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Synthesis, characterization and DNA-Binding properties of the novel mononuclear Zn(II), Cd(II), and Mn(II) complexes with Pantoprazole

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Abstract: A novel mononuclear Mn(II), Zn(II) and Cd(II) complexes of pantoprazole (PA) was synthesized and characterized by elemental analysis, molar conductivity, magnetic susceptibility measurements, IR, UV-visible spectral studies, and thermal analysis. The electronic spectra along with magnetic data suggest octahedral geometry for Mn(II), Zn(II) and Cd(II) complexes. PA acts as an anionic bi-dentate ligand being coordinated by (S=O) oxygen and benzimdazolyl nitrogen atoms. The interaction of the complexes with calf thymus DNA (CT-DNA) was monitored by blue shift and hyperchromism in the UV-vis spectra. The observed intrinsic binding constants together with structural analysis of the complexes indicate the groove binding. The binding constants were determined at 303°K, 308°K and 313°K. A thermodynamic analysis showed that the reaction is spontaneous with ΔG being negative. The enthalpy ΔH and the entropy ΔS of reactions were all determined.

Keywords: Pantoprazole; Complexes; Binding constant; hyperchromism.

Introduction

Proton pump inhibitors are highly effective in the management of acid-related diseases, including duodenal ulcer (DU), gastric ulcer (GU), gastroesophageal reflux disease (GERD), errosive oesophagitis, hypersecretory syndroms like Zollinger -Ellison and Helicobacter pylori (H. pylori) infections [1-4]. There are currently five different proton pump inhibitors (PPIs) available, including esomeprazole, lansoprazole, omeprazole, pantoprazole and rabeprazole [5-10]. These agents are all substituted benzimidazoles that inhibit the final common pathway of gastric acid secretion [2,3]. Proton pump inhibitors irreversibly inhibit the proton pump and acid production can only be restored through endogenous synthesis of new proton pumps [6,7,8,9]. Metal complexes are gaining increasing importance in the design of respiratory, slow release and long acting drugs. Metal ions are therefore known to accelerate drug actions [11].

The efficacies of some therapeutic agents are known to increase upon coordination [12]. Some metal complexes are known to exhibit remarkable antitumor, antifungal, antiviral and special biological activities [13,14]. Therefore, complexation of chemotherapeutic agents has been found to be applicably useful in medicine and pharmacy [15].

Deoxyribonucleic acid (DNA) is the primary target molecule for most anticancer and antiviral therapies according to cell biology [16,17]. Investigations of the interaction between small molecules and DNA are basic work in the design of new types of pharmaceutical molecules [18]. Binding studies of small molecules with DNA are important in the design of new and more efficient drugs targeted to DNA [19]. Several aromatic hydrocarbons and their derivatives have been shown to be carcinogenic, and in several instances, the carcinogenicity was attributed to their activity at the DNA level [20,49-50]. Metal complexes, porphyrins, natural antibiotics, and a host of other planar heterocyclic cations have been investigated for their DNA binding affinity. Recently, the DNA sequence recognition by drugs as well as by small molecules that are conjugated to peptides or oligonucleotides has been of great interest. Binding studies with these various small molecules are valuable for the rational design of drugs as well as in understanding how

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proteins recognize and bind to specific DNA sequence [21,22].

Experimental Section

Materials

All chemicals were of A.R. grade and were used without further purification; pure (how pure) Pantoprazole sodium sesquihydrate (PANa) was obtained from Smilax Laboratories Limited, India. Cadmium (II) chloride dihydrate ($CdCl_2{\cdot}2H_2O$), zinc (II) chloride hexahydrate ($ZnCl_2{\cdot}6H_2O$) and manganese (II) chloride hexahydrate ($MnCl_2{\cdot}6H_2O$) were purchased from (Merck Co.). All solvents used are of analytical grade quality from Sigma-Aldrich.

Methods

All experiments involving the interaction of the complexes with DNA was carried out in tris buffer (5 mM Tris-HCl, 50 mM NaCl, pH 7.0). In solution this DNA had a ratio of UV absorbance at 260 and 280 nm of about 1.90 indicating its purity [23]. DNA concentration per nucleotide was determined by absorbance at 260 nm using the molar absorption coefficient

(6600 $M^{-1}cm^{-1}$) [24,25]. All the experiments involving the binding of complexes with CT-DNA were carried out in a bidistilled water buffer with tris(hydroxymethyl)-aminomethane (Tris, 5 mM) and sodium chloride (50 mM) and adjusted to pH 7.2. Absorption titration experiments were performed with fixed concentrations of the complexes (1 x 10^{-4} $molL^{-1}$) with varying concentration of DNA(0-60 μM). While measuring the absorption spectra, an equal amount of DNA was added to both the test solution and the reference solution to eliminate the absorbance of DNA itself. The values of the intrinsic binding constants K_b were calculated by regression analysis using the equation (1) [26].

$$\frac{[DNA]}{\varepsilon_a-\varepsilon_f} = \frac{[DNA]}{\varepsilon_b-\varepsilon_f} + \frac{1}{k_b.(\varepsilon_a-\varepsilon_f)} \qquad (1)$$

where [DNA] is the concentration of CT-DNA in base pairs and ε_a, ε_f and ε_b are extinction coefficients of the apparent, free and bound metal complex, respectively and K_b is the equilibrium binding constant. In the plots of [DNA]/(ε_a- ε_f) versus [DNA], K_b is given by the ratio of slope to the intercept.

