Impact of aprotic solvent on binary complexes of bioactive metals with L-Valine

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Abstract

A pH metric investigation of biologically essential acid containing amino group (L-valine) with metals (Ca^{2+}, Mn^{2+} and Zn^{2+} ions) at a specific ionic concentration 0.16 mol l^{-1} in 10.0 % to 60.0 % vol/vol of aprotic solvent-aqua composition form anticipated protonated (LH_2^+, LH) forms and deprotonated (L^-) forms of L-valine.

The computer augmented and statistical parameters show that the binary complexes are ML^+, MLH^{2+} and ML_2H^+. The differences in log β with respect to dielectric constant (1/D) of solvent and the influence of some experimental parameters on log β were explained. The order of influence is $[OH^-] > [H^+] >$ [valine]> [M] > log F.

Keywords: Binary complexes, bioactive metals, L-valine, aprotic solvent.

Introduction

The binary speciation of bioactive metals like Ca^{2+}, Mn^{2+} and Zn^{2+} ions with biologically essential acid containing amino group (L-valine) in aprotic solvent acetonitrile (AN) and their aqua mixtures studies exploits the active positions, chemical bonding behavior, acido-basic equilibrium with respect to temperature, dielectric constant at different ionic strengths. It is very difficult to measure dielectric constant (D) due to less polarity of proteins rather than bulk[30].

Calcium is a major essential metal in metabolic activities mainly on muscle growth, contradiction, blood flow and it controls relaxation and the release of few hormones and central nerves system[36]. Absorption of calcium through vitamin D[5,15] is very slow. More amounts of calcium consumption result in adverse effects on kidney function, sometimes toxic as well. Availability of Zinc is almost at trace levels even though it works as a critical biological function.[8,9,19,22,27]

Another trace nutrient is Mn in living beings. Its deficiency causes excess bone growth and lack of bone healing functions. It is mostly concentrated on important organs like liver and kidney[10,31]. L-Valine is an essential biological amino acid has large applications in pharmaceutical[4] and food industries. Some authors reported log β constants of binary complexes of L-valine by potentiometric, paper electrophoretic and SCOGS[2,16,18,32] methods. AN behaves protophilic, dipolar solvent[1,11,21,23] and existed in to dimers.

Material and Methods

Preparation of Reagents: Pure tri distilled water is used for 0.05 mol l^{-1} solution of L-valine. 0.1 mol l^{-1} of chlorinated salts of Ca^{2+}, Mn^{2+} and Zn^{2+} were prepared. 0.4 mol l^{-1} solution of NaOH and 0.2 mol l^{-1} of HCl were prepared. During titration, 2.0 mol l^{-1} of sodium chloride solution was added to the titrand. From Gran plot method[12,13,28], strength of acid and alkali was analyzed. Acetonitrile is added without further purification. The binary stability constants of valine determined from graphical curves like alkalimetric curves in different compositions of acetonitrile and respective quantities of valine in the titrands were maintained. A digital pH meter (readability 0.01) is calibrated with standard solution. The useful parameters are log *F*, asymmetric and liquid junction potential data from SCPHD program[29].

Modeling Method: Computer program MINIQUAD75[14] is executed on primary alkalimetric titration data resulting different number of species, out of that few species are best in fitted. The results[35] are shown in table 1.

Results and Discussion

Prime species was investigated by operating trial exhaustive study on 10% v/v AN–aqua mixture and the results are shown in table 2. These prime species (ZnL, ZnLH and ZnL_2H) are after concurrent existence of possible combinations of species through expert system CEES and MINIQUAD75 shown in table 3. Less values of U_{corr} support the prime species. Deviation of the values of best fit factors like kurtosis and skewness from three and zero respectively shows the tendency of these residuals to concentrate more to the left or right of the mean and broadening of the peak. From the above data, the kurtosis factor values show that the residuals form both leptokurtic and platykurtic patterns and few are in mesokurtic patterns[7,20,33].

