(2B)...Cl(1)#1	0.86	2.73	3.528(4)	155.3
N(4)-H(4B)...Cl(1)	0.86	2.43	3.197(4)	149.7

Table 3—Bond lengths and angles for the Co(II) complex

Bond	Bond length (Å)	Angle	Bond angle (°)
Co(1)-Cl(1)	2.2677(14)	N(1)-Co(1)-Cl(1)	113.53(10)
Co(1)-Cl(2)	2.2471(13)	N(1)-Co(1)-Cl(2)	110.13(10)
Co(1)-N(1)	2.021(4)	N(1)-Co(1)-N(3)	105.19(14)
Co(1)-N(3)	2.034(4)	N(3)-Co(1)-Cl(1)	108.75(10)
S(1)-C(6)	1.744(4)	N(3)-Co(1)-Cl(2)	108.23(10)
S(1)-C(8)	1.736(5)	C(1)-N(1)-Co(1)	120.9(3)
S(2)-C(14)	1.741(4)	C(8)-N(1)-Co(1)	128.9(3)
S(2)-C(16)	1.737(5)	H(2A)-N(2)-H(2B)	120.0
N(1)-C(8)	1.321(5)	N(1)-C(8)-S(1)	116.2(3)
N(2)-H(2A)	0.8600	C(9)-N(3)-Co(1)	121.3(3)
N(2)-H(2B)	0.8600	C(16)-N(3)-Co(1)	128.1(3)
C(1)-C(2)	1.384(6)	C(8)-N(1)-C(1)	110.2(4)
C(1)-C(6)	1.400(6)	C(8)-S(1)-C(6)	88.9(2)
N(2)-C(8)	1.339(5)	C(16)-S(2)-C(14)	89.3(2)
C(15)-H(15A)	0.9800	C(3)-C(2)-H(2)	120.4
C(5)-C(6)	1.385(6)	C(2)-C(1)-N(1)	126.8(4)
N(1)-C(8)	1.321(5)	C(1)-C(6)-S(1)	110.0(3)

The packing diagram of the complex given in Fig. 2 shows both the intermolecular and the intramolecular interactions which stabilize the solid state structure.

Spectral, thermal and magnetic studies

The complex is stable in solution and in the solid state at room temperature. It is insoluble in water but soluble in common organic solvents like ethanol, acetonitrile, DMSO and DMF. The molar conductance of the complex in 10^{-3} *M* solution is negligible indicating its non-electrolytic behavior. The electronic transitions in the complex are observed at 263, 310, 420 and 730 nm. The characteristic band at 625 nm for the tetrahedral complex is not observed in the complex due to coordination of DMSO,which makes it distorted octahedral[27].

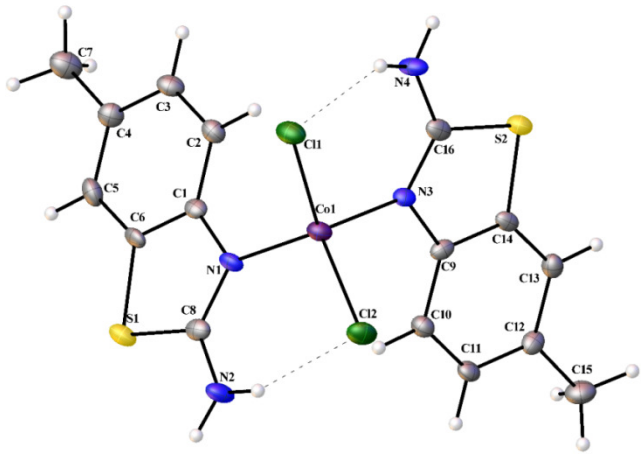

Fig. 1 – Thermal ellipsoid plot of the Co(II) complex.