Synthesis of the complexes

To a colorless solution of PANa (431 mg, 1 mmol) in ethanol/ water (EtOH/ H_2O, 1:1) (10 ml), a solution of hydrated metal chloride (1 mmol) in ethanolic aqueous (H_2O/EtOH, 1:1) (10 ml) was added drop wise then the reaction mixture was stirred at room temperature for 1 hr. After that, the isolated solid was filtered off, washed with cold acetone and dried under vacuum at room temperature to yield M(II) pantoprazolate complexes.

Instruments

Elemental analyses for C, H, and N were performed with a Perkin-Elmer 2400 elemental analyzer. FTIR spectra were recorded on a BRUKER Tensor -37 FTIR spectrophotometer in the range 400-4000 cm^{-1} as KBr discs. For signal intensities the following abbreviations were
Used: br (broad), sh (sharp), w (weak), m (medium), s (strong), vs (very strong). The UV/vis absorption measurements were conducted at room temperature with concentration (10^{-4} M) on a Shimadzu UV-1601 spectrophotometer, in the range 200-800 nm, using quartz cuvettes (1 cm). Molar conductivities of freshly prepared 1×10^{-3} $molL^{-1}$ DMF solutions were measured using WPACM 35 conductivity meter. Finally the thermogravimetric analysis (TGA and DTG) were carried out in dynamic air atmosphere (30 mL/min) with a heating rate of 10°C/min using a Shimadzu TGA-50H thermal analyzer.

Results and Discussion

Chemistry and synthesis

The metal complexes were prepared by the reaction of an equimolar amount of $MCl_2{\cdot}6H_2O$ ($M = Mn^{2+}$, Zn^{2+} and Cd^{2+}) with PANa in ethanol/ water (1:1) media. The ease of synthesis and high yield in single step reaction from commercially inexpensive reagents make these extremely attractive in coordination compounds. These metal complexes are stable, soluble in DMF and DMSO and insoluble in all other organic solvents and in water. The elemental analysis and conductivity data of the free ligand and its complexes are presented in Table 1. All the metal complexes possess 1:1 (M: L) stoichiometry and the analytical data are in a good agreement with these proposed stoichiometry. The molar conductivity values for the complexes in DMF solvent (1.0×10^{-3} $molL^{-1}$) which were in the range (0.016-0.022 mhos cm^2mol^{-1}) (Table 1) reveal their non-electrolytic nature [27] and absence of Cl^- outside the coordination sphere which supported by negative $AgNO_3$ test.

Table 1. Elemental analytical results and some properties of the PANa and complexes

Compound	m.p	Y	Elemental Analysis (%) Calc. / (found)					Λ_η
(Empiric formula)	(%)	C	H	N	S	M	mhos	
PANa ($C_{16}H_{15}F_2N_3NaO_4$ SNa)	198	–	–	–	–	–	–	0.046
[Cd(PA)Cl_2(H_2O)2] ($C_{16}H_{19}Cl_2CdF_2N_3O_6S$)	200	70	31.88 (31.76)	3.18 (3.26)	6.97 (6.88)	5.32 (5.48)	18.65 18.37	0.023
[Zn(PA)Cl_2(H_2O)2] ($C_{16}H_{19}Cl_2ZnF_2N_3O_6S$)	186	73	34.58 (34.35)	3.45 (3.28)	7.56 (7.44)	5.77 (5.48)	11.77 (11.28)	0.018
[Mn(PA)Cl_2(H_2O)2] ($C_{16}H_{19}Cl_2MnF_2N_3O_6S$)	194	72	35.24 (35.13)	3.51 (3.41)	7.71 (7.54)	5.88 (5.60)	10.08 (9.89)	0.016

IR spectra and mode of chelation

The study of the IR spectral data was quite informative in characterizing the metal-PA binding modes. The diagnostic IR spectral bands of the free ligand with those of its metal complexes were recorded in Table 2.

