

Scientific paper

# Complexation Equilibria and Coordination Aspects of Zn(II) Complexes Contain 2–Aminobenzamide and some Bioactive Amino acid Mixed Ligands: pH–metric, Spectroscopic and Thermodynamic Studies

Jeyaprakash Dharmaraja,<sup>1</sup> Paramasivam Subbaraj,<sup>2</sup>  
Thirugnanasamy Esakkidurai,<sup>2,\*</sup> Sutha Shobana<sup>3</sup> and Saravanan Raji<sup>4</sup>

<sup>1</sup> Division of Chemistry, Faculty of Science and Humanities, Sree Sowdambika College of Engineering, Chettikurichi, Aruppukottai – 626 134, Virudhunagar District, Tamil Nadu, India.

<sup>2</sup> Department of Chemistry, Devanga Arts College (Autonomous), Aruppukottai – 626 101, Virudhunagar District, Tamil Nadu, India.

<sup>3</sup> Department of Chemistry, Rajas Institute of Technology for Women, Ozhuginasery, Nagercoil–629 001, Kanyakumari District, Tamil Nadu, India.

<sup>4</sup> Department of Chemistry, Islamiah College (Autonomous), New Town, Vaniyambadi–632 752, Tamil Nadu, India.

\* Corresponding author: E-mail: tesakkidurai.dac@gmail.com  
Telephone: +91 94420 56667, Fax: +91 4566 240324.

Received: 04-04-2014

## Abstract

Mixed ligand complexation of 2–aminobenzamide (2AB) as ligand [L] with Zn(II) in the presence of some bio–relevant amino acid constituents like glycine (gly), L–alanine (ala), L–valine (val) and L–phenylalanine (phe) as ligand [B] have been investigated using pH–metric measurements with a combined pH electrode at different temperatures (300, 310, 320 and 330 ± 0.1 K) in 50% (v/v) ethanol–water mixture containing  $I = 0.15$  M NaClO<sub>4</sub> as supporting electrolyte. Computer assisted analysis of the experimental titration data showed the presence of ZnLB and ZnLB<sub>2</sub> species as mixed ligand complexes in addition to various binary species. In ZnLB/ZnLB<sub>2</sub> species, both primary and secondary ligands act as bidentate to form a stable six, five membered chelate ring. The calculated stabilization parameter  $\Delta \log K$ ,  $\log X$ ,  $\log X'$  and % R.S. values clearly show the mixed ligand complexes have higher stabilities than their binary. Thermodynamic parameters  $\Delta G$ ,  $\Delta H$  and  $\Delta S$  have been derived from the temperature dependence of the stability constants. The complexation behavior of ZnLB species has been studied by means of electronic spectra. The percentage distribution of various binary and mixed ligand species of each type of the complexes in solution depending on pH and the ratio of Zn(II) to 2–aminobenzamide/amino acid of the systems.

**Keywords:** 2–Aminobenzamide; amino acids; mixed ligand complexes; stability constants; thermodynamic study.

## 1. Introduction

In recent year, much attention has been paid to investigate the formation of mixed ligand complexes derived from the interaction of bioactive ligands or molecules with transition metal ions which showed numerous physico–chemicals, biological and pharmaceutical significance of our living systems.<sup>1–3</sup> The bioactive ligands

containing amide moieties are the basic structural constituent in peptides and protein synthesis. Benzamide and its derivatives like sultopride and tiapride are used as a better antipsychotic, anti–emetic, anti–dyskinetic, anti–malarial and anti–hypertensive agents in clinical and therapeutic fields.<sup>4,5</sup> 2–Aminobenzamide (Antranilamide; 2AB) and its derivatives are frequently used as a fluorescent reagent for the analysis of protein glycosylation<sup>6</sup> and

they act as selective serine protease factor  $X_a$  ( $FX_a$ ) inhibitors for blood coagulation cascade. Zinc is recognized as the second most abundant trace element for plants, animals and human.<sup>7</sup> It is highly present in the retina and essential for the growth and repair of tissues like ligament, teeth, bone, nail, skin and hair in our human body.<sup>7,8</sup> Zinc is an essential co-factor for several enzymes controlling many cellular processes including DNA synthesis, growth, reproduction, behavioural response and development.<sup>9</sup> Amino acids are the fundamental structural units of proteins, peptide hormones and antibiotics. The mixed ligand complexes of amino acids are involved in the exchange and transport mechanisms.<sup>10</sup> In a sequel of continuation,<sup>11–14</sup> the main goal of the present work is to find the solution equilibria of the mixed ligand complex systems of Zn(II) with 2-aminobenzamide (2AB) as a primary ligand(L) and some biologically important amino acid *viz.*, glycine (gly), L-alanine (ala), L-valine (val) and L-phenylalanine (phe) as secondary ligands(B) (Figure 1) were investigated by pH-metrically in 0.15 M NaClO<sub>4</sub> medium at different temperatures (300, 310, 320 and 330 ± 0.1 K) in 50% (v/v) ethanol–water mixture. From this study, the corresponding thermodynamic parameters of  $\Delta G$ ,  $\Delta H$  and  $\Delta S$  was evaluated. In addition, the coordination environment and the stability constants of mixed ligand complexes formed in solutions have been determined using spectrophotometrically at different pH in 50% (v/v) ethanol–water medium.

## 2. Experimental and Methods

### 2.1. Materials

All the chemicals and ligands (Figure 1) used in this present work were analytical grade purity of Sigma Aldrich and Fluka (Puriss) products and were used without further purification. Carbonate free, sodium hydroxide (0.3 M) solution was prepared from a Titrisol solution (Merck) and standardized against standard potassium hydrogen phthalate solution by means of the appropriate Gran titrations.<sup>15</sup> The ionic strength of each solution was adjusted to 0.15 M by the addition of NaClO<sub>4</sub> as supporting electrolyte and other solutions were prepared

and estimated as described earlier.<sup>11,12</sup> Double distilled CO<sub>2</sub> free water with specific conductance equal to (1.81 ± 0.1  $\Lambda^{-1} \text{ cm}^{-1}$ ) was used for the preparation of all the solutions.