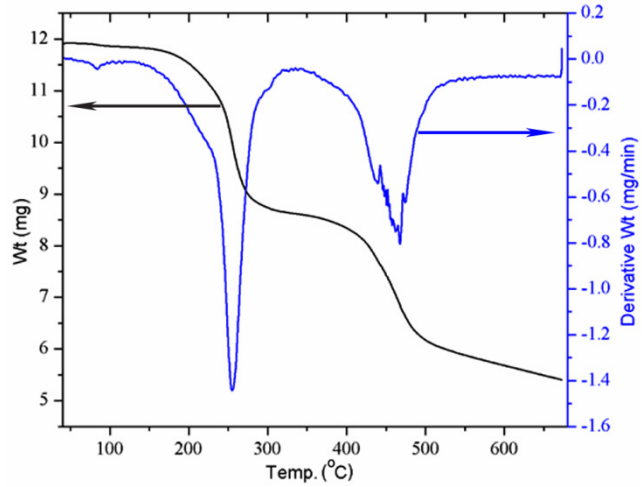

Fig. 3 – Thermogram of the Co(II) complex.

Thermogravimetric analysis was carried out from 35 to 670 °C at a heating rate of 10 °C/min in Ar. The TGA curve shows that the complex is stable up to 254 °C. The ligand (2-amino-6-methylbenzothiazole) is eliminated in two decomposition steps at 254 and 468 °C leaving a stable metal oxide. The thermogram of the Co(II) complex is given in Fig. 3.

The observed magnetic moment of the Co(II) complex (4.12 BM) is characteristic of tetrahedral Co(II) complex[28].The magnetic property of the complex was analyzed using a vibrational sample magnetometer at room temperature. The saturation magnetization (Ms) (0.00754 emu/g) and coercivity (Hc) (410.35 G) values were extracted from M-H curves. The low saturation magnetization and the presence of coercivity for the complex indicate its ferromagnetic nature.

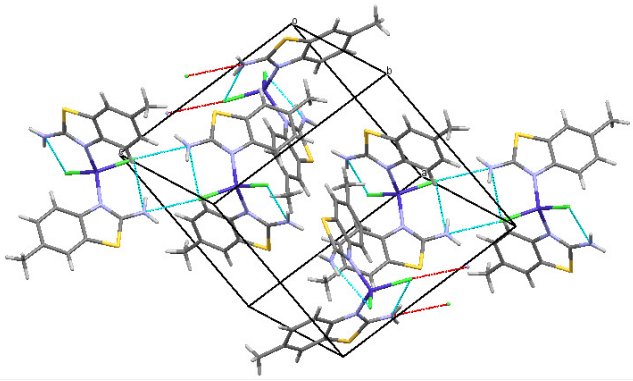

Fig. 2 – Packing diagram of the Co(II) complex showing hydrogen bonds along ***a*** axis.

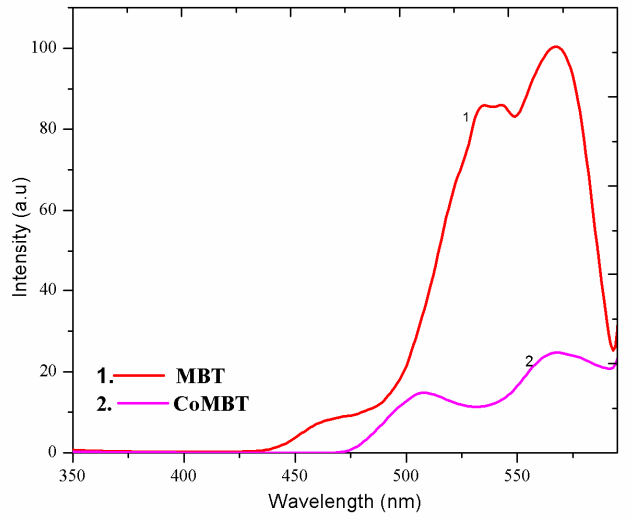

Fig. 4 – Emission spectra of the ligand and its Co(II) complex [1, MBT; 2, COMBT].