Table 2. IR spectral assignments of PANa and its bivalent transition metal complexes

Compound	*ν* (O-	*ν* (C=N	*ν* (C-	*ν* (C-	*ν* (S=O	γ, δ	*ν* (M-	*ν* (M-
PANa	3430	1590	1320	1120	1069	720, 630	-	-
	(m, br)	(s, sh)	(s, sh)	(s, sh)	(s, sh)	(w, br), (w, br)		
[Cd(PA)Cl_2(H_2O	3432	1592	1304	1119	1040	718, 630	426	627
	(m, br)	(s, sh)	(m, sh)	(s, sh)	(s, sh)	(w, br), (w, br)	(w, br)	(w, br)
[Zn(PA)Cl_2(H_2O	3417	1590	1303	1119	1039	719, 631	421	631
	(m, br)	(s, sh)	(m, sh)	(s, sh)	(s, sh)	(w, br), (w, br)	(w, br)	(w, br)
[Mn(PA)Cl_2(H_2	3435	1592	1301	1120	1041	716, 629	419	629
	(m, br)	(s, sh)	(s, sh)	(s, sh)	(s, sh)	(w, br), (w, br)	(w, br)	(w, br)

sh, sharp; br, broad; s, strong; m, medium; w, week.

All complexes exhibit very similar infrared spectral features. When comparing the spectroscopic data of complexes with those of the free ligand, marked changes may be noticed in the ligand bands arising from various modes of donor groups involved in bonding to cadmium, zinc and manganese ions (Figure 1). The diagnostic IR spectral bands with their assignments of the free ligands and their metal complexes are shown in (Table 2). The IR stretching bands due to *ν*(C-N, imidazole) register a blue-shift of 10-11 cm^{-1} in the complexes thus, indicating the coordination of the imidazole nitrogen to the ions [28], which is further confirmed by the appearance of a new band in the spectra of chelates at 443-445 cm^{-1} assigned to a *ν*M(II)-N vibration (M= Mn, Zn, Cd) [29].

Strong bands attributable to sulfonyl oxygen *ν*(S=O) are evident; these all show a shift of 28-30 cm^{-1} to lower energy in the complexes from the free ligand values indicative of co-ordination to Mn(II), Zn(II) and Cd(II) respectively [30]. The new IR band (456-475 cm^{-1}) is assigned to M-O vibrations [31] and supports the ligation of the sulfonyl oxygen to metal ions. The bands ascribed to the vibration of the imidazole *ν*(C=N) and pyridine moiety remains unchanged in the complexes revealing that, the nitrogen atom of the (C=N) group does not take part in metal coordination [32]. Finally, very broad bands centered at ca. 3400 cm^{-1} in all complexes can be assigned to the *ν*(OH) modes of lattice water in the corresponding framework [33-36].

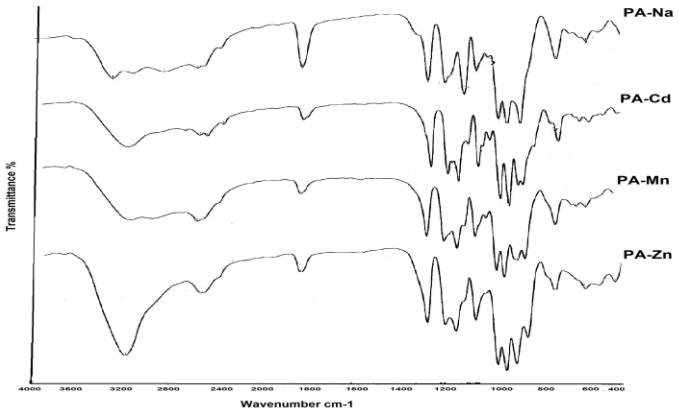
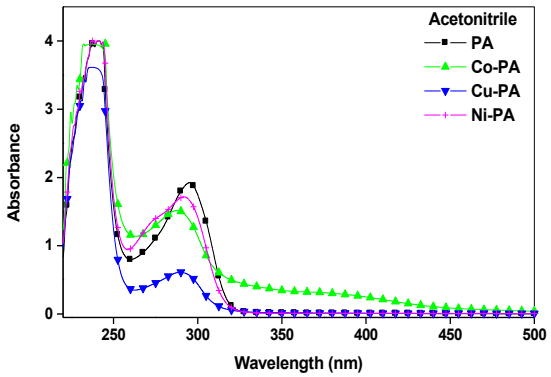


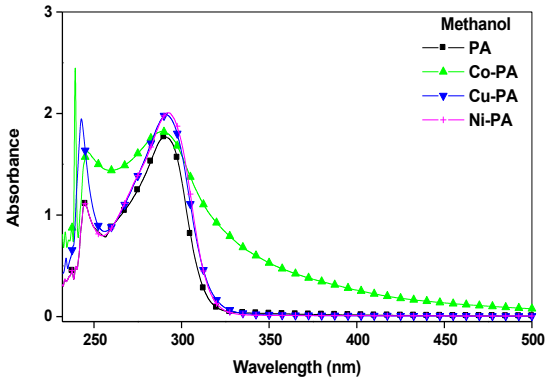
Figure 1. FTIR spectra, for comparison the sulfonyl and benzimidazolyl stretches and their splitting patterns from PANa and its complexes.