### 2.2. pH-metric and Spectrophotometric Equilibrium Measurements

The pH titrations were carried out in a digital pH meter (Elico LI System 127) with a combined glass and calomel electrodes (accuracy ± 0.01 pH unit) under an N<sub>2</sub> atmosphere (free from oxygen and CO<sub>2</sub>). The instrument was calibrated using standard buffer solutions.<sup>16</sup> The temperature of the sample solutions at 300, 310, 320 and 330 ± 0.1 K was maintained by circulating water from a double wall glass jacketed titration cell (100 mL capacity) connected to a constant temperature thermostat of Toshniwal GL 15.01 constant temperature bath. All the titration of the titled systems was performed in 50 mL portions of solution containing low concentrations [ $3 \times 10^{-3}$  M] of zinc(II) perchlorate, 2AB(L) and amino acid(B) ligands in 1:1:1 and 1:1:2 ratios at constant ionic strength ( $I = 0.15$  M) with a known volume of standard carbonate free sodium hydroxide solution. Oxygen free nitrogen gas was bubbled through the solution before and during the titrations. All the calculations involved in this study within the pH range 2.5–9.0 (51–59 number of observations; volume of base/pH) are given in Table 1. By increasing the pH level (> 9.0), the titled systems undergo hydroxylation and form [Zn(OH)<sub>2</sub>] as a precipitate and thus, no calculations have been implemented beyond this point. This pH-metric data were computed with the aid of SCOGS computer program<sup>17</sup> to determine the stability constants. Under the present experimental conditions, the pH-meter readings in 50% (v/v) ethanol–water medium were corrected by Van Uitert and Haas relation.<sup>18</sup> The ionic product of water ( $K_w$ ) was calculated based on the measurement of [H<sup>+</sup>] and [H<sup>-</sup>] in 50% (v/v) ethanol–water medium at constant ionic strength ( $I = 0.15$  M NaClO<sub>4</sub>) and the obtained ( $K_w = 14.42 \pm 0.03$  at 300 K) value is well agreed with the reported value.<sup>19,20</sup> Spectrophotometric determinations of Zn-LB complexes at each pH level was performed on a Hitachi U-2000 double beam spectrophotometer (cell length,

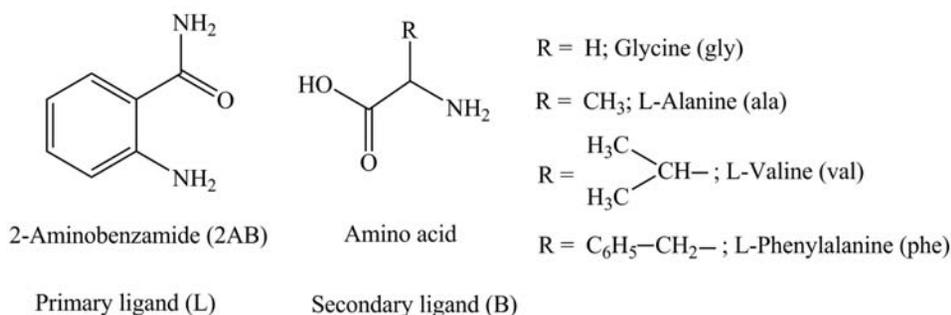


Figure 1. Structure of primary and secondary ligands.

**Table 1.** Experimental details of potentiometric measurements at different temperature in  $I = 0.15$  M ( $\text{NaClO}_4$ ) medium.

Systems	Temp (K)	Concentrations <sup>a</sup> ( $\times 10^{-3}$ M)				pH range	$n^a$
		$C_M$	$C_L$	$C_B$	$C_H$		
Zn(II)–2AB–gly	300						
	310	3.032	2.978	2.992	1.141	2.5–8.4	58
	320	3.003	3.012	5.997	1.140	2.9–8.2	56
	330						
Zn(II)–2AB–ala	300						
	310	3.008	3.005	3.015	1.141	2.7–8.1	57
	320	3.029	3.029	6.026	1.141	3.0–8.4	54
	330						
Zn(II)–2AB–val	300						
	310	2.998	2.987	3.012	1.140	3.0–8.0	59
	320	3.004	3.021	5.989	1.140	3.2–8.3	55
	330						
Zn(II)–2AB–phe	300						
	310	2.991	3.019	3.029	1.140	2.8–8.3	57
	320	3.015	3.036	6.019	1.141	3.3–8.5	51
	330						

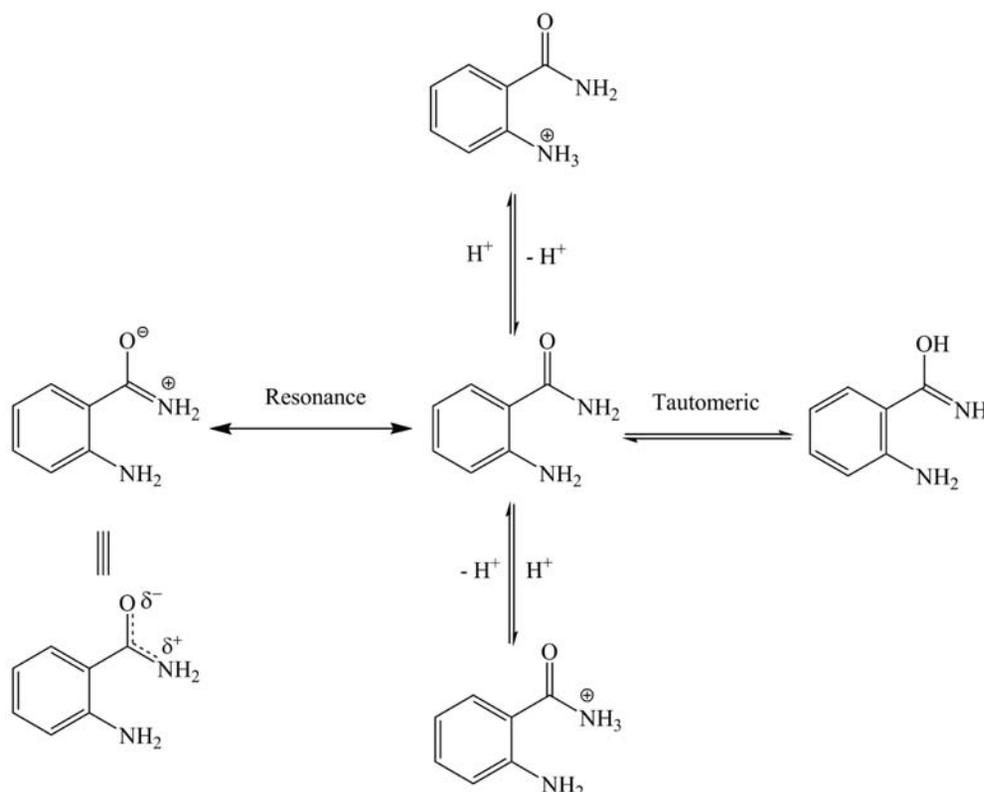
<sup>a</sup>Initial concentration of metal ( $C_{Zn}$ ), primary ligand ( $C_L$ ), secondary ligand ( $C_B$ ), perchloric acid ( $C_H$ ) and number of experimental observations ( $n$ ) at different temperatures with  $I = 0.15$  M  $\text{NaClO}_4$

1 cm) in the range of 200–1100 nm at 310 K. Multiple titrations were carried out for each system and the formation of various species distribution curves of the metal speciation in solution were calculated by HySS program<sup>21</sup> by using the stability constant values.