The photoluminescence property of 2-amino-6-methylbenzothiazole (MBT) and its Co(II) complex (CoMBT) was studied at room temperature for 10^{-4} *M* solution in DMSO (Fig. 4). The most striking feature was that the ligand excited at 280 nm gave an intense emission. The emission of the ligand was inhibited on complexation. Quenching of fluorescence of the ligand by transition metal ions during complexation is a rather common phenomenon, which can be explained by processes including magnetic perturbation, redox-activity and electronic energy transfer[29].

***In vitro* antimicrobial activity**

The *in vitro* antimicrobial activity of the complex was tested against various bacteria *A. hydrophila, S. marcescens, T. thidurance, P. aeruginosa* and *A. baumanii,* and fungi *A. niger* and *C. tropicalis*. The standard error for the experiment was ±0.001 cm and the experiment was repeated three times under identical conditions. DMSO was used as the negative control and amikacin was used as the standard for antibacterial study. Nystatin was used as the reference for antifungal study. The zone of inhibition for various species is given in Table S1 (Supplementary Data). The Co(II) complex showed very good activity against *A. niger, T. thidurance* and *S. marcescens*. In all the cases, the antimicrobial activity of the Co(II) complex was greater than that of the ligand. It was evident from the data that the activity significantly increased by 50% on coordination.

Compared to the antimicrobial agents with various heterocyclic rings reported in the literature[30-32], the synthesized Co(II) complex showed decreased or increased activity depending on the hetero atom and the substituents. In most of the cases, the Co(II) complexes showed enhanced activity (82-100%) against the test pathogens (~18-22 mm). The synthesized Co(II) complex showed moderate antimicrobial activity against all pathogens except against *A. niger* which shows pronounced activity, although this activity is not greater than the standards used or the literature value.

***In vitro* anticancer activity**

Cisplatin has many side effects and many attempts are being made to replace it with suitable alternatives. In this direction, a number of non-platinum complexes have been synthesized and screened for their potential anticancer activity. The ligand, 2-amino-6-methylbenzothiazole and its Co(II) complex were evaluated for their cytotoxicity against human breast cancer cell line MCF-7 by MTT assay method which measures mitochondrial dehydrogenase activity as an indication of cell viability. The results were analysed by cell viability curves and expressed in terms of IC_{50} values in the studied concentration range from 0.1 to 100 μ*M*. The results revealed that the complex showed promising cytotoxic effect as compared to the ligand. The IC_{50} values of the ligand and complex are 80.19 and 14.12 μ*M* respectively. The compounds showed cytotoxicity during a short incubation period of 48 h. The cytotoxic activity of the Co(II) complex is only slightly less than that of cisplatin (IC_{50}: 12.75 μ*M*)[33].

Europium(III) and terbium(III)-2-thioacetate benzothiazole complexes with a potent DNA-binding anti-tumour agent have been reported by Hussein *et al.*[34] The Tb(III)-complex was the most potent compound in this screening, and exhibited a higher cytotoxic activity (IC_{50} = 4.5 μ*M*) against MCF-7 when compared with the reference drug cisplatin followed by Eu(III)-complex with IC_{50} = 5.1 μ*M*. Pd(II) and Pt(II) complexes of derivatives of 2-(4′-aminophenyl)benzothiazole have been synthesized by Mavrodi *et al.*[35] They also studied the selective anticancer action of phenylbenzothiazole. From the *in vitro* cytotoxic activity against the MCF-7 human breast cancer cell line, the complexes showed IC_{50} value ranging from 20–71 μ*M* and are less active than the standard drug cisplatin. Though the Co(II) complex has lower cytotoxicity than the Eu(III) and Tb(III) complexes reported by Hussain *et al.*, it shows activity comparable to cisplatin. Further, compared to the Pd(II) and Pt(II) complexes reported by Mavrodi *et al.*[35], the Co(II) complex shows higher activity.

