Pantoprazole Sodium Sesquihydrate Complexes: Synthesis, Characterization, Potentiometric Determination and DNA interaction

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ABSTRACT

The synthesis and characterization of solid complexes for pantoprazole sodium sesquihydrate (PNZ) with Cd(II), Hg(II) and Zn(II) metals in molar ratios M:L = 1:2 was studied. The complexes are stable in the solid state and are soluble only in DMF and DMSO. The metal complexes were characterized by elemental analysis, molar conductivity measurements, magnetic susceptibility, UV spectrophotometry, IR, Mass spectra, TGA/DTG analysis. Potentiometric measurements for these metal complexes were studied.

Keywords: Pantoprazole, complexes, potentiometry, Proton Pump Inhibitors, DNA interaction.

INTRODUCTION

Pantoprazole sodium sesquihydrate is benzimidazole derivative which have biological activity to inhibit gastric acid secretion1. Pantoprazole acts as good ligand as it has several coordination modes2-4. Many drugs enhance its pharmacological and toxicological properties by their complexation with metal ions. Cd(II), Hg(II) and Zn(II)5. In this paper, several techniques were used to characterize the prepared pantoprazole complexes. DNA interaction of these complexes was given.

EXPERIMENTAL

Solid complexes

All complexes were prepared according to the following procedure. The pantoprazole ligand (0.5 mmol) is dissolved in 10 cm³ H₂O. The metal salt (0.25 mmol) dissolved in 10 cm³ H₂O
is added dropwise with continues stirring to the ligand solution. The formed precipitate was filtered, washed with hot water and dried. Synthesized solid complex were characterized by elemental analysis, IR, mass spectrometry, electrical conductivity, magnetic susceptibility, UV spectroscopy and thermal analysis.

**Physical measurements**

The electronic absorption spectra were obtained in 10⁻⁵ mol/L DMF solution in 1 cm quartz cell using Shimadzu-1601PC UV-Visible automatic recording spectro-photometer. The CHNS elemental analysis was estimated using Thermo Flasha Eager 300. The infrared spectra were recorded as KBr discs in the 400-4000 cm⁻¹ range using perkin Elmer 1650 FT-IR instrument. TGA were obtained using a Shimazdu DTG-60H in a dynamic air atmosphere (30 cm min⁻¹) at a heating rate of 10 °C min⁻¹. Conductivity of the dissolved complexes were carried out at room temperature on freshly prepared 10⁻³ mol/L DMF solutions using Jenco Model 1671 Dual Display Bench Top instrument pH/ORP (redox)/conductive. Magnetic susceptibility measurements were carried out using the modified Gouy method on MSB-MK1 balance at room temperature using murcuru (II) tetrathiocyanatecobaltate(II). The effective magnetic moment µ_eff per metal atom was calculated from the expression µ_eff = 2.83√x.T B.M., where x is the molar susceptibility corrected using Pascal’s constant for the diamagnetism of all atoms in the complexes. Mass spectra were done by AMD Intectra Gmb HDP10. Data system EI/8 Kv spectrometer.

**Kinetic parameters**

In order to assess the influence of the structural properties of the ligand and the type of metal on thermal behavior of the complexes, the order n and the heat of activation E at the various decomposition stages were determined from TGA and DTG thermograms using the Coats-Redfern equations in the following form ¹²,

\[
\ln \left[ \frac{1 - (1 - \alpha)^{1-n}}{(1-n)T^2} \right] = \ln \left( \frac{AR}{BE} \right) \left[ 1 - \frac{2RT}{E} \right] - \left( \frac{E}{2.303RT} \right) \quad \text{for } n \neq 1
\]

\[
\ln \left[ \frac{\ln(1 - \alpha)}{T^2} \right] = \ln \left( \frac{AR}{BE} \right) \left[ 1 - \frac{2RT}{E} \right] - \left( \frac{E}{2.303RT} \right) \quad \text{for } n = 1
\]

Where: \( \alpha \) is fraction of weight loss, \( T \) is temperature (K), \( n \) is order of reaction, \( A \) is pre-exponential factor, \( R \) is molar gas constant, \( E_a \) is activation energy, \( \dot{\alpha} \) is heating rate.