### 3. Results and Discussion

#### 3.1. Stability and Structure of Binary Species

The protonation and stability constants of 2-aminobenzamide and their binary Zn(II)–2AB(L) complex has



**Scheme.** Protonation and deprotonation sites in 2-aminobenzamide(L).

**Table 2.** Stability constant values for the parent binary Zn(II) with 2AB(L), gly, ala, val and phe(B) systems in 50% (v/v) ethanol–water mixture

Parameters	log $\beta$ value (at 300 K)					log $\beta$ value (at 310 K)				
	2AB <sup>a</sup>	gly	ala	val	phe	2AB <sup>a</sup>	gly	ala	val	phe
log $\beta_{HB}$	-2.57(4)	9.77(3)	10.07(4)	10.11(3)	9.49(5)	-2.41(3)	9.57(2)	9.72(3)	9.84(3)	9.22(4)
log $\beta_{H_2B}$	2.83(5)	12.05(5)	12.38(5)	12.66(6)	11.95(7)	2.75(4)	11.74(4)	12.15(5)	12.45(4)	11.68(6)
log $\beta_{ZnB}$	3.84(3)	4.96(4)	4.89(5)	4.59(5)	4.46(5)	3.73(4)	4.84(5)	4.76(4)	4.46(5)	4.33(6)
log $\beta_{ZnB_2}$	7.16(5)	9.09(4)	8.94(6)	8.42(4)	8.18(5)	7.01(6)	8.97(6)	8.80(6)	8.27(7)	8.05(8)
log $K_{ZnB}^{ZnB}$	3.32	4.13	4.05	3.83	3.72	3.28	4.13	4.04	3.81	3.72
$\Delta R$	–	–	-0.07	-0.37	-0.50	–	–	-0.08	-0.38	-0.51
log $K_1/\log K_2$	0.54	0.55	0.55	0.55	0.55	0.53	0.54	0.54	0.54	0.54

<sup>a</sup> 2AB become primary ligand(L) in the mixed ligand systems.

been determined by pH–metrically in 50% (v/v) ethanol–water medium at different temperatures using the constant ionic strength ( $I = 0.15$  M NaClO<sub>4</sub>) and the stability constant values are given in Table 2. The primary 2AB(L) ligand offers two well separated buffer regions, due to successive deprotonation of NH<sub>3</sub><sup>+</sup> and –CONH<sub>2</sub>–moieties (Scheme).<sup>22</sup> In general, the thermodynamically preferred sites for the protonation of amide moieties in acidic medium occur only at amido–O atom<sup>23</sup> and the chelation of amido–N atom takes place only at very high basic medium.<sup>24,25</sup> The complex formation of Zn(II) with 2AB(L) ligand generally starts the pH above 3.0 to 9.0 since increasing the pH (> 9.0) level leads to form [Zn(OH)<sub>2</sub>] precipitate. The computer analysis of the pH–metric data shows HA, H<sub>2</sub>A, ZnL and ZnL<sub>2</sub> species (Table 2). Under the experimental conditions, the first  $pK_a$  value of -2.41 (at 310 K) for 2AB(L) corresponding to amido–O atom which is very close to the reported (-2.67) value<sup>26</sup> and the second protonation constant value of 2.67 corresponding to amino–N atom which is as lower as compared to the parent aniline (4.63) due to the presence of electron withdrawing amide (–CONH<sub>2</sub>–) moiety present in 2–aminobenzamide(L).<sup>27</sup> No precipitate was observed in the titration vessel which indicating that the possibility of [Zn(OH)<sub>2</sub>] formation can be excluded. From Table 2, the log $\beta_{ZnL}$  and log $\beta_{ZnL_2}$  values are 3.73 and 7.01 respectively

at 310 K and these values suggest that 2–aminobenzamide(L) acts as bidentate *i.e.*, it chelates with Zn(II) ion through amino–N and amido–O atoms to form a stable six membered chelate ring. In ZnL<sub>2</sub> species, both the ligands bind the Zn(II) ion in a bidentate manner forming two 6–membered chelate rings with the distorted octahedral environment and the remaining position is satisfied with solvent water molecules. This type of binding has already been established in [M(II)–(2AB)<sub>2</sub>–Cl<sub>2</sub>] complexes in their solid state.<sup>28</sup>

The protonation and stability constant values (Table 2) of amino acids were redetermined under the present experimental conditions and the values agree well with the reported values.<sup>29</sup> The amino acids bind Zn(II) ion in a bidentate manner through carboxylato–O and amino–N atoms forming a stable 5–membered chelate ring. Small differences are within the limit of our experimental errors which is due to the variation in experimental conditions like ionic strength ( $I$ ), temperature effect, *etc.* Moreover, the stability constant values (Table 2) show that ZnB complexes are more stable than ZnL. The complex formation of Zn(II) with 2AB(L) is accompanied by the sharp change of colour in the solution. In 1:2 solution of Zn(II) and 2AB gives pale yellow coloration ( $\lambda_{max} = 380$  nm) at pH 6.5 and the  $\lambda_{max}$  values doesn't shift with the change of pH of the solution. Formation of ZnL and ZnL<sub>2</sub> complexes

**Table 3.** Stability constant and stabilization effects of mixed ligand systems in 50% (v/v) ethanol–water mixture at different temperatures

Parameters	Ligand (B) (at 300 K)				Ligand (B) (at 310 K)			
	gly	ala	val	phe	gly	ala	val	phe
og $\beta_{ZnLB}$	9.13(3)	8.97(4)	8.67(6)	8.52(7)	8.95(4)	8.79(5)	8.53(6)	8.39(8)
log $\beta_{ZnLB_2}$	13.36(4)	13.18(5)	–	–	13.19(6)	12.99(6)	–	–
log $K_{ZnLB}^{ZnLB}$	5.29	5.13	4.83	4.68	5.22	5.06	4.80	4.66
log $K_{ZnLB}^{ZnLB}$	4.17	4.08	4.08	4.06	4.11	4.03	4.07	4.06
log $K_{ZnL}^{ZnL}$	9.52	9.34	–	–	9.46	9.26	–	–
log $K_{ZnLB_2}^{ZnLB_2}$	4.27	4.24	–	–	4.22	4.19	–	–
log $K_{ZnLB_2}^{ZnLB_2}$	4.23	4.21	–	–	4.24	4.20	–	–
$\Delta \log K_{ZnLB}$	0.33	0.24	0.24	0.22	0.38	0.30	0.34	0.33
$\Delta \log K_{ZnLB_2}$	0.43	0.40	–	–	0.49	0.46	–	–
log $X$	2.01	1.84	1.76	1.70	1.92	1.77	1.78	1.72
log $X'$	0.85	0.76	0.76	0.74	0.83	0.75	0.79	0.78
%R.S.	6.65	4.91	5.23	4.93	7.85	6.30	7.62	7.62

at different temperatures in  $I = 0.15$  M NaClO<sub>4</sub> medium [error limit:  $\pm (0.02-0.05)$ ]. Standard deviations are given in parentheses.