The skewness values are tabulated in table 3 resulting in range of -3.56 to 1.10 for Ca(II), -0.02 to 1.01 for Mn(II) and - 0.07 to 0.78 for Zn(II). Best suitable factors like χ^2 (4.15 to 89.4 is less than table values) and very low U_{corr} support prime species to the present data. Literature results are correlated with reported values in table 4.

Embodiment of errors: MINIQUAD75 has no provision to vary the influential restriction. Then some representative systems were studied in order to have a cognizance of the effects of errors in concentrations of ingredients on the stability constants (Table 5) of binary metal complexes for Mn(II)-valine system in 30% v/v AN-aqua mixture studied

by incorporation of few influent specifications. The enlarged standard deviation (SD) in stability constants and few species are not feasible to form when applying influent things confirming the correctness of the prime species.

Table 1
log β's of valine in acetonitrile-aqua mixtures

AN content in % w/v	1/D of AN-aqua	log β_1	log β_2
0	78.30	9.41	11.70
10	74.68	9.71	12.19
20	70.52	9.72	12.32
30	65.78	9.74	12.63
40	60.20	9.78	12.79
50	55.71	9.91	13.20
60	50.78	10.02	13.58

Table 2
Trial exhaustive study of Zn^{2+}-valine complex in 10% v/v acetonitrile-aqua mixture

Model Number	log β_{mlh}(*SD*)			U_{corr} [a] $*_{10}^{8}$	χ^2	Skewness	Kurtosis	*R*-factor
	ML^+	MLH^{2+}	ML_2H^+					
1	4.83(25)	NF	NF	6.32	36.32	0.03	4.11	0.0089
2	NF	11.68(36)	NF	21.23	76.29	0.22	17.26	0.0164
3	NF	NF	16.82(28)	6.83	35.61	0.06	4.24	0.0093
4	5.10(23)	11.73(16)		4.95	63.70	0.79	7.71	0.0079
5	NF	11.74(16)	17.02(22)	5.39	67.73	0.75	7.54	0.0083
6	4.83(25)	NF	16.85(15)	6.32	36.32	0.03	4.11	0.0089
7	4.88(39)	11.76(14)	16.81(28)	5.13	74.36	0.78	7.58	0.0081

NF: Not feasible

Table 3
Prime species of valine with Ca(II), Mn(II) and Zn(II) in AN-aqua mixtures

% v/v AN	log β_{mlh}(*SD*)			*NP*	U_{corr} [a] $*_{10}^{8}$	Skewness	χ^2	Kurtosis	*R*-factor	pH-Range
	ML^+	MLH^{2+}	ML_2H^+							
Ca(II)										
0.0	2.43(47)	11.41(45)	14.05(52)	36	21.11	-0.15	79.41	4.22	0.0406	2.8-10.6
10.0	2.72(12)	11.95(11)	15.09(97)	58	17.62	1.10	74.28	3.72	0.0532	1.5-11.6
20.0	3.73(20)	12.78(14)	16.30(53)	43	20.53	-2.67	50.78	10.97	0.0252	1.5-11.6
30.0	4.06(36)	13.61(26)	16.88(40)	42	19.3	-3.56	37.30	8.89	0.0242	1.5-11.6
40.0	3.54(58)	14.04(42)	17.17(34)	45	2.76	0.67	85.62	2.01	0.0244	1.5-11.6
50.0	4.69(43)	14.25(39)	17.99(64)	40	4.21	0.49	89.4	2.00	0.0346	1.5-11.6
60.0	5.18(63)	15.05(55)	18.30(39)	53	3.50	-0.83	44.32	9.25	0.0232	1.5-11.6
Zn(II)										
0.0	5.08(41)	11.66(13)	16.53(19)	45	6.83	0.29	11.79	3.54	0.0094	1.6-8.6
10.0	4.88(39)	11.76(14)	16.81(27)	45	5.13	0.78	74.36	7.58	0.0081	1.5-9.0
20.0	5.62(41)	12.33(16)	17.01(26)	44	14.66	0.14	24.24	2.67	0.0139	1.5-9.0
30.0	5.94(31)	12.64(13)	17.48(24)	41	8.89	0.41	13.65	3.67	0.0128	1.5-9.0
40.0	6.36(60)	12.61(21)	17.71(30)	46	18.5	-0.07	6.93	2.84	0.0158	1.5-9.0
50.0	6.08(30)	12.78(15)	18.35(24)	38	5.69	-0.06	27.33	3.45	0.0124	1.5-9.0
60.0	7.62(60)	14.82(39)	19.93(65)	45	22.79	0.63	32.41	2.33	0.0173	1.5-9.0
Mn(II)										
0.0	3.06(16)	11.50(5)	14.74(19)	44	0.60	-0.02	46.02	11.00	0.0027	1.6-9.0
10.0	4.25(31)	12.01(7)	16.03(57)	45	1.46	0.28	26.01	4.34	0.0043	1.5-9.5
20.0	4.45(41)	13.05(18)	16.10(83)	40	7.86	0.46	7.47	2.74	0.0119	1.5-9.5
30.0	4.71(15)	12.87(5)	16.55(33)	36	0.79	1.01	19.11	7.35	0.0045	1.5-9.5
40.0	4.75(30)	13.11(11)	16.37(83)	41	4.30	0.46	4.15	2.98	0.0088	1.5-9.5
50.0	5.17(37)	13.39(12)	16.93(38)	41	5.35	0.35	4.67	3.06	0.0098	1.5-9.5
60.0	5.54(37)	14.00(19)	17.70(59)	37	13.85	0.63	12.17	2.81	0.0191	1.5-9.5