The anti-cancer activity of the ligand and the Co(II) complex towards MCF, are not much significant compared to the known metal bound anticancer reagent, cisplatin. Nevertheless this work could be a good starting point to synthesize newer potent cytotoxic complexes with different substituted ligands.

Antituberculosis activity

The emergence of multidrug resistant strains highlighted the need for new drugs for the treatment of TB. The ligand and Co(II) complex were checked for their anti-TB activity against *M. tuberculosis* (H37 RV strain) while the standards used were pyrazinamide (3.125 μg/mL), streptomycin (6.25 μg/mL) and ciprofloxacin (3.125 μg/mL). The ligand shows a moderate activity (MIC =12.5 μg/mL) but complex shows a MIC value of 6.2 μg/mL which is equal to the tested standard streptomycin[36].

The anti-tuberculosis activity of the first row transition metal complexes with belnzothiazole core shows an IC_{50} value of 0.8 μg/mL in the earlier reports[37], the synthesized complex shows IC_{50} equal to that of the standard streptomycin.

Antioxidant activity

2, 2′-Diphenyl-2-picrylhydrazyl (DPPH) assay is widely used for assessing the radical scavenging ability, and it is measured in terms of IC_{50} value. DPPH shows a strong absorption band at 517 nm. When the odd electron becomes paired off in the presence of a free radical scavenger, this absorption vanishes and the resulting decolourisation is stoichiometric with respect to the number of electrons taken up. It is seen from the results that the Co(II) complex (750 μ*M*) exhibited low activity compared to the standard ascorbic acid (46 μ*M*)[38].

UV-visible absorption spectral titrations

UV-visible spectral study provides preliminary information regarding the binding behavior between DNA and small molecules. The concentration of the complex was kept constant and DNA was added to that solution in increasing amounts. Generally, when metal complexes bind with DNA, if hypochromism with red shift is observed in the absorption spectrum of the complex, it indicates an intercalative mode involving a strong stacking interaction between the complex and the base pairs of DNA, whereas a non-intercalative mode of interaction shows hyperchromism with blue shift[39]. The binding constant (K_b) for the complexes was determined from the following equation,

$$\frac{[DNA]}{(\epsilon_A-\epsilon_F)} = \frac{[DNA]}{(\epsilon_B-\epsilon_F)} + \frac{1}{K_b(\epsilon_B-\epsilon_F)}$$

where ε_A, ε_B and ε_F correspond to the apparent, bound and free metal complex extinction coefficients respectively. A linear plot of [DNA] / (ε_A-ε_F) versus [DNA] gave a slope of 1/(ε_B-ε_F) and a Y intercept equal to 1/K_b(ε_B-ε_F), where K_b is the ratio of slope to

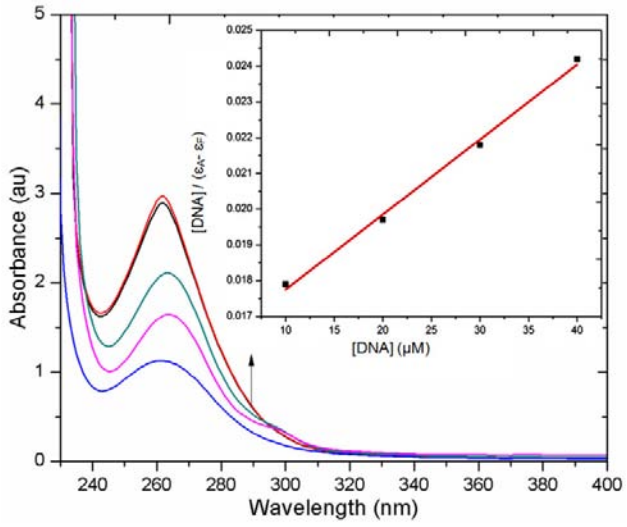

Fig. 5 – Absorption spectrum of Co(II) complex in the presence and absence of CT-DNA. {Cond.: [M] = 10 μ*M*, [DNA] = 0–40 μ*M*. Arrow (↑) shows the increasing absorbance upon increasing DNA concentration. Inset: Linear plot for the calculation of the intrinsic DNA binding constant (K_b)}.