2AB <sup>a</sup>	log $\beta$ value (at 320 K)				2AB <sup>a</sup>	log $\beta$ value (at 330 K)			
	gly	ala	val	phe		gly	ala	val	phe
-2.23(5)	9.28(3)	9.48(5)	9.65(4)	8.96(6)	-2.05(6)	8.97(4)	9.30(6)	9.42(5)	8.78(4)
2.69(6)	11.48(5)	11.92(6)	12.17(7)	11.48(8)	2.62(8)	11.21(6)	11.68(8)	11.96(7)	11.27(6)
3.63(6)	4.73(4)	4.65(6)	4.36(6)	4.24(7)	3.55(7)	4.61(5)	4.56(6)	4.23(7)	4.13(8)
6.87(7)	8.82(5)	8.68(8)	8.14(8)	7.92(9)	6.75(9)	8.69(7)	8.58(8)	8.04(9)	7.81(8)
3.24	4.09	4.03	3.78	3.68	3.20	4.08	4.02	3.81	3.68
–	–	-0.08	-0.37	-0.49	–	–	-0.05	-0.38	-0.48
0.53	0.54	0.54	0.54	0.54	0.53	0.53	0.53	0.53	0.53

start at pH 3.5 and it has been found to be maximum in the pH range of 4.0–8.5 and accounted *ca.* 65–80% of the total Zn(II) ion at different temperatures in 1:1, 1:2 and 1:5 ratios.

### 3. 2. Stability and Structure of Mixed Ligand ZnLB/ZnLB<sub>2</sub> Species

From the pH–metric data illustrate that the mixed ligand Zn(II)–2AB(L)–amino acid(B) systems to form ZnLB and ZnLB<sub>2</sub> types of mixed ligand complex species in addition to various binary species HL, H<sub>2</sub>L, ZnL, ZnL<sub>2</sub>, HB, H<sub>2</sub>B, ZnB and ZnB<sub>2</sub> have been identified. The stability constant values for the mixed ligand systems were reported in Table 3. In order to characterize the stability of mixed ligand equilibria with respect to their corresponding binary analogues, it can be expressed quantitatively to support the terms like  $\Delta \log K$ ,  $\log X$ ,  $\log X'$  and % R.S. The log  $K_{ZnLB}^{ZnB} / \log K_{ZnLB_2}^{ZnB_2}$  values (Table 3) obtained at different temperatures in Zn(II)–2AB(L)–amino acid(B) systems are compare favorably with log  $K_{ZnL}^{Zn}$  value in Zn(II)–2AB(L) binary systems (Table 2). This shows that, the ligand 2AB(L) in mixed ligand system binds with Zn(II) ion in a manner similar to its binding in their binary ZnL system *i.e.*, the ligand 2AB(L) acts as bidentate and binds through amino–N and amido–O atoms.

Again, log  $K_{ZnLB}^{ZnL} / \log K_{ZnLB_2}^{ZnL}$  values (Table 3) in ZnLB / ZnLB<sub>2</sub> systems compare favorably with log  $K_{ZnLB}^{Zn} / \log K_{ZnB_2}^{Zn}$  values in Zn(II)–amino acid systems (Table 2) and this show that the binding mode of secondary amino acid ligands(B) in mixed ligand ZnLB/ZnLB<sub>2</sub> species is similar to its bidentate binding mode in the corresponding binary systems. Thus, the four coordinating positions in Zn(II)–2AB–amino acid systems would be occupied by the bidentate binding of 2AB(L) and amino acids(B) respectively. The remaining positions in ZnLB systems would be occupied by solvent water molecules (Figure 2) to form a stable hexa coordinated environment. The binding of amino acid(B) ligands in ZnLB species in the presence of 2AB(L) ligand involves a stable five–six membered chelate ring. This is also confirmed from the plot (Figure 3) of log  $K_{ZnL}^{Zn} / \log K_{ZnLB}^{ZnB}$  vs.  $pK$  values of 2AB(L) which is evident that all the points due to the binary complexes fit on a straight line.<sup>30</sup> Also, the points due to the ZnLB complexes form a straight line parallel to those of the binary complexes. From Table 3, the overall stability of mixed ligand ZnLB system follows the stability order as: Zn(II)–2AB–gly > Zn(II)–2AB–ala > Zn(II)–2AB–val > Zn(II)–2AB–phe.

In order to characterize the stability of the mixed ligand ZnLB complexes with respect to the corresponding binary analogues can be expressed quantitatively in terms of  $\Delta \log K$ ,  $\log X$ ,  $\log X'$  and % R.S. are computed as:

in  $I = 0.15$  M (NaClO<sub>4</sub>) medium [error limit:  $\pm (0.02-0.05)$ ]. Standard deviations are given in parentheses.

	Ligand (B) (at 320 K)					Ligand (B) (at 330 K)			
	gly	ala	val	phe		gly	ala	val	phe
8.81(6)	8.64(7)	8.36(5)	8.22(7)	8.63(7)	8.49(8)	8.22(6)	8.09(9)		
13.02(7)	12.83(8)	–	–	12.83(6)	12.68(8)	–	–		
5.18	5.01	4.73	4.59	5.08	4.94	4.67	4.54		
4.08	3.99	4.00	3.98	4.02	3.93	3.99	3.96		
9.39	9.20	–	–	9.28	9.13	–	–		
4.20	4.15	–	–	4.14	4.10	–	–		
4.21	4.19	–	–	4.20	4.19	–	–		
0.45	0.36	0.37	0.35	0.47	0.38	0.44	0.41		
0.57	0.52	–	–	0.59	0.55	–	–		
1.93	1.73	1.71	1.65	1.82	1.65	1.65	1.62		
0.84	0.75	0.76	0.74	0.82	0.73	0.79	0.76		
9.51	7.74	8.49	8.25	10.20	8.33	10.40	9.93		

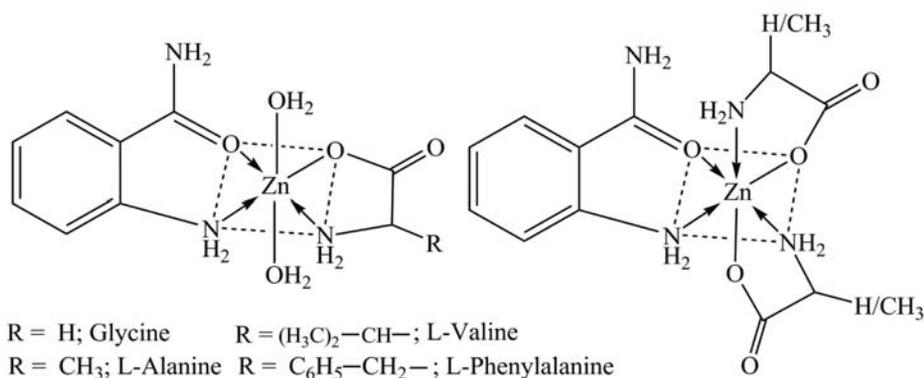


Figure 2. Proposed structures of ZnLB and ZnLB<sub>2</sub> species in Zn(II)-2AB(L)-amino acid(B) systems.