Electronic spectra and magnetic susceptibility data

The formation of the metal complexes was also confirmed by UV/vis spectra. The absorption spectrum of PA ($1x10^{-4}$ molL^{-1}) in ethanol:DMF (1:9) (v/v) shows a maximum absorption band at 242 nm and around 295 nm due to the π-π* transition with high extinction coefficient $1.85x10^{4}$ mol^{-1} cm^{-1} L which can be assigned to the intra-pantoprazolate charge transfer (π→π*) transition, in the phenyl and imidazole parts of the PA ligand [37]. In comparison to the ligand, the electronic spectra of the mononuclear complexes ($1x10^{-4}$mol^{-1}L^{-1}) exhibit similar features, where all display blue shift which confirms the coordination of the ligand to the metal ions [38], which indicate that the benzimdazolyl nitrogen atom and the oxygen atom were involved in coordination with the metal ions. For Mn-complex, the absorption bands at 291 and 242 nm are assigned to ligand-centered π→π* transition [39]. The Mn(II) complexes, exhibit new bands over 450 nm corresponding to the $^{6}A_{1g}$ (F) → $^{4}T_{2g}$ (G) transitions, as has been reported for Mn(II) octahedral complexes [40,41]. In the spectra of the complexes, the d-d transitions were not very well defined and were observed as shoulder bands. The geometry of Mn(II) complex is further confirmed [42,43] by the high *μeff* value (5.85 BM).

The diamagnetic Zn(II) and Cd(II) complexes show absorption bands at 292 nm and 242 nm. These bands are attributed to the charge transfer MLCT as the electronic configuration of these complexes confirmed the absence of any d-d transition [44-46]. Effect of different solvents on UV-vis spectra for complexes is shown in Figure 2. The π-π* (295 nm) band shifted to lower wavelength as the polarity of solvent increase, following the order: ethanol ~methanol > DMF > acetonitrile > DMSO > water.





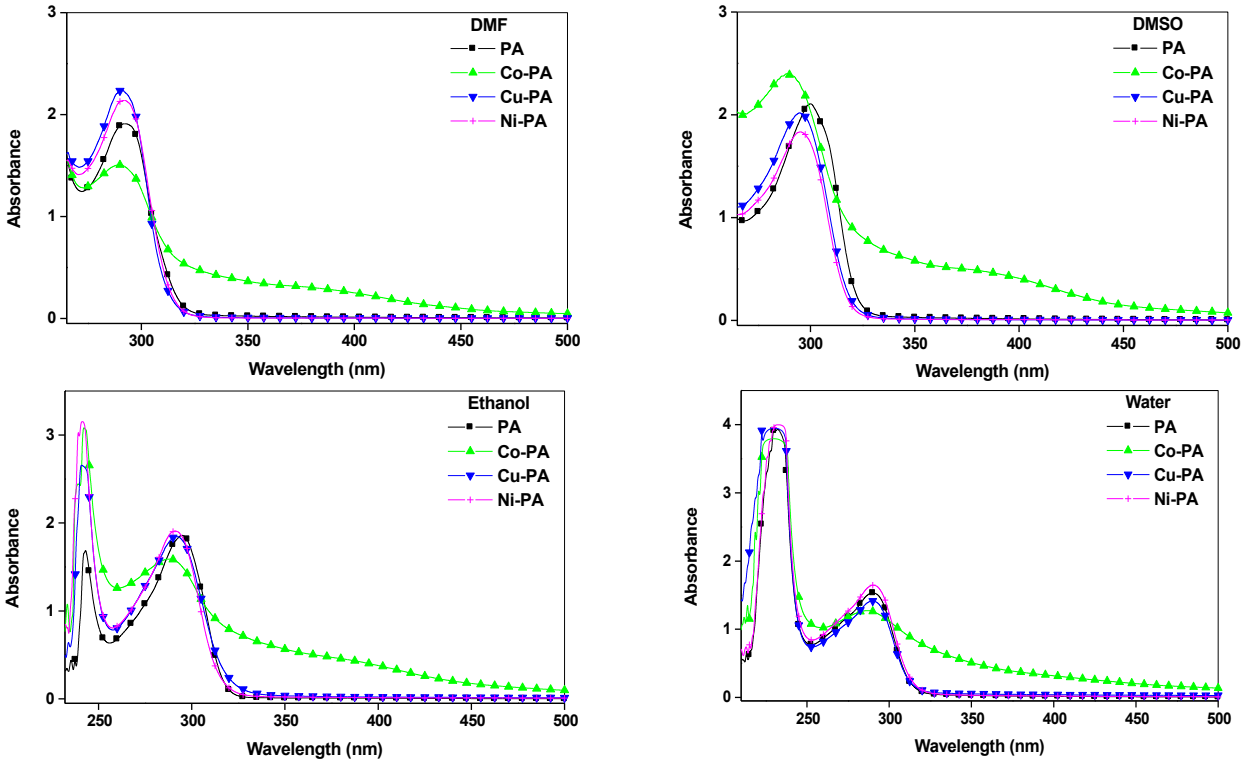


Figure 2. Electronic absorption spectra for Pantoprazole and their complexes at different solvent