The correlation factor \( r \) is computed using the least squares method for equations (1) and (2). Linear curves were drawn for values equal 0.5, 1, 1.5, 2, 2.5 and 3. The value of \( n \) which gave the best linear plot was chosen as the order parameter for the decomposition stage of interest and the heat of activation was calculated from its slope ¹⁰, ¹³.

The activation entropy \( \Delta S \), the activation enthalpy \( \Delta H \) and the free energy of activation \( \Delta G \) were calculated using the following equations:

\[
\Delta S = R \ln \left( \frac{Ah}{kT} \right)
\]

\[
\Delta H = E - RT
\]

\[
\Delta G = \Delta H - T\Delta S
\]

\( K \) and \( h \) are the Boltzman’s and Plank’s constants.

**DNA Interaction**

All the experiments involving the binding of complexes with CT-DNA were carried out in double distilled water and adjusted to pH 7.2. Absorption titration experiments were performed with fixed concentrations of the compounds (1×10⁻⁴ mol/L) with varying concentration of DNA (0–60 µmol/L). 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 ¹⁰.

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

where \([\text{DNA}]\) is the concentration of CT-DNA in base pairs and \(\varepsilon_a\), \(\varepsilon_f\) and \(\varepsilon_b\) are molar absorbitivities of the apparent, free and bound metal complex, respectively and \(K_b\) is the equilibrium binding constant. In the plots of \([\text{DNA}]/([\text{DNA}] - [\text{DNA}])\) versus \([\text{DNA}]\), \(K_b\) is given by the ratio of slope to the intercept.
Potentiometric study

All materials employed in the present investigation were of A.R. grade products. [amino succinic acid] \( \text{C}_4\text{H}_7\text{NO}_2 \) (Aspartic acid), [2-amino-propanoic acid] \( \text{C}_3\text{H}_7\text{NO}_2 \) (Alanine), [2-amino-3-imidazole propanoic acid] \( \text{C}_6\text{H}_9\text{N}_3\text{O}_2 \) (Histidine), \( \text{C}_4\text{H}_9\text{NO}_3 \) (Threonine), \( \text{C}_3\text{H}_7\text{NSO}_2 \) (Cysteine), and \( \text{C}_9\text{H}_{11}\text{NO}_2 \) (Phenylalanine), were purchased from Sigma-Aldrich Company and were used without purification. To account for preparation of metal ion amino acid solutions of exactly a 1:1 ratio, we also determined, by potentiometric pH titration, the molecular weight of these amino acids.

RESULTS AND DISCUSSIONS

Elemental analysis

The elemental analyses of the solid complexes of pantoprazole are recorded in Table (1). It is clear that the formula of the \( \text{Hg}^{2+} \) and \( \text{Zn}^{2+} \) complexes may be represented as \([\text{M(PNZ})(\text{H}_2\text{O})\text{Cl}]\text{H}_2\text{O}\), while \( \text{Cd}^{2+} \) complex is represented as \([\text{Cd(PNZ)}_2(\text{H}_2\text{O})_2]\text{H}_2\text{O}\).

Molar conductivity measurements

The complexes were dissolved in DMF and the molar conductivities of \(10^{-3}\) mol/L of their solutions at 25±2 °C were measured. Table (2) shows the molar conductance values of the complexes. It is concluded from the results that the complexes are found to have molar conductance values of 6–18.8 \( \Omega^{-1} \) cm\(^2\) mol\(^{-1}\) indicating that these complexes are non-electrolytes. It also, indicates the bonding of the chloride anion to the metal ions.

Electronic spectra measurements and magnetic susceptibility

The UV-Visible spectra of the ligand

Scheme 1: Fragmentation pattern for PNZ-complexes
and its complexes were recorded in DMF at room temperature. The electronic spectrum of the ligand showed only one intense band at 342 cm$^{-1}$, which was assigned to $n \rightarrow \pi^*$ transition of the C=N chromophore. The complexes of Zn(II), Hg(II) and Cd(II) are diamagnetic and have only one peak in the UV region. According to the empirical formula, Cd(II) complex has an octahedral geometry while both Zn(II) and Hg(II) have tetrahedral geometry.