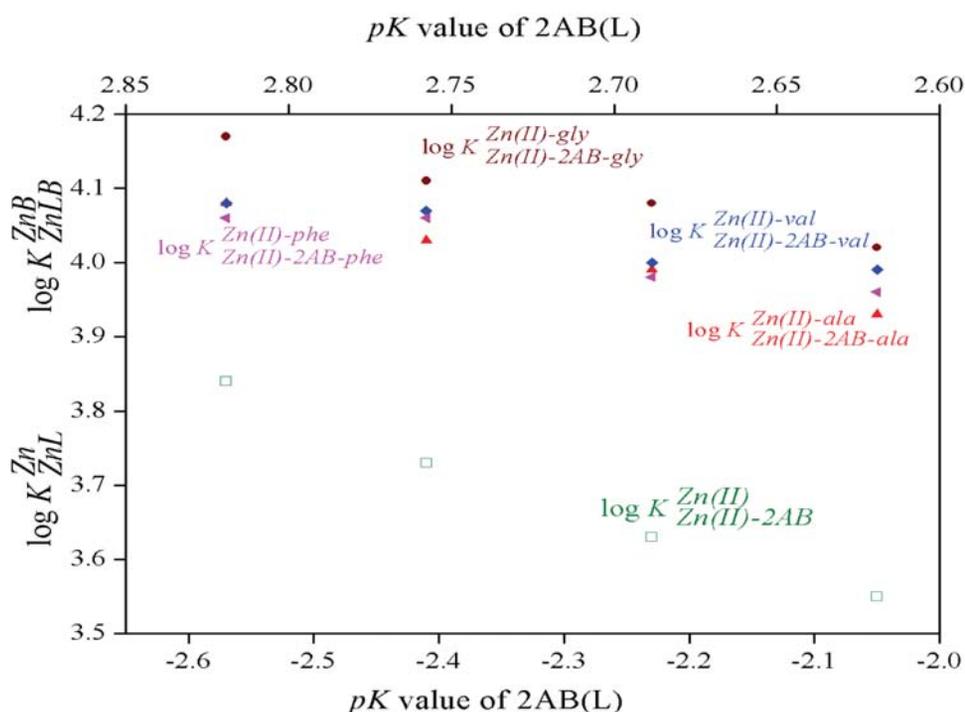
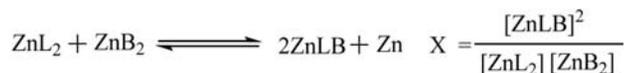


Figure 3. Relationship between the logarithm values with  $pK$  values of primary 2AB(L) ligand.



$$\Delta \log K_{\text{ZnLB}} = \log \beta_{\text{ZnLB}}^{\text{Zn}} - (\log \beta_{\text{ZnL}}^{\text{Zn}} + \log \beta_{\text{ZnB}}^{\text{Zn}})$$



$$\log X_{\text{ZnLB}} = 2 \log \beta_{\text{ZnLB}}^{\text{Zn}} - (\log \beta_{\text{ZnL}_2}^{\text{Zn}} + \log \beta_{\text{ZnB}_2}^{\text{Zn}})$$

From Table 3, the calculated  $\Delta \log K_{\text{ZnLB}}$  values for all these systems are more positive compared to the statistically expected values<sup>31</sup> which indicating that the mar-

ked stabilities of mixed ligand complexes as compared to their binary analogues. The calculated disproportionation parameter ( $\log X$ ) values for all the complexes are very much higher than the statistically expected (+0.6) value<sup>31</sup> which suggest that the preference for the formation of mixed ligand ZnLB complexes compared to the formation of corresponding binary ZnL<sub>2</sub>/ZnB<sub>2</sub> complexes *i.e.*, the inter-ligand and electronic interactions are present in the mixed ligand complexes. The  $\log X$  values can only indicate the coordination tendency of the secondary ligand towards binary ZnL complex, but it fails to explain the stabilizing order of metal-ligand bonds after the complex formation. Hence, a new parameter  $\log X'$

$$[ = (\log \beta_{ZnLB}^{Zn} + \log K_{ZnL}^{Zn}) - (\log \beta_{ZnL_2}^{Zn} + \log K_{ZnB}^{Zn}) ]$$

value<sup>31</sup> is considered and the observed  $\log X'$  values are greater than 0.3, suggesting that ZnL and ZnB bonds in mixed ligand complexes are stronger than in binary complexes. Also, the percentage relative stabilization % R. S.

$$[ = (\log K_{ZnLB}^{ZnL} - \log K_{ZnB}^{ZnL}) \times 100 / (\log K_{ZnB}^{ZnL}) ]$$

parameter<sup>32</sup> indicates a noticeable stabilization is present in the mixed ligand NiAB complexes than corresponding binary. The  $ZnLB_2$  species in Zn(II)–2AB(L)–gly/ala(B) systems, the solvent water molecules of  $ZnLB$  species would be replaced by a second molecule of glycine/alanine ligands(B). The obtained  $\log K_{ZnLB_2}^{ZnB_2} / \log K_{ZnLB_2}^{ZnL}$  values (Table 3) in Zn(II)–2AB–gly/ala systems were comparable with  $\log K_{ZnLB_2}^{ZnB_2}$  and  $\log K_{ZnLB_2}^{ZnL}$  values (Table 2) in the binary systems and the  $ZnLB_2$  species in the Zn(II)–2AB(L)–gly/ala(B) systems would be six coordinated due to the bidentate binding of nature of one molecule of 2AB(L) and two molecules of gly/ala(B) ligand respectively. The calculated  $\Delta \log K_{ZnLB_2}$  values are more positive while compared to the statistically expected values<sup>31</sup> indicating that enhanced stabilities for  $ZnLB_2$  systems.

### 3. 3. Effect of Temperature

The protonation constant values for 2AB(L) and amino acid ligands(B), as well as the stability constant values of their binary Zn(II) complexes in 50% (v/v) etha-

nol–water mixture has been investigated at different temperatures in  $I=0.15$  M  $NaClO_4$  (Table 2). From Table 2, it is clear that the protonation and their binary stability constant values decrease with the increase of temperature. The change in enthalpy ( $\Delta H$ ) and entropy ( $\Delta S$ ) values were obtained by linear least squares fit (Van't Hoff plot) of  $\log \beta_{ZnLB} / \log \beta_{ZnLB_2}$  values vs.  $1/T$  (Figure 4) leading to a slope  $-(\Delta H/RT)$  and an intercept ( $\Delta S/R$ ) are as follows:

The thermodynamic parameter ( $\Delta G$ ,  $\Delta H$  and  $\Delta S$ ) values for binary Zn(II) systems are given in Table 4. The calculated  $\Delta H$  and  $\Delta S$  values can be considered as the sum of two contributions such as the release of solvent ( $H_2O$ ) molecules and metal–ligand bond formation. From Table 4, the binary Zn(II) systems, (i) the negative  $\Delta G$  values (except the first protonation constant values of 2AB(L) ligand) show that the driving tendency of the complexation reaction is spontaneous process,<sup>11</sup> (ii) the  $\Delta H$  values are negative, indicating that the exothermic nature of the complexation process and (iii) the  $\Delta S$  values are positive, confirming the complexation process is entropically favorable. The abnormal high positive  $\Delta S$  values of the binary systems are consistent with the hypothesis that a large number of water molecules are released upon complexation.<sup>11,12,33</sup> The thermodynamic parameters for all the mixed ligand  $ZnLB$  and  $ZnLB_2$  systems are given in Table 5. The stability constant  $\log \beta_{ZnLB} / \log \beta_{ZnLB_2}$  values decrease with the increase of temperature (Figure 4). A negative  $\Delta G$  values for all these complexes suggest the complexation process is spontaneous.<sup>11,12,33</sup> A negative  $\Delta H$  values

$$\Delta G = -RT \ln K = \Delta H - T\Delta S$$

$$\ln K = -\frac{\Delta H}{RT} + \frac{\Delta S}{R} \quad \text{and} \quad \Delta S = \frac{(\Delta H - \Delta G)}{T}$$

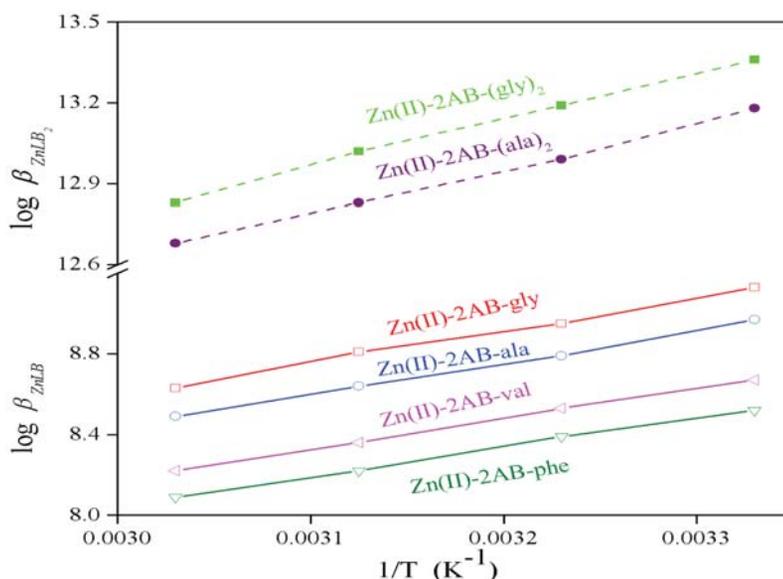


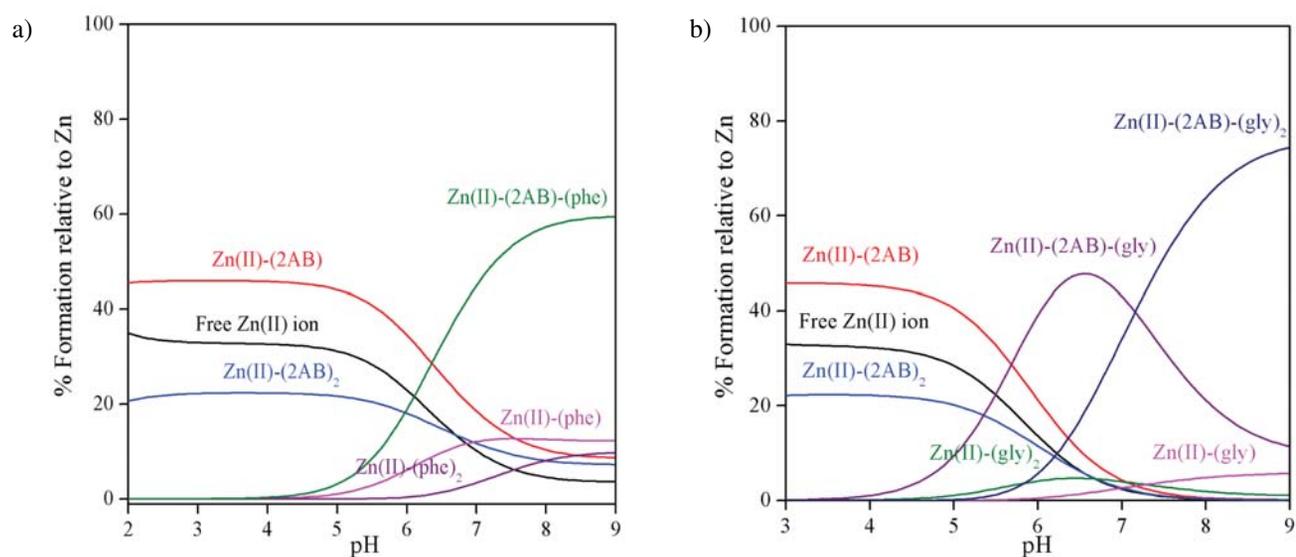
Figure 4. Van't Hoff plot of  $\beta_{ZnLB} / \log \beta_{ZnLB_2}$  values vs.  $1/T$ .

**Table 4.** Thermodynamic parameter of binary Zn(II)–2-aminobenzamide(L) and Zn(II)–amino acid(B) systems.

System	Species	$-\Delta G$ (kJ mol <sup>-1</sup> )				$-\Delta H$ (kJ mol <sup>-1</sup> )		$\Delta S$ (J K <sup>-1</sup> mol <sup>-1</sup> )			
		300 K	310 K	320 K	330 K	300 K	330 K	300 K	310 K	320 K	330 K
Zn(II)–2AB	HL	-14.76	-14.35	-13.66	-12.95	32.94	60.59	60.11	60.24	60.56	
	H <sub>2</sub> L	16.26	16.32	16.48	16.56	13.08	10.57	10.45	10.62	10.52	
	ZnL	22.06	22.14	22.24	22.43	18.41	12.15	12.03	11.97	12.18	
	ZnL <sub>2</sub>	41.13	41.61	42.09	42.65	25.99	50.46	50.38	50.32	50.48	
Zn(II)–gly	HB	56.12	56.80	56.86	56.68	50.83	17.65	19.28	18.85	17.73	
	H <sub>2</sub> B	69.22	69.68	70.34	70.83	52.71	55.01	54.74	55.08	54.90	
	ZnB	28.49	28.73	28.98	29.13	21.98	21.72	21.78	21.89	21.68	
	ZnB <sub>2</sub>	52.21	53.24	54.04	54.91	25.56	88.84	89.29	89.00	88.93	
Zn(II)–ala	HB	57.84	57.69	58.09	58.76	48.51	31.10	29.62	29.91	31.06	
	H <sub>2</sub> B	71.11	72.12	73.04	73.80	44.13	89.95	90.29	90.33	89.92	
	ZnB	28.09	28.25	28.49	28.81	20.89	24.00	23.76	23.76	24.02	
	ZnB <sub>2</sub>	51.35	52.23	53.18	54.21	22.78	95.24	95.01	95.01	95.25	
Zn(II)–val	HB	58.07	58.41	59.13	59.52	42.86	50.70	50.14	50.82	50.48	
	H <sub>2</sub> B	72.72	73.90	74.57	75.57	45.09	92.12	92.94	92.13	92.38	
	ZnB	26.37	26.47	26.71	26.73	22.35	13.37	13.29	13.62	13.25	
	ZnB <sub>2</sub>	48.37	49.09	49.87	50.80	24.12	80.82	80.54	80.48	80.85	
Zn(II)–phe	HB	54.51	54.73	54.90	55.48	45.38	30.42	30.14	29.73	30.58	
	H <sub>2</sub> B	68.64	69.33	70.34	71.21	42.51	87.11	86.51	86.97	86.97	
	ZnB	25.62	25.70	25.98	26.10	20.48	17.12	16.83	17.17	17.01	
	ZnB <sub>2</sub>	46.99	47.78	48.53	49.35	23.52	78.24	78.28	78.16	78.28	