Thermal stability

The TG-DTA analysis of manganese complex shows loss in weight corresponding to decomposition of water molecules in the temperature range 152 to 200 °C accompanied with the two endothermic peaks in first step decomposition. In that second step, there is continuous loss of the complex supported by an endothermic peak and the final product is metal oxide. The TG - DTA analysis of Cd-complex shows loss in weight in temperature range 160-220 °C may correspond the elimination of coordinated water molecules accompanied with an endothermic peak in the first step of decomposition. The decomposition continues up to 700°C and on further increasing the temperature no weight loss is observed which may be attributed to formation of stable metal oxide.

Structure of the complexes

The fact that these compounds were isolated as powders and not as single crystals means that no complete structure determination can be made. Accordingly, physicochemical and spectral as well as thermal analyses could help us to predict structure; the suggested structures of the Hydrated Mn(II), Zn(II) and Cd(II) pantoprazolate complexes can be represented below (Figure 4).

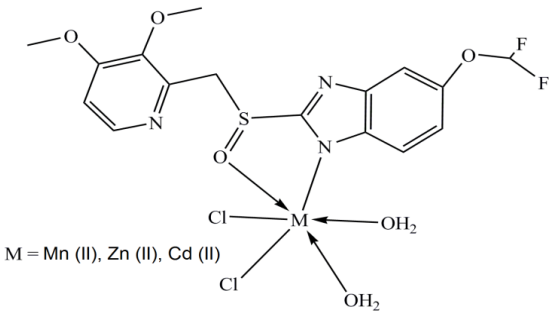


Figure 4. PANa coordination modes in metal complexes

DNA-binding experiments

DNA-binding studies are important for the rational design and construction of new and more efficient drugs targeted to DNA. Electronic absorption spectroscopy is one of the most useful techniques for DNA-binding studies of metal complexes. The spectral changes reflect the corresponding changes in DNA in its conformation and structures after the drug bound to DNA. Intercalative mode of binding usually results in hypochromism and bathochromism due to strong stacking interaction between an aromatic

chromophore and the base pairs of DNA. On the other hand, metal complexes which non-intercalatively or electrostatically bind with DNA may result in hyperchromism and hypsochromism. The absorption spectra show clearly that the addition of DNA to the complexes lead to strong hyperchromism accompanied by the slight hypsochromism to the [DNA]/[complex] (Figure 5). Obviously, these spectral characteristics suggest that all the complexes interact with DNA via electrostatically with the base pairs of DNA [47-50]