**IR spectra and mode of bonding**

IR spectra for the ligand and its complexes are shown in Table (3). In the free ligand, the band at 1373 cm$^{-1}$ is assigned to $\nu$(C-N). After complexation, this band is shifted to higher frequency in the three complexes. Shifting of the $\nu$(C-N) vibration is due to C-N $\rightarrow$ M$^{2+}$ coordination. Characteristic band at 3498 cm$^{-1}$ is assigned to presence of water in the ligand structure; similarly presence of coordinated water is confirmed by the presence of band at 3372-3440 cm$^{-1}$. Coordinated water molecule is also noticed as a weak band at 815-820 cm$^{-1}$ due to rocking mode while band at 450-630 cm$^{-1}$ indicated the presence of water of crystallization. In addition, IR spectrum of the ligand revealed a sharp band at 1035 cm$^{-1}$ due to $\nu$(S=O) of side chain, which is shifted to higher frequency after complexation in all complexes, suggesting that oxygen atom of the side chain also contributes to the complexation. New bands appeared in the spectra of the complexes at 633-733 cm$^{-1}$, corresponding to O $\rightarrow$ M and 410-540 cm$^{-1}$ due to N $\rightarrow$ M vibrations which support the involvement of N and O atoms in complexation with metal ions under investigation. Characteristic strong band at 1486 cm$^{-1}$ is assignable to the stretching vibration of aromatic C=N group in benzimidazole ring that remained unchanged after complexation which confirmed the non-coordination of this group. Another band appears at the spectra of Hg(II) and Zn(II) complexes at 865-900 cm$^{-1}$ due to Cl$^-$ vibration which support the involvement of Cl atom in complexation of these chelates. all these discussions indicate that the ligands are bidentate and coordinating via O, N atoms.

**Mass spectra**

The mass spectral data did not show any of the required molecular ion peaks, but it could be deduced through studying of the assigned fragmentation peaks. All complexes have the same fragmentation, which have the main fragments [a], [b], [c], [d], [e], [f] at m/z= 180(4.5), 116(8.5), 90(10.2), 78(14), 50(50.3) and 64(36.2) (as fragments of ligand), which confirm the proposed structure of complexes. This was also confirmed by the appearance of a peak at 179.5(7.9), 127(2.8), 291.5(5.1) and 321(5.6) for fragments [g], [h], [i] and [j] respectively. The most prominent peaks were assigned as shown in the following fragmentation (Scheme.1).

**Thermal analysis**

The thermal behavior of the PNZ-Complexes was characterized using TGA/DTG method. The decomposition stages, temperature ranges and decomposition products as well as the found and calculated weight loss are given in Table (4). The activation energies and kinetic parameters were calculated using Coats-Redfern equation and the values are given in Table (5).

Cadmium complex undergo decomposition in four steps. Dehydration of the complex takes...
place in the 39-121°C range with DTG peak at 72°C associated with weight loss of 3.1% (Calcd. 3.86%). Coordination sphere decomposition for the cadmium complex is concerned with the elimination of the coordinated water and partial decomposition of the ligand. It takes place with DTG maxima at 233°C in the 120.4-302.9°C range. The ligand is continued to decompose at maxima 306.5 and 421.7 °C in the

Fig.1: Linearization curves of [Cd(PNz)(H$_2$O)$_2$] H$_2$O complex (first decomposition step)

Fig. 2: Linearization curves of [Hg(PNz)(H$_2$O)Cl]H$_2$O complex (first decomposition step)

Fig. 3: Linearization curves of [Hg(PNz)(H$_2$O)Cl] H$_2$O complex (second decomposition step)

Fig. 4: Linearization curves of [Hg(PNz)(H$_2$O)Cl] H$_2$O complex (third decomposition step)

Fig. 5: Linearization curves of [Zn(PNz)(H$_2$O)Cl] H$_2$O complex (first decomposition step)

Fig. 6: Linearization curves of [Zn(PNz)(H$_2$O)Cl] H$_2$O complex (second decomposition step)
range of 302.9-388.7 and 388.7-801 °C, respectively with no definite final product since the decomposition process is not complete at 800 °C.

TGA/DTG curves of the mercury complex are characterized by three decomposition steps. The first step takes place in the 35.4-256.7 °C range with DTG peaks at 38.2 and 228°C. Observed mass loss is 33.6% against calculated one of 33.1% corresponding evolution of crystallization water, coordinated water, chloride ion and partial decomposition of the ligand. The ligand is continued to decompose at 256.7 °C and end with final decomposition at 398.4 °C. The final decomposition is attributed to the evaporation of Hg metal with weight loss of 33.8% against calculated one of 33.6%. Carbon is remained as final product.