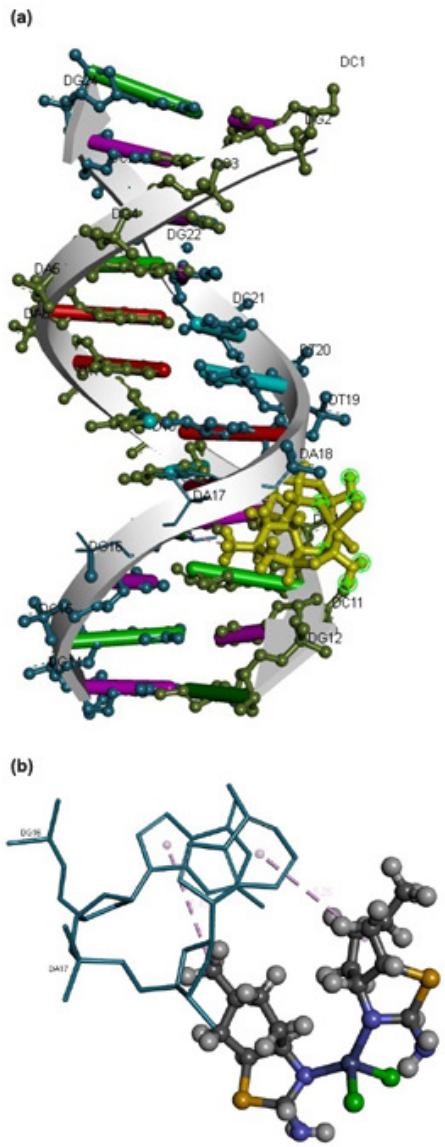

Fig. 6 – The docking poses of the complex with the DNA. {(a) 2D interaction diagram showing various interactions of the complex with DNA through minor groove binding; (b) Formation of hydrogen bonds between Co(II) complex and DNA residues}.

the intercept. The observation of hyperchromism is indicative of the breakage of the secondary structure of DNA.

The absorption spectrum of the Co(II) complex on the addition of the CT-DNA is shown in Fig. 5. Upon increasing the concentration of DNA to the Co(II) complex, the absorption band exhibited hyperchromism of 25-60% with a slight red shift of 2-4 nm at 266 nm. The observation of hyperchromism with a slight red shift for the synthesized complex shows that they interact with the secondary structure of CT-DNA by breaking its double helix structure. The observed binding constant (K_b) value for the complex is $1.24\times10^4\ M^{-1}$. This value is lesser than that of the classical intercalators[40], for e.g., ethidium bromide with binding constant of the order of 10^6-$10^7\ M^{-1}$. Also, by comparing the binding constant values reported in literature for various transition metal complexes as DNA groove binders[41-44], we can deduce that the Co(II) complex binds to CT-DNA via groove binding.

Docking with DNA

Possible binding modes of ligands with DNA can be identified using docking analysis. Therefore molecular docking study was carried out with HEX 6.3 package and the energetically most probable poses are given in Fig. 6. The binding energy of the complex is −6.0 kcal/mol with a IC_{50} value of 39.02 μ*M*. The Co(II) complex with benzothiazole derivative binds with the DNA in minor groove fashion with the help of hydrogen bonds[45].