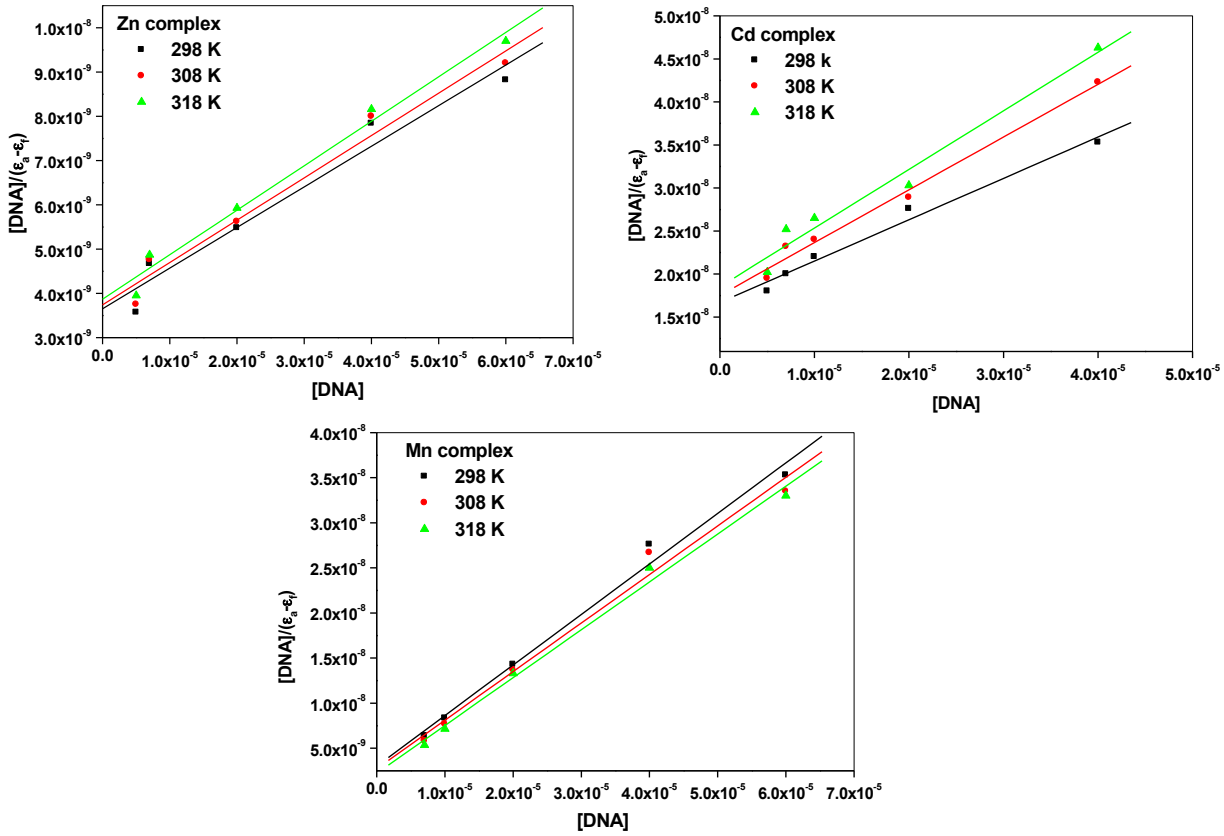


Figure 5: Plot of [DNA]/($\varepsilon_a - \varepsilon_f$) versus [DNA]

The values of intrinsic DNA-binding constant, K_b of the complexes determined at different temperature are listed in the Table 3.

Table 3. Binding constants and Thermodynamic parameters for the interaction of pantoprazole complexes with CT-DNA

	Temp.	Binding constant K_{b_1}	R	ΔH (kj/mol)	ΔS (j/mol.k)	ΔG (kj/mol)
	298 K	2.88x 10^4	0.9910	9.07x10^3	116.10	-25.4
Cd-complex	308 K	3.50x10^4	0.9935			-26.8
	318 K	3.68x10^4	0.9825			-27.8
	298 K	1.86x10^5	0.9945	9.45x10^3	132.4	-30.1
Mn-complex	308 K	1.97x10^5	0.9924			-30.2
	318 K	2.39x10^5	0.9963			-32.7
Zn-complex	298 K 308 K 318 K	2.5x10^4 2.56x10^4 2.58x10^4	0.9786 0.9851 0.9915	1.13x10^3	88.04	-25.1 -26.0 -26.9

The thermodynamic parameters associated with temperature variation were analyzed in order to further characterize the acting forces between CT-DNA and complexes. The thermodynamic parameters, enthalpy change (ΔH) and entropy change (ΔS) of binding reaction, are the main evidence for confirming binding modes. From the thermodynamic standpoint, $\Delta H > 0$ and $\Delta S > 0$ implies a hydrophobic interaction; $\Delta H < 0$ and $\Delta S < 0$

reflects the van der Waals force or hydrogen bond formation; and $\Delta H \approx 0$ and $\Delta S > 0$ suggesting an electrostatic force [48].

The temperature-dependence of the binding constants was studied at three different temperatures (25, 35, and 45 °C). According to the following thermodynamic equations:

$$\text{Ln K} = -\frac{\Delta H}{RT} + \frac{\Delta S}{R} \quad (2)$$

$$\Delta G = \Delta H - T\Delta S = -RT\text{LnK} \quad (3)$$

Where K is the binding constant at corresponding temperature and R is the gas constant, in which ΔH and ΔS of reaction could be determined from the linear relationship between ln K and the reciprocal absolute temperature. The free energy (ΔG) could be calculated by Eq. (3). The results from the plots of ln K versus $1/T$ (Figure 6 which is based on the K values of binding constant) are given in Table 3. The reaction of complexes with DNA is spontaneous as indicated from the negative value for ΔG, both ΔH and ΔS are positive. This attributed to hydrophobic interactions being the leading contributor to the binding [49-51]. The binding constant increase with temperature suggesting that some covalent type interactions are at play in the binding.

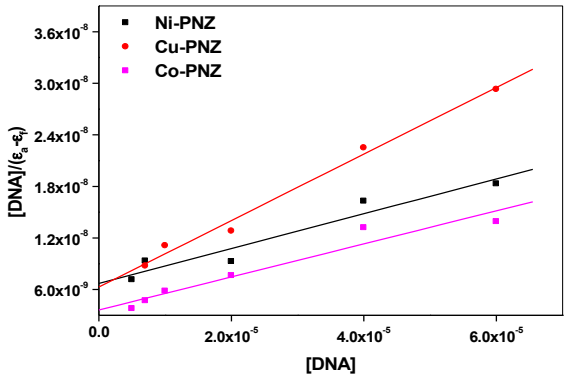


Figure 6. Correlation between ln K versus 1/T

Conclusion

Three new Mn(II), Zn(II) and Cd(II) complexes with pantoprazole sodium sesquihydrate (PANa) have been synthesized by mixing equimolar aqueous ethanolic solution of PANa and $MCl_2{\cdot}6H_2O$ (M = Mn^{2+}, Zn^{2+} and Cd^{2+}). IR, UV-visible spectral studies, conductance measurements and thermogravimetric (TGA) and differential thermal analyses (DTG) have been used to characterize the isolated solid complexes.