Thermal decomposition of zinc complex takes place in four stages. The first stage starts at 117.9-321.9 °C range. This was accompanied with mass loss of 30.3% (Calcd. 29.9%) with maximum DTG at 228.5 °C, which attributed to the volatilization of the hydrated water, coordinated water, chloride ion and partial decomposition of the ligand. The second decomposition stage takes place in the 322.9-425.5°C range with maxima at 410°C, which correspond decomposition of ligand. The third decomposition stage takes place at 426.4-506.4 °C range with maximum DTG at 491.6°C attributed to further decomposition of ligand with mass loss of 4.6% (Calcd. 4.4%). The final decomposition stage occurs in the range 506.9-797 °C with maxima at 603 and 781°C with no definite final product since the decomposition process is not complete at 800 °C.

From the TGA curves, the order n, activation energy E, and pre-exponential factor A of the different thermal decomposition steps of the complexes have been elucidated by the method of Coats-Redfern. Some examples of the linearization curves for the complexes, which were obtained, presented in Figs. (1-6). The values of correlation coefficients of linearization curves of the complexes and their reaction orders are given in Table (5). The activation energy E and enthalpy of activation ΔH of the three complexes are expected to increase proportional to decrease in their radii. The activation energy of the
tetrahedral $[\text{Zn(PNZ)}(\text{H}_2\text{O})\text{Cl}]\text{H}_2\text{O}$ complex is higher than $[\text{Hg(PNZ)}(\text{H}_2\text{O})\text{Cl}]\text{H}_2\text{O}$ complex.

The smaller the radius of metal ion, the easier the ligand approaches the central atom. As a result, metal-ligand interaction becomes stronger, the detachment of the link becomes more difficult and $E$ values increase\textsuperscript{15,16}. The negative values of the entropies in the decomposition reactions of the complexes Table (5) indicates that the reactions are slower than normal\textsuperscript{17-19} and the activated complexes have more ordered structure than the reactants\textsuperscript{20,21}.

Based on the above analytical data and physicochemical properties, the following structures are proposed in which the metal ion is coordinated through C-N, sulphonyl groups $\text{S=O}$, the coordinated water and the coordinated anion.

**DNA Interaction**

UV-Vis Absorption spectra (Figs. 7,8) were obtained by titration of $(1 \times 10^{-5} - 1 \times 10^{-4} \text{ M})$ complex solution with increasing concentration of DNA. In absence of DNA, the spectrum is characterized by a peak at 293 nm. The absorbance of the peak increased gradually as DNA concentration increased.

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 $[\text{DNA}/\text{complex}]$ (Fig. 9). Obviously, these spectral characteristics suggest that all the complexes interact with DNA via electrostatically with the base pairs of DNA\textsuperscript{22}.

### Table 1: Analytical data and magnetic moments of the PNZ and its complexes

<table>
<thead>
<tr>
<th>Compound</th>
<th>Chemical formula</th>
<th>C (%)</th>
<th>H (%)</th>
<th>N (%)</th>
<th>S (%)</th>
<th>M (%)</th>
<th>$\mu_{\text{eff.}}$ (298°K) (B.M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNZ</td>
<td>$\text{C}<em>{16}\text{H}</em>{14}\text{F}<em>{2}\text{N}</em>{3}\text{O}<em>{4}\text{S}\cdot\text{Na}\cdot1.5\text{H}</em>{2}\text{O}$</td>
<td>43.2</td>
<td>3.0</td>
<td>9.4</td>
<td>6.5</td>
<td>—</td>
<td>Diamagnetic</td>
</tr>
<tr>
<td>Zn-PNZ</td>
<td>$[\text{Zn(PNZ)}(\text{H}_2\text{O})\text{Cl}]\text{H}_2\text{O}$</td>
<td>36.3</td>
<td>3.2</td>
<td>8.0</td>
<td>5.8</td>
<td>12.1</td>
<td>Diamagnetic</td>
</tr>
<tr>
<td>Cd-PNZ</td>
<td>$[\text{Cd(PNZ)}(\text{H}_2\text{O})_2]\text{H}_2\text{O}$</td>
<td>40.7</td>
<td>3.4</td>
<td>8.9</td>
<td>6.5</td>
<td>11.8</td>
<td>Diamagnetic</td>
</tr>
<tr>
<td>Hg-PNZ</td>
<td>$[\text{Hg(PNZ)}(\text{H}_2\text{O})\text{Cl}]\text{H}_2\text{O}$</td>
<td>28.5</td>
<td>2.6</td>
<td>6.1</td>
<td>4.5</td>
<td>29.9</td>
<td>Diamagnetic</td>
</tr>
</tbody>
</table>