**Table 5.** Thermodynamic parameter of mixed ligand Zn(II)–2-aminobenzamide(L)–amino acid(B) systems.

System	Species	$-\Delta G$ (kJ mol <sup>-1</sup> )				$-\Delta H$ (kJ mol <sup>-1</sup> )		$\Delta S$ (J K <sup>-1</sup> mol <sup>-1</sup> )			
		300 K	310 K	320 K	330 K	300 K	330 K	300 K	310 K	320 K	330 K
Zn(II)–2AB–gly	ZnLB	52.44	53.12	53.98	54.53	31.07	71.25	71.14	71.59	71.09	
	ZnLB <sub>2</sub>	76.74	78.29	79.78	81.07	33.32	144.75	145.07	145.18	144.69	
Zn(II)–2AB–ala	ZnLB	51.53	52.17	52.94	53.65	30.16	71.22	71.017	71.19	71.17	
	ZnLB <sub>2</sub>	75.71	77.10	78.61	80.12	31.50	147.38	147.12	147.24	147.35	
Zn(II)–2AB–val	ZnLB	49.80	50.63	51.22	51.94	28.80	70.02	70.44	70.08	70.13	
Zn(II)–2AB–phe	ZnLB	48.94	49.80	50.37	51.12	27.66	70.94	71.43	70.96	71.09	

**Figure 5.** Species distribution diagrams of mixed ligand (a) Zn(II)–2AB(L)–phe(B) system in (1:1:1) and (b) Zn(II)–2AB(L)–gly(B) in (1:1:2) complexes in 50% (v/v) ethanol–water medium at 310 K.

show that the chelation process is exothermic and the complexation process favorable at very low temperature. All the complexes show a positive  $\Delta S$  values<sup>34</sup> suggest the complexation of 2AB(L) ligand with Zn(II) ion in the presence of amino acids(B) ligand is entropically favorable.

### 3. 4. Species Distribution Diagram

In order to show the quantitative trends found in the species distribution plots obtained for Zn(II)–2AB–phe and Zn(II)–2AB–(gly)<sub>2</sub> systems (at 310 K) are given in Figure 5. The formation of ZnLB complexes start at pH 5.0 and it has been found to be maximum in the pH range of 7.0 to 8.5 and accounted ca. 50–85% of the total Zn(II) ion. The ZnLB<sub>2</sub> species in Zn(II)–2AB(L)–gly/ala(B) systems has been found to be favoured above pH 7.0 and accounted for 65–80% of the total Zn(II) ion in 1:1:2 system. At lower pH range the ZnL and ZnL<sub>2</sub> species are present in considerable amount (ca. 20–45%). At higher pH less than 20% of total Zn(II) ions are present as ZnB and ZnB<sub>2</sub> complexes.

### 3. 5. Electronic Absorption Spectra

The electronic absorption spectra of Zn(II)–2AB(L)–amino acid(B) complexes of ZnLB systems [ $3 \times 10^{-3}$  M] in the range of 200–1100 nm were recorded at different pH levels in 50% (v/v) ethanol–water medium at 310 K. The diamagnetic nature of Zn(II) ion does not show any d–d transition in the visible region. However, the Zn(II)–2AB(L)–gly, ala, val and phe(B) complexes show only one band at 26385, 26247, 26455 and 26371 cm<sup>-1</sup> respectively in the UV region due to LM charge transfer (LMCT) transition which corresponds to six–coordinated distorted octahedral environment around the Zn(II) ion with two water molecules are present in the z–axes of the cartesian coordinate.<sup>35, 36</sup>

## 4. Conclusion

In the present work, we determined the protonation and stability constants of binary and their mixed ligand complexes in 50% (v/v) ethanol–water mixture at different temperatures (300, 310, 320 and 330 ± 0.1 K) of  $I = 0.15$  M (NaClO<sub>4</sub>) medium. In solution equilibria, the ZnLB/ZnLB<sub>2</sub> species, both 2AB(L) and amino acid(B) ligands act as bidentate to form a stable six, five membered chelation around the central Zn(II) ion. The percentage distribution of various binary and mixed ligand species in solution was evaluated. From the stabilization parameters, the complexation of 2AB(L) with Zn(II) ion in the presence of amino acids(B) is more favorable than the binary complex formation and the calculated thermodynamic parameters explain the nature of the complexation process. Both the pH–metric and electronic absorption spectral

studies predict stable distorted octahedral geometry for the title complexes.

## 5. Acknowledgement

The authors express their sincere gratitude to the Managing Board and Principal of Sree Sowdambika College of Engineering and Devanga Arts College (Autonomous), Aruppukottai for their moral support and constant encouragement throughout this investigation.