References

1- G. Novacek, A. Geppert, L. Krame, F. Wrba, F. Herbst, W. Schim, A. Gangl, and R.Potzi,, J. Clin Gastroent., **2001**, 33-56.

2- C. W Howden,. R. H Hunt, *Am J Gastroent.,* **1998**, 93

3- K. R DeVault,. D. O Castell, *Am J Gastroent.,* **1999**, 94, 1434.

4- L. S Welage, R. R Berardi,., *J Am Pharm Assoc (Wash).*, **2000**, 40, 52.

5- X. Q. Li, T. B Andersson, M Ahlstrom, and L .Weidolf,., *Drug Metab Dispos.,* **2004**, 32,

6- J. G Hatlebakk,., *Aliment Pharm Ther.,* **2003**, 17, 10S.

7- R. M Khoury, and P. O Katz,., *Aliment Pharmac.,* 1999, 13, 675. [8] Langtry, H. D. and Wilde, M. I., *Drugs,* **1997**, 54, 473.

8- J. G Hatlebakk, *Aliment Pharm Ther.,* **2003**, 17, 10S.

9- A. O .Ajibola,., *Essential of Medicinal Chemistry*; 2nd Edition, Sharson Jersey, 1990.

10- Reedijk, A., *J Pure Appl Chem*., **1987**, 59, 181.

11- R. C Sharma, and R. K Parashar,., *J Inorg Biochem.,* **1988**, 32, 163.

12- Z. H Abdel-waheb., M. M Mashaly, ,A. A Salman., B. A El-shetary, A A,Faheim,, *Spectrochim Acta A,* **2004**, 60, 2861.

13- J. A Obaleye,., , J. B Nde-aga. and E. A Balogun, *Afr J Sci.,* **1997**, 1, 10.

14- K Jiao, Q.X Wang, W Su., F.F Jian,. Synthesis, characterization and DNA- binding properties of a new cobalt(II) complex: Co (bbt)2Cl2. J Inorg Biochem, **2005**, 99, 1369-1375.

15- D.S Sigman,, D.R Graham, V.D Aurora, A.M Ster,. Oxygendependent cleavage of DNA by the 1,10-phenanthroline cuprous complex. Inhibition of Escherichia coli DNA polymerase I. J. Biol. Chem., **1979**, 254, 12269-12272.

16- H. A. Azab, E. M. Mogahed, F. K. Awad, R. M. Abd El Aal, R. M. Kamel, J Fluoresc, **2012**, 22:971-992

17- B. Lambert, J.B LePecq, *DNA-Ligand Interactions, from Drugs to Proteins*; Guschibaver, W., Saenger, W., Eds.; Plenum: New York, **1986**, p 141.

18- C Heidelberger, Polycyclic Hydrocarbons and Carcinogenesis. *Annu. ReV. Biochem.* **1977**, *44*, 79.

19- D Porschke, *DNA-Ligand Interactions, Specificity and Dynamics of protein-Nucleic Acid Interactions*;.; Plenum: New York, **1986**, p 85.

20- H. A. Azab , I. I. Abd El-Gawad, and R. M. Kamel, *J. Chem. Eng. Data* **2009**, 54(11) pp 3069-3078.

21- Y Wang, Z.Y Yang, Synthesis, Characterization and DNA-binding Properties of Three 3d Transition Metal Complexes of the Schiff Base Derived from Diethenetriamine with PMBP. Transition Met. Chem., **2005**, 30, 902-906.