### Table 2: Physical data of the PNZ ligand and its complexes

<table>
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<tr>
<th>Compound</th>
<th>Chemical formula</th>
<th>M. Wt</th>
<th>% Yield</th>
<th>Color</th>
<th>$\Lambda_m$ (Ω$^{-1}$cm$^2$mol$^{-1}$)</th>
<th>Melting Point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNZ</td>
<td>$\text{C}<em>{16}\text{H}</em>{14}\text{F}<em>{2}\text{N}</em>{3}\text{O}<em>{4}\text{S}\cdot\text{Na}\cdot1.5\text{H}</em>{2}\text{O}$</td>
<td>432.38</td>
<td>82</td>
<td>Off white</td>
<td>—</td>
<td>137</td>
</tr>
<tr>
<td>Zn-PNZ</td>
<td>$[\text{Zn(PNZ)}(\text{H}_2\text{O})\text{Cl}]\text{H}_2\text{O}$</td>
<td>519.26</td>
<td>70</td>
<td>Off white</td>
<td>6</td>
<td>170</td>
</tr>
<tr>
<td>Cd-PNZ</td>
<td>$[\text{Cd(PNZ)}(\text{H}_2\text{O})_2]\text{H}_2\text{O}$</td>
<td>931.16</td>
<td>73</td>
<td>Faint brown</td>
<td>5.4</td>
<td>160</td>
</tr>
<tr>
<td>Hg-PNZ</td>
<td>$[\text{Hg(PNZ)}(\text{H}_2\text{O})\text{Cl}]\text{H}_2\text{O}$</td>
<td>654.47</td>
<td>62</td>
<td>Faint red</td>
<td>7</td>
<td>155</td>
</tr>
</tbody>
</table>
In order to evaluate quantitatively the DNA-binding strength, the intrinsic DNA-binding constants, $K_b$ of the complexes have been estimated to be in the range $[0.121–0.382 \text{ mol/L}]$ and is are listed in the Table (6).

**pH-metric Measurements**

The formation of various 1:1:1 ternary complex species are inferred from the potentiometric-pH titration curves. Initial estimates of the stability constants of the resulting species and the acid dissociation constants of pantoprazole, and amino acids have been refined with the HYPERQUAD computer program. The quality of the fit during this refinement was judged by the values of the sample standard deviations and the goodness of fit $\chi^2$ (Pearson's Test). At $\sigma_E = 0.1 \text{ mV (0.001 pH error)}$ and $\sigma_\gamma = 0.005 \text{ cm}^3$, the values of $S$ in different sets of titrations were between 1.0 and 1.7 and $\chi^2$ was between 12.0 and 13.0. The scatter of residuals ($E_{\text{calc}}-E_{\text{obs}}$) versus pH reasonably random, without any significant systematic trends, thus indicating a good fit of the experimental data of the expected model systems under our experimental conditions. Furthermore, the formation constants values of the different 1:1 metal ion- amino acids have been determined under identical conditions. This is made with the aim to compare the stability of the formed 1:1:1 ternary complex with of the corresponding 1:1 binary metal complexes.

All the initial estimates of the formation constants of the different binary and ternary complexes formed in the present investigation have been refined using HYPERQUAD computer program.

$$K = \frac{[M_{(PNZ)}(AA)]}{[M]_q[PNZ]^p[AA]^r[H]^s}$$

Which refers to the addition of amino acids to the binary complex $M_q(PNZ)_p$. The overall complexation reaction involving protonation is,$$
pM + q \text{PNZ} + r \text{AA} + sH \rightarrow M_{(PNZ)}q(\text{AA})r(H)s$$

Of the 20 $\alpha$-amino acids that commonly occur in proteins; about half contain side chain donor atoms that are at least potentially capable of forming a chelate ring with metal ion bound at the $\alpha$-amino nitrogen. If the $\alpha$-amino and $\alpha$-carboxylate groups that occur in the free amino acids also chelate the metal ion, then two chelate rings will be formed.