Conclusions

Co(II) complex bearing amino benzothiazole ligand was synthesized and characterized. The structure of the complex was confirmed by single crystal XRD. The complex was found to be paramagnetic. The synthesized complex was evaluated for biological properties like DNA binding, antioxidant and cytotoxicity under *in vitro* experimental conditions. The DNA binding ability of the ligand and complex has been assessed by absorption spectra reveals a minor groove binding with binding constant $1.24\times10^4\ M^{-1}$. The results were validated from docking studies. The antioxidant activity showed that it has a low activity against DPPH radical. The *in vitro* antimicrobial activity against various bacteria and fungi showed that the Co(II) complex showed a better activity than the free ligand. The *in vitro* cytotoxicity of the Co(II) complex against MCF-7 cell line was found to be comparable to that of cisplatin. In addition, the Co(II) complex showed a good anti-TB activity equal to the test standard streptomycin.

Supplementary Data

Supplementary X-ray crystallographic data for the complex (CCDC 1025347) can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (+44) 1223-336-033 or Email: deposit@ccdc.cam.ac.uk). Other Supplementary data associated with this article, viz., Figs S1-S3, and, Table S1, are available in the electronic form at http://www.niscair.res.in/jinfo/ijca/IJCA_55A(11)1297-1304_SupplData.pdf.

Acknowledgement

One of the authors (SJ) thanks University Grants Commission-Hyderabad, India for financial support (MRP No. 4995/14 (SERO-UGC).

References

1 Bryson M, Fulton B & Benfield P, *Drugs*, 52 (1996) 549.
2 Akhtar T, Hameed S, Al-Masoudi N, Loddo R & Colla P L, *Acta Pharm*, 58 (2008) 135.
3 Shi D, Bradshaw T, Wrigley S, McCall C, Lalieveld P, Fichhtner I & Stevens M, *J Med Chem*, 39 (1996) 3375.
4 Slawinski J & Brzozowski Z, *Eur J Med Chem*, 41 (2006) 1180.
5 Catalano A, Carocci A, Defrenza I, Muraglia M, Carrieri A, Van Bambeke F, Rosato A, Corbo F & Franchini C, *Eur J Med Chem*, 64 (2013) 357.
6 Soni B, Ranawat M, Sharma R, Bhandari A & Sharma S, *Eur J Chem*, 45 (2010) 2938.
7 Nagarjan S, Crescenzo G, Getman D, Lu H, Sikorski J, Walker J, McDonald J, Houseman K, Kocan G, Kishore N, Mehta P, Shippy C & Blystone L, *Bioorg Med Chem*, 11 (2003) 4769.
8 Delmas F, Avellaneda A, Giorgio C, Robin M, Clercq E, David P & Galy J P, *Eur J Med Chem*, 39 (2004) 685.
9 Abbas E M H, Amin K M, El-Hamouly W S, Dawood D H & Abdulla M M, *Res Chem Intermed*, 41 (2015) 2537.
10 Lemoine P, Viossat B, Huy Dung N, Tomas A, Morgant G, Greenaway F T & Sorenson J R J, *J Inorg Biochem*, 98 (2004) 1734.
11 Pattan S R, Suresh C, Pujar V D, Reddy V V K, Rasal V P & Koti B C, *Indian J Chem*, 44B (2005) 2404.
12 Ibrahim D A, Lasheen D S, Zaky M Y, Ibrahim A W, Vullo D, Ceruso M, Supuran C T & Abou El-Ella D A, *Bioorg Med Chem*, 23 (2015) 4989.
13 Racane L, Kulenovic V, Kitson R & Zamola G, *Monatsh Chem*, 137 (2006) 1571.
14 El-Shazly M F, Salem T, El-Sayed M A & Hedewy S, *Inorg Chim Acta*, 29 (1978) 155.
15 Chaurasia M R, Shukla P & Singh N K, *Def Sci*, 32 (1982) 75.