## 6. References

1. a) H. Kraatz, N. M. Nolte, Concepts and Models in Bioinorganic Chemistry: Wiley, New York, **2006**.  
b) A. Pladzyk, K. Baranowska, D. Gudat, S. Godlewska, M. Wieczerszak, J. Chojnacki, M. Bulman, K. Januszewicz, A. Dolega, *Polyhedron* **2011**, 30(6), 1191–1200.
2. M. Darawsheh, H.A. Ali, A.L. Abuhijleh, E. Rappocciolo, M. Akkawi, S. Jaber, S. Maloul, Y. Hussein, *Eur. J Med. Chem.* **2014**, 82, 152–163.
3. H. Sigel, Metal Ions in Biological Systems: Dekker, New York, vol 1–37, **1971–1997**.
4. R. F. Spano, M. Trabucchi, G. U. Corsini, G. L. Gessa, Sulpiride and other benzamides: Experimental and Clinical Pharmacology: Raven Press, New York, **1979**.
5. D. Oltmanns, M. Eisenhut, W. Mier, U. Haberkorn, *Curr. Med. Chem.* **2009**, 16(17), 2086–2094.
6. S. B. Katiyar, I. Bansal, J. K. Saxena, P. M. Chauhan, *Biorg. Med. Chem. Lett.* **2005**, 15(1), 47–50.
7. a) L. M. Plum, L. Rink, H. Haase, *Int. J. Environ. Res. Public Health* **2010**, 7(4), 1342–1365.  
b) R. I. Cousins, Zinc in present knowledge in nutrition: E. E. Zeigler, L. J. Filer, (Eds.), ILSI Press, Washington, DC, **1996**.
8. a) P. Ozturk, E. Kurutas, A. Ataseven, N. Dokur, Y. Gumusalen, A. Gorur, L. Tamer, S. Inaloz, *J. Trace Elem. Med. Bio.* **2014**, 28(3), 266–270.  
b) A. S. Prasad, *Adv. Nutr.* **2013**, 4, 176–190.
9. a) D. K. Dhawan, V. D. Chadha, *Indian J. med. Res.* **2010**, 132, 676–682.  
b) P. Frost, J. C. Chen, I. Rabbani, J. Smith, A. S. Prasad, The effect of Zn deficiency on the immune response. In: Zinc metabolism. Current aspects in health and disease. G. J. Brewer, A. S. Prasad (Eds.), Alan R Liss Inc, New York, **1977**.
10. S. Lau, B. Sarkar, *Can. J. Chem.* **1975**, 53(5), 710–715.
11. M. A. Neelakantan, S. S. Mariappan, J. Dharmaraja, K. Muthukumar, *Acta Chim. Slov.* **2010**, 57(1), 198–205.
12. J. Dharmaraja, T. Esakkidurai, P. Subbaraj, S. Shobana, *Spectrochim. Acta* **2013**, 114, 607–621.
13. S. Shobana, J. Dharmaraja, S. Selvaraj, *Spectrochim. Acta* **2013**, 107, 117–132.
14. J. Dharmaraja, P. Subbaraj, T. Esakkidurai, S. Shobana, *Spectrochim. Acta* **2014**, 132, 604–614.

15. G. Gran, *Analyst* **1952**, 77(920), 661–671.
16. H. Irving, M. G. Miles, L. D. Pettit, *Anal. Chim. Acta* **1967**, 38, 475–488.
17. a) I. G. Sayce, *Talanta* **1971**, 18(6), 653–654.  
b) I. G. Sayce, V. S. Sharma, *Talanta* **1971**, 19(6), 831–832.
18. L. G. Van Uitert, C. G. Haas, *J. Am. Chem. Soc.* **1953**, 75(2), 451–455.
19. L. G. Hepler, E. M. Woolley, D. G. Hurkot, *J. Phys. Chem.* **1970**, 74(22), 3908–3913.
20. N. Durust, M. A. Akay, Y. Durest, E. Kilic, *Anal. Sci.* **2000**, 16, 825–827.
21. L. Alderighi, P. Gans, A. Ienco, D. Peters, A. Sabatini, A. Vacca, *Coord. Chem. Rev.* **1999**, 184(1), 311–318.
22. J. R. Allan, B. McCloy, A. D. Paton, W. E. Smith, D. L. Gerrard, *Thermochim. Acta* **1992**, 205, 127–137.
23. a) R. B. Homer, C. D. Johnson, In *The Chemistry of Amides*: J. Zabicky, (Ed.), Wiley Interscience, New York, **1970**.  
b) R. B. Martin, *J. Chem. Soc., Chem. Commun.* **1972**, 13, 793–794.
24. E. T. Nomkoko, G. E. Jackson, B. S. Nakani, *Dalton Trans.* **2004**, 9, 1432–1440.
25. D. Chen, Y. Sun, A. E. Martell, M. J. Welch, *Inorg. Chim. Acta* **2002**, 335, 119–124.
26. B. Garcia, R. M. Casado, J. Castillo, S. Ibeas, I. Domingo, J. M. Leal, *J. Phys. Org. Chem.* **1993**, 6(2), 101–106.
27. Z. Z. Rappoport, *The Chemistry of Anilines–Part 1*: John Wiley & Sons Ltd., The Atrium, England, **2007**.
28. a) D. L. Dinsel, T. R. Sweet, *Anal. Chem.* **1963**, 35(13), 2077–2081.  
b) R. C. Jagessar, D. Rampersaud, *Life Sci. J.* **2007**, 4(4), 46–49.
29. a) I. Sovago, T. Kiss, A. Gergely, *Pure Appl. Chem.* **1993**, 65(5), 1029–1080.  
b) L. D. Pettit, *Pure Appl. Chem.* **1984**, 56(2), 247–292.
30. R. B. Martin, H. Sigel, *Comments Inorg. Chem.* **1988**, 6, 285–314.
31. a) H. Sigel, *IUPAC Coordination Chemistry–20*, D. Banerjee, (Ed.), Pergamon Press, Oxford, New York, **1980**.  
b) H. Sigel, *Angew. Chem., Int. Ed. Engl.* **1975**, 14(6), 394–402.  
c) R. DeWitt, J. I. Watters, *J. Am. Chem. Soc.* **1954**, 76(14), 3810–3814.
32. a) S. N. Limaye, M. C. Saxena, *J. Indian Chem. Soc.* **1984**, 61, 448–450.  
b) S. N. Limaye, M. C. Saxena, *J. Indian Chem. Soc.* **1985**, 62, 352–354.
33. A. A. Al-Sarawy, A. A. El-Bindary, A. Z. El-Sonbati, T. Y. Omar, *Chem. Pap.* **2005**, 59(4), 261–266.
34. A. T. Mubarak, *J. Solution Chem.* **2004**, 33(2), 149–155.
35. A. B. P. Lever, *Electronic spectra of d<sup>n</sup> ions in Inorganic Electronic Spectroscopy: second ed.*, Elsevier, Amsterdam, The Netherlands, **1984**.
36. C. J. Ballhausen, *Introduction to Ligand Field Theory*: McGraw Hill, New York, **1962**.

## Povzetek

Proučevali smo kompleksacijo mešanih ligandov 2-aminobenzamida (2AB) kot prvega liganda [L] s Zn(II) v prisotnosti liganda [B], ki ga predstavljajo nekatere bio-relevantnih sestavin amino kislin kot so glicin (gly), L-alanin (ala), L-valin (val) in L-fenilalanin (phe). Proces smo zasledovali z merjenjem pH pri različnih temperaturah (300, 310, 320 in  $330 \pm 0.1$  K) v 50 % (v/v) mešanici etanola in vode, v prisotnosti 0.15 M NaClO<sub>4</sub>. Analiza eksperimentalnih podatkov dobljenih pri titracijah kaže na prisotnost ZnLB in ZnLB<sub>2</sub> kompleksov mešanih ligandov, in tudi binarnih kompleksov. Tako primarni kot sekundarni ligandi delujejo kot bidentati z možnostjo tvorbe stabilnega šest-ali petčlanskega ketalnega obroča. Izračunane vrednosti stabilizacijskih parametrov  $\Delta \log K$ ,  $\log X$ ,  $\log X'$  in % R.S. kažejo, da imajo mešani kompleksi večjo stabilnost od binarnih. S pomočjo temperaturne odvisnosti konstante stabilnosti smo določili termodinamske parametre  $\Delta G$ ,  $\Delta H$  and  $\Delta S$  za proučevani proces.