The order of stability constants of $M + \text{PNZ} + \text{Alanine}$ is $\text{Cd} > \text{Zn}$.

Phenylalanine, as its name indicates, contains a phenyl ring attached in place of one of the
Table 3: IR spectral data of the PNZ and its complexes (cm⁻¹)

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<tbody>
<tr>
<td>Ligand</td>
<td>3498</td>
<td>3376 (assym)</td>
<td>1590</td>
<td>1486</td>
<td>1373</td>
<td>1298</td>
<td>1116</td>
<td>1035</td>
<td>—</td>
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<tr>
<td></td>
<td></td>
<td>3190 (sym)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1166 (sym)</td>
<td>1172 (sym)</td>
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<tr>
<td>Zn-Complex</td>
<td>3408</td>
<td>3088 (assym)</td>
<td>1585</td>
<td>1484</td>
<td>1423</td>
<td>1299</td>
<td>1119</td>
<td>1064</td>
<td>817</td>
<td>865</td>
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<tr>
<td>Cd-Complex</td>
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<td>3095 (assym)</td>
<td>1587</td>
<td>1490</td>
<td>1408</td>
<td>1303</td>
<td>1121</td>
<td>1066</td>
<td>820</td>
<td>—</td>
<td>410</td>
<td>683</td>
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<tr>
<td></td>
<td></td>
<td>2990 (sym)</td>
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<tr>
<td>Hg-Complex</td>
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<td>3079 (assym)</td>
<td>1619</td>
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<td>1122</td>
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<td>930</td>
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<tr>
<td>Compound</td>
<td>Temp. range °C</td>
<td>DTG °C</td>
<td>Mass loss% Found</td>
<td>Process</td>
<td>Product</td>
<td>Residue % and type Found (Calcd.)</td>
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<tr>
<td>[Zn(PNZ)(H$_2$O)Cl]$H_2$O</td>
<td>117.96-321.99</td>
<td>228.53</td>
<td>30.27</td>
<td>Dehydration+Coordination sphere partial decomposition</td>
<td>2H$_2$O + Cl + 0.22</td>
<td>Not complete</td>
<td></td>
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<tr>
<td></td>
<td>322.96-425.49</td>
<td>410</td>
<td>7.09</td>
<td>Ligand partial decomposition</td>
<td>0.1 Ligand</td>
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<tr>
<td></td>
<td>426.41-506.41</td>
<td>491.64</td>
<td>4.646</td>
<td>Ligand partial decomposition</td>
<td>0.06 Ligand</td>
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<td></td>
<td>506.9-797.41</td>
<td>603.34</td>
<td>27.49</td>
<td>Ligand partial decomposition</td>
<td>0.37 Ligand</td>
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<tr>
<td>[Cd(PNZ)$_2$(H$_2$O)$_2$]$H_2$O</td>
<td>39.22-121.1</td>
<td>72</td>
<td>3.1</td>
<td>Dehydration+Coordination sphere partial decomposition</td>
<td>2H$_2$O</td>
<td>Not complete</td>
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<tr>
<td></td>
<td>121.1-302.91</td>
<td>233.1</td>
<td>32.26</td>
<td>Ligand partial decomposition</td>
<td>H$_2$O + 0.42</td>
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<tr>
<td></td>
<td>302.91-388.77</td>
<td>306.51</td>
<td>5.94</td>
<td>Ligand partial decomposition</td>
<td>0.15 Ligand</td>
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<tr>
<td></td>
<td>388.77-801.09</td>
<td>421.67</td>
<td>20.93</td>
<td>Ligand partial decomposition</td>
<td>0.43 Ligand</td>
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<tr>
<td>[Hg(PNZ)(H$_2$O)Cl]$H_2$O</td>
<td>35.36-256.77</td>
<td>38.24</td>
<td>33.56</td>
<td>Dehydration+Coordination sphere partial decomposition</td>
<td>2H$_2$O + Cl</td>
<td>1.83 Carbon (1.75)</td>
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<tr>
<td></td>
<td>256.77-398.45</td>
<td>347.78</td>
<td>31.45</td>
<td>Final decomposition</td>
<td>0.54 Ligand</td>
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<td></td>
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<tr>
<td></td>
<td>398.45-680.02</td>
<td>588.44</td>
<td>33.814</td>
<td>Final decomposition</td>
<td>0.05 Ligand + Hg</td>
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</table>
hydrogen of alanine. The order of stability constants of M + PNZ + Phenylalanine is Zn > Cd.