16 Bhagat T M, Swamy D K & Deshpande M N, *J Chem Pharm Res*, 4 (2012) 100.

17 Maji M, Sengupta P, Chattopadhyay S, Mostafa G, Schwalbe C H & Ghosh S, *J Coord Chem*, 54 (2006) 13.

18 Chen Q, Yang E, Zhang R, Wang X & Zhao X, *J Coord Chem*, 61 (2008) 1951.

19 Joseph J & Boomadevi Janaki G, *J Mater Environ Sci*, 5 (2014) 693.

20 *Methods for Anti-Microbial Dilution and Disk Susceptibiliy Testing of Infrequently Isolated or Fastidious Bacteria; Approved Guideline Document M45-A 26(19)*, (National Committee for Clinical Laboratory Standard, NCCLS, Vilanova PA USA) 1999.

21 Monks A, Scudiero D, Skehen P, Shoemaker R, Paull K, Vistica D, Hose C, Langley J, Cronise P & Vaigro-Wolff A, *J Natl Cancer Inst*, 83 (2009) 757.

22 Collins L A & Franzblau S G, *Antimicrob Agents Chemother*, 41 (1997) 1004.

23 Sheldrick G M, *ActaCryst*, A64 (2008) 112.

24 Dolomanov O V, Bourhis L J, Gildea R J, Howard J A K & Puschmann H, *J Appl Cryst*, 42 (2009) 339.

25 Sampath K, Sathiyaraj S & Jayabalakrishnan C, *Med Chem Res*, 23 (2014) 858.

26 Zheng K, Liu F, Xu X, Li Y, Wu Z & Yan C, *New J Chem*, 38 (2014) 2964.

27 Selwin Joseyphus R & Sivasankaran Nair M, *Arab J Chem*, 3 (2010) 195.

28 Motaung M P & Ajibade P A, *Int J Electrochem Sci*, 10 (2015) 8087.

29 Jin Q, Chen J, Pau Y, Zhang Y & Jiu D, *J Coord Chem*, 63 (2010) 1492.

30 Nanda Srivatva A, Pal Singh N & Kiran Shriwastaw C, *Arab J Chem*, 9 (2016) 48.

31 Awad I M A, Osman A H & Aly A A M, *Phosph, Sulph Silicon*, 178 (2003) 1339.

32 Chohan Z H, Munawar A & Supuran C T, *Metal Based Drugs*, 8 (2001) 137.

33 Ohsaki Y, Gazdar A F, Chen H C & Johnson B E, *Cancer Res*, 52 (1992) 3534.

34 Hussein B H M, Azab H A, El-Azab M F & El-Falouji A I, *Eur J Med Chem*, 51 (2012) 99.

35 Mavroida B, Sagnou M, Stamatakis K, Paravatou-Petsotas M, Pelecanou M & Methenitis C, *Inorg Chim Acta*, 444 (2016) 63.

36 Yamori S, Ichiyama S, Shimokata K & Tsukamura M, *Microbiol Immunol*, 36 (1992) 361.

37 Netalkar P P, Netalkar S P, Budagumpi S & Revankar V K, *Eur J Med Chem*, 79 (2014) 47.

38 Sampath K, Sathiyaraj S & Jayabalakrishnan C, *Spectrochim Acta A*,115 (2013) 287.

39 Chandrasekaran S, Sameena Y & Muthu Vijayan Enoch I V, *Turk J Chem*, 38 (2014) 725.

40 Alonso S, Almendral M J, Curto Y, Criado J J, Rodriquez E & Manzano J L, *Anal Biochem*, 355 (2006) 157.

41 Kurdekar G S, Puttanagouda S M, Kulkarni N V, Budagumpi S & Revankar V K, *Med Chem Res*, 20(4) (2011) 421.

42 Raman N, Sobha S & Mitu L, *J Saudi Chem Soc*, 17 (2013) 151.

43 Gomathi R, Ramu A & Murugan A, *Bioinorg Chem Appl*, 215392 (2014) 1.

44 Subburaj P, Ramu A, Raman N & Dharmaraja J, *J Saudi Chem Soc*, 19 (2015) 207.

45 Chandrasekaran S, Sameena Y & Muthuvijayan Enoch I V, *Aust J Chem*, 67(2) (2013) 256.