Role of protic solvent: Dielectric constant (D) of the acetonitrile influences the magnitude of the log β through the van der waals interactions between chemical species. Impact of AN percent content on overall binary stability constant depends on strong electric and weak non electric forces well defined by Born's[6] theory.

According to his theory, the energy of strong electric interactions is related to dielectric constant of the medium. log β values fluctuate linearly as a function of reciprocal of the dielectric constant (1/D) of the acetonitrile.

Distribution diagrams: The ligand valine is a bidentate amino acid with one associated and dissociated proton. Its protonated forms are LH_2^+, LH at low pH 1.5 to 9.0 and unprotonated form L^- at high pH regions 9.0-11.0. The most fit prime species are ML^+, MLH^{2+} and ML_2H^+ for Ca^{2+}, Mn^{2+} and Zn^{2+} in AN-aqua composition from possible equilibrium.

Table 4
Correlation of log β of L-valine complexes.

M	Prime species	Reported	Literature
Ca^{2+}	ML^+	2.43	
	MLH^{2+}	11.41	
	ML_2H^+	14.05	
Zn^{2+}	ML^+	5.08	4.44[30]
	MLH^{2+}	11.66	
	ML_2H^+	16.53	
Mn^{2+}	ML^+	3.06	3.77[31]
	MLH^{2+}	11.50	
	ML_2H^+	14.74	

Table 5
Embodiment of errors

	log β(*SD*)			
Ingredient	**% Error**	**ML^+**	**MLH^{2+}**	**ML_2H^+**
	0	4.719(15)	12.87(05)	16.55(33)
	-5			
NaOH	-2	3.81(16)	12.37(11)	NF
	+2	5.75(37)	13.17(09)	
	+5	10.55(12)	13.12(16)	
	-5	20.10(**)	26.78(**)	
HCl	-2	6.13(30)	13.62(09)	NF
	+2	3.40(15)	11.08(13)	
	+5			
	-5	4.57(12)	12.54(06)	
valine	-2	4.70(11)	12.75(05)	NF
	+2	4.88(11)	12.98(04)	
	+5	5.01(11)	13.15(04)	
	-5	4.88(12)	12.91(05)	
Mn(II)	-2	4.82(12)	12.88(05)	NF
	+2	4.76(11)	12.85(04)	
	+5	4.71(10)	12.83(04)	
	-5	5.06(11)	13.17(04)	
Log F	-2	4.89(11)	12.99(04)	NF
	+2	4.69(12)	12.75(05)	
	+5	4.55(13)	12.58(06)	