Aspartic acid contains two acidic side chains. This amino acid is often called aspirate to emphasize that its side chain is usually negatively charged at physiological pH. The order of stability constants of M + PNZ + Aspartic acid is Cd > Zn.

The amino acid histidine in its dicatonic form contains four acidic protons. As the pH increased the successive pKa values for potone removal are carboxylic acid imidazolium. –N(3)-H, side chain ammonium imidazole –N(1)-H. The imidazole (1)-NH is very weakly acidic (pKa = 14.4) and thus it does not dissociate in the measureable pH range. It has been argued strongly that metal ion binding on the aromatic imidazole ring occurs only at pyridine nitrogen, as the energy required for binding to occur at a pyrrole nitrogen is prohibitive. The order of stability constants of M + PNZ + Histidine is Zn > Cd.

Threonine contains aliphatic hydroxyl group. It can be thought of as hydroxylated version of valine with hydroxyl group in place of one of the valine methyl groups. The hydroxyl groups of threonine make them much more hydrophilic and reactive than valine. As the alcoholic hydroxy group is so weakly acidic (pKa> 14) that it does not undergo dissociation. The order of stability constants of M + PNZ + Threonine is Zn > Cd.

Cystein contains three dissociable protons, the last two of these deprotonations, those of the ammonium and the thiol groups take place

### Table 5: Kinetic parameters for the first decomposition step of the PNZ-complexes

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Step</th>
<th>E</th>
<th>A</th>
<th>n</th>
<th>R</th>
<th>∆H</th>
<th>∆G</th>
<th>∆S</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Zn(PNZ)(H₂O)Cl]H₂O</td>
<td>1</td>
<td>324.2186</td>
<td>1.03E+16</td>
<td>3</td>
<td>0.9977</td>
<td>320.0488</td>
<td>291.3221</td>
<td>57.2781</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>92.07861</td>
<td>3432.793</td>
<td>1.5</td>
<td>0.8861</td>
<td>83.3123</td>
<td>281.2472</td>
<td>-187.723</td>
</tr>
<tr>
<td>[Cd(PNZ)₂(H₂O)₂]H₂O</td>
<td>1</td>
<td>48.86083</td>
<td>859168.6</td>
<td>1.5</td>
<td>0.9717</td>
<td>44.6531</td>
<td>113.3337</td>
<td>-135.706</td>
</tr>
<tr>
<td>[Hg(PNZ)(H₂O)Cl]H₂O</td>
<td>1</td>
<td>61.81923</td>
<td>3828334</td>
<td>1</td>
<td>0.9772</td>
<td>57.65342</td>
<td>119.3837</td>
<td>-123.199</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>26.67542</td>
<td>3605656</td>
<td>1</td>
<td>0.9651</td>
<td>21.51425</td>
<td>87.52501</td>
<td>-106.335</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>189.056</td>
<td>57501102</td>
<td>3</td>
<td>0.9273</td>
<td>181.894</td>
<td>272.4992</td>
<td>-105.179</td>
</tr>
</tbody>
</table>

E, ∆H, ∆G in KJ.mol⁻¹
∆S in J.mol⁻¹.k⁻¹
A in S⁻¹

### Table 6: The Binding constant of complexes with DNA

<table>
<thead>
<tr>
<th>Complex</th>
<th>Binding constant (Kb)</th>
<th>R</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hg-PNZ</td>
<td>0.121</td>
<td>0.9596</td>
<td>0.1904</td>
</tr>
<tr>
<td>Cd-PNZ</td>
<td>0.137</td>
<td>0.9685</td>
<td>0.0769</td>
</tr>
</tbody>
</table>

R = Correlation coefficients
SD = Standard deviations

### Table 7: Formation constants for the binary M + amino acids (AA) and M-PNZ ligand complexes at 25 ± 0.1°C and I = 0.1 mol.L⁻¹ KNO₃