22- D Lawrence, V. G Vaidyanathan, , B Unni Nair, Synthesis, characterization and DNA binding studies of two mixed ligand complexes of ruthenium(II). Journal of Inorganic Biochemistry. J. Inorg. Biochem. 100, **2006**, 1244-1251.
23- R Eshkourfu, B Čobeljić, M. Vujčić, I. TurelPevec, A Sepčić, K., Zec, M., Radulović, S., Srdić-Radić, T., Mitić, D., Andjelković, K., Sladić, D.,. Synthesis, characterization, cytotoxic activity and DNA binding properties of the novel dinuclear cobalt(III) complex with the condensation product of 2-acetylpyridine and malonic acid dihydrazide. J. Inorg. Biochem. 105, **2011**, 1196-1203.
24- A Wolf, G. H Shimer.,T Meehan. Polycyclic aromatic hydrocarbons physically intercalate into duplex regions of denatured DNA. Biochemistry 26, **1987**, 6392-6396.
25- W. J Geary, The use of conductivity measurements in organic solvents for the characterisation of coordination compounds. Coord. Chem. **1971**. 7, 81-122.
26- C Mingquan., H Chuanhua,., W Xiaoling, L Lan, P Jiankun, Q Yu, Faming Zhuanli Shenqing Gongkai Shuomingshu, **2002** 8. Patent: CN 2002-113294 20020130.
27- K Nakomoto, Infrared and Raman Spectroscopy of Inorganic and Coordination Compounds. **1978**, 3rd ed., Wiley Interscience, New York.
28- M Revanasiddappa, C Basavaraja, T. Suresh, S. D Angadi, Synthetic, spectral and antimicrobial activity studies of first row transition metal complexes derived from lansoprazole drug. Journal of the Indian Chemical Society, **2009** 86(2), 127-132.
29- S. S Garje, V. K Jain. Chemistry of arsenic, antimony and bismuth compounds derived from xanthate, dithiocarbamate and phosphorus based ligands Coord. Chem. Rev., **2003**, 236, 35-56.
30- J Huang, X Fu., G Wang, Q Miao, G Wang, Axially coordinated chiral salen Mn(III) anchored onto azole onium modified ZnPS-PVPA as effective catalysts for asymmetric epoxidation of unfunctionalized olefins. Dalton Trans. **2012**, 41, 10661-10669.
31- K Nakamato, Infrared and Raman Spectra of Inorganic and Coordination Compounds. **1986** 4th ed., Wiley, New York, pp. 242.
32- W. N Wassef,, N. M Ghobrial., S. M Agami, Spectroscopic studies on the electron donor-acceptor interaction between 1-propanamine-3-triethoxysilyl and π- acceptors, Spectrochim. **1991**, Acta A 47, 623.
33- E.M Nour, L.A Shahada, Electronic spectral studies and solvent effects on the reaction of iodine with 1,4,8,11-tetraazacyclotetradecane Spectrochim. Acta A 44, **1988**, 1277.
34- S.Y AlQaradawi, Nour, E. M, Spectroscopic investigation of the charge-transfer interactions between 1,4,7-trimethyl-1,4,7-triazacyclononane and the acceptors iodine, TCNE, TCNQ and chloranil. Spectorchim., Acta A 68, **2007**, 908.
35- M Pandeeswaran, E.H El-Mossalamy, K. P Elango, Spectroscopic studies on the dynamics of charge-transfer interaction of pantoprazole drug with DDQ and iodine. Inc. Int J Chem Kinet, **2009**, 41, 787-799.
36- Friedel, R. A., Orchin, M.,. Ultraviolet Spectra of Aromatic Compounds Chemistry. John Wiley, **1958** New York.
37- M Mohan, P Sharma, Metal(II) complexes of 1-formylisoquinoline thiosemicarbazone: their preparation, characterization and antitumour activity. Inorg. Chem. Acta, **1985**, 106, 117-121.
38- A. B. P. Lever, *Electronic Spectra of Ions. In Inorganic Electronic Spectroscopy*, 2nd Ed.; Elsevier: Amsterdam, **1984**, 449.
39- V. Philip, V. Suni, M. R. P. Kurup, M. Nethaji, *Spectrochim. Acta Part A*, 64, **2006**, 171.
40- B N Figgis, *Introduction to Ligand Fields*; Willey Eastern Ltd., New Delhi, **1976**.
41- M.Y Aljanabi,. *The Physical Methods in Inorganic Chemistry*, University of Baghdad: Iraq; 1983.
42- A.S Shayma, K Hamid, M.A Hapipah,. *Chem. Papers* **2011**, 65, 299.
43- P Nagababu, J Naveena, L Latha, Y, Prashanthi, S Satyanarayana, Journal of Chemical and Pharmaceutical Research, 1(1), **2009**, pp. 238-241
44- P. D. Ross and S. Subranmanian, *Biochemistry* 20, **1981**, 3096.
45- X. Li and X. Y. Jiang, *Spectrosc. Lett.* 4, **2009**, 210.
46- J. N. Tian, J. Q. Liu, X. Tian, Z. D. Hu and X. G. Chen, *J. Mol. Struct.,* **2004**, 1-3, , 197.
47- L.H. Abdel-Rahman., El-Khatib, R. M., Nassr, L., Spectrochim. Acta A, **2013**, 111, 266-276
48- L. H Abdel-Rahman, R.M El-Khatib, L.A.E Nassr, A.M Abu-Dief, M Ismael, and A.A Seleem, Spectrochim. Acta,, **2014**, vol. 117, 366.
49- L. H Abdel Rahman, , A. M Abu-Dief, N Ali Hashem, A Abdou Seleem, Int. J. Nano.Chem.,**2015**, 1 (2), 79-95.
50- L. H. Abdel-Rahman, A. M Abu-Dief, M Ismael, M.A Mohamed, N. A Hashem, J. Mol. Struct., **2016**, 1103, 232-244.
51- B. Zhou, Z. D. Qi, Q. Xiao, J. X. Dong, Y. Z. Zhang and Y. Liu. *J. Biochem. Biophys. Methods* 70, **2007**, 743.