<table>
<thead>
<tr>
<th>Metal Ions</th>
<th>logK₅₉(Ala)</th>
<th>logK₅₉(Phe)</th>
<th>logK₅₉(Asp)</th>
<th>logK₅₉(Thr)</th>
<th>logK₅₉(His)</th>
<th>logK₅₉(Cys)</th>
<th>logK₅₉(PNZ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cd (II)</td>
<td>4.12±0.02</td>
<td>4.11±0.03</td>
<td>5.86±0.02</td>
<td>4.16±0.02</td>
<td>3.98±0.04</td>
<td>8.89±0.02</td>
<td>6.21±0.03</td>
</tr>
<tr>
<td>Zn (II)</td>
<td>5.81±0.02</td>
<td>4.96±0.02</td>
<td>6.97±0.02</td>
<td>4.9±0.02</td>
<td>4.94±0.02</td>
<td>8.45±0.03</td>
<td>7.15±0.02</td>
</tr>
</tbody>
</table>
Table 8: Formation Constants for $M + \text{Pantoprazole (PNZ)} + \text{Amino Acids (AA)}$ 1:1:1 Ternary Complexes at $25.0 \pm 0.1^\circ\text{C}$ and $I = 0.1 \text{mol.L}^{-1}$

<table>
<thead>
<tr>
<th>Metal ion</th>
<th>$\log_{M(\text{Ala})(PNZ)}$</th>
<th>$\log_{M(\text{Phe})(PNZ)}$</th>
<th>$\log_{M(\text{Asp})(PNZ)}$</th>
<th>$\log_{M(\text{Thr})(PNZ)}$</th>
<th>$\log_{M(\text{His})(PNZ)}$</th>
<th>$\log_{M(\text{Cys})(PNZ)}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cd (II)</td>
<td>15.47±0.02</td>
<td>2.18±0.02</td>
<td>19.11±0.02</td>
<td>1.96±0.02</td>
<td>1.56±0.02</td>
<td>19.58±0.02</td>
</tr>
<tr>
<td>Zn (II)</td>
<td>3.91±0.02</td>
<td>3.59±0.02</td>
<td>17.83±0.03</td>
<td>3.91±0.02</td>
<td>2.89±0.02</td>
<td>18.29±0.03</td>
</tr>
</tbody>
</table>

in overlapping processes. Cystein is typical ambidentate ligand, the possible metal binding sites are different in nature. COO$^-$ is rather hard, $S^-$ is fairly soft and NH$_2^+$ groups have relatively high pKa values, and the sulfur atoms behaves as bridging ligands. Thus a great variety of metal complexes may be formed, including protonated and polynuclear complexes with monodentate and different bidentate and tridentate bonding modes. The order of stability constants of $M + \text{PNZ} + \text{Cystein}$ is $\text{Cd} > \text{Zn}$.

The observed different orders may be attributed to different types of interactions depending on metal ion different geometrical behavior during the formation of binary and ternary complexes in solution.

CONCLUSION

From elemental analysis it can be concluded that the formula of the Zn$^{2+}$ and Hg$^{2+}$complexes can be represented as $[M(\text{PNZ})(\text{H}_2\text{O})\text{Cl}]\text{H}_2\text{O}$,while Cd$^{2+}$ represented as $[\text{Cd}(\text{PNZ})_2(\text{H}_2\text{O})_2]\text{H}_2\text{O}$, the molar conductance for the complexes were measured in DMF and showed that PNZ-complexes are non-electrolytes. From magnetic susceptibility and UV spectroscopy it's found that Zn-PNZ, Cd-PNZ and Hg-PNZ complexes are diamagnetic where Zn and Hg have tetrahedral geometry, while Cd have octahedral geometry. IR spectra for ligand and its complexes showed that the pantoprazole act as bidentate ligand which form complexes with metals through C-N and S=O groups, also the spectra showed new peaks due to M-N and M-O which confirmed the involvement of N and O atoms in complexation with metal ions. The mass spectral data showed that three complexes formed with molar ratio $M:L = 1:2$. Thermal analysis showed the different decomposition stage of the metal complexes, which appear the presence of water of hydration in all complexes. The activation energy $E$ and enthalpy of activation $\Delta H$ of the complexes are expected to increase proportional to decrease in their radii.

REFERENCES

5. Tiwari, C. R. JERAD 2012, 6, No. 3A.