NF: Not feasible

$M^{2+} + LH_2^+ \rightleftharpoons MLH^{2+} + H^+$ (1)

$MLH^{2+} \rightleftharpoons ML^+ + H^+$ (2)

$M^{2+} + LH \rightleftharpoons ML^+ + H^+$ (3)

$MLH^{2+} + LH \rightleftharpoons ML_2H^+ + H^+$ (4)

$ML^+ + LH_2^+ \rightleftharpoons ML_2H^+ + H^+$ (5)

The best prime species ML^+, MLH^{2+} and ML_2H^+ with high percentile (Fig. 2) are predicted in physiological pH regions 1.5-11.6 for Ca^{2+}, 1.5-9.0 for $Zn^{2+}$and 1.5-9.5 for Mn^{2+}. With reference to chemical equilibria 1, for all M^{2+}-valine complexes, MLH^{2+} complex is constructed through interaction of free metal ion with LH_2^+ where the % of FM and LH_2^+ is descending with ascending % of MLH^{2+}. There is possibility to form ML^+ species through deprotonation of MLH^{2+} from chemical equilibria 2 and there is another possible way to form ML^+ species by interaction of FM with LH from chemical equilibria 3.

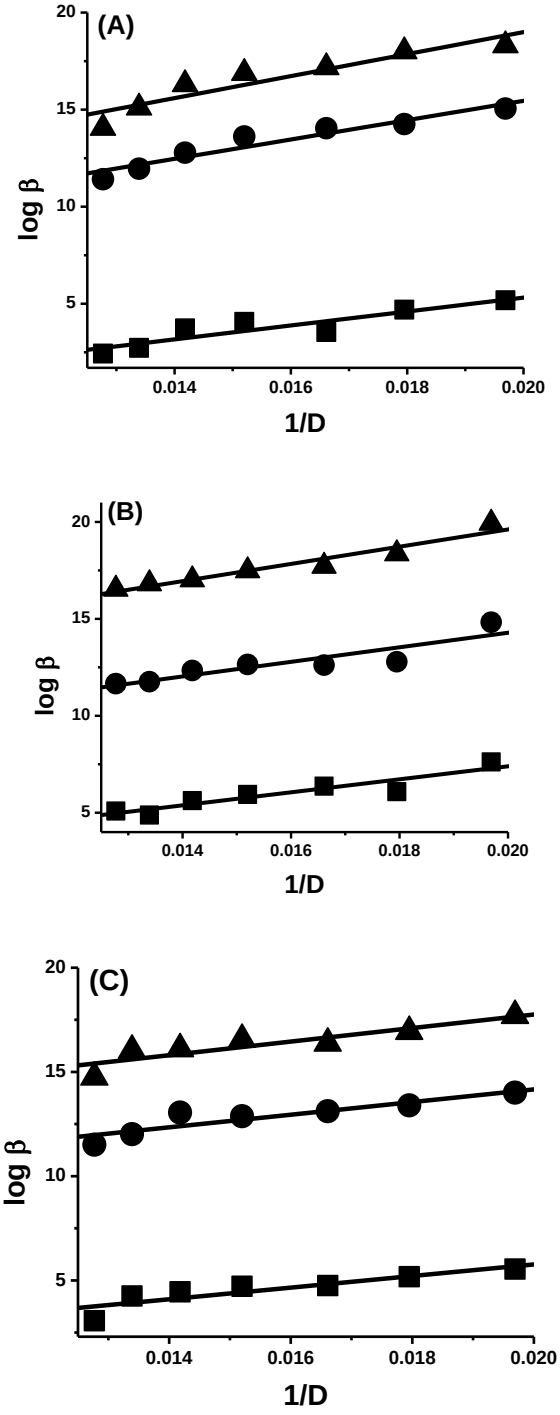

Fig. 1: Effect of AN (1/D) on log β of metal-valine complexes of (A) Ca^{2+}, (B) Zn^{2+} and (C) Mn^{2+}-(■)log β_{ML^+} (●)log $\beta_{MLH^{2+}}$ (▲)log β_{ML2H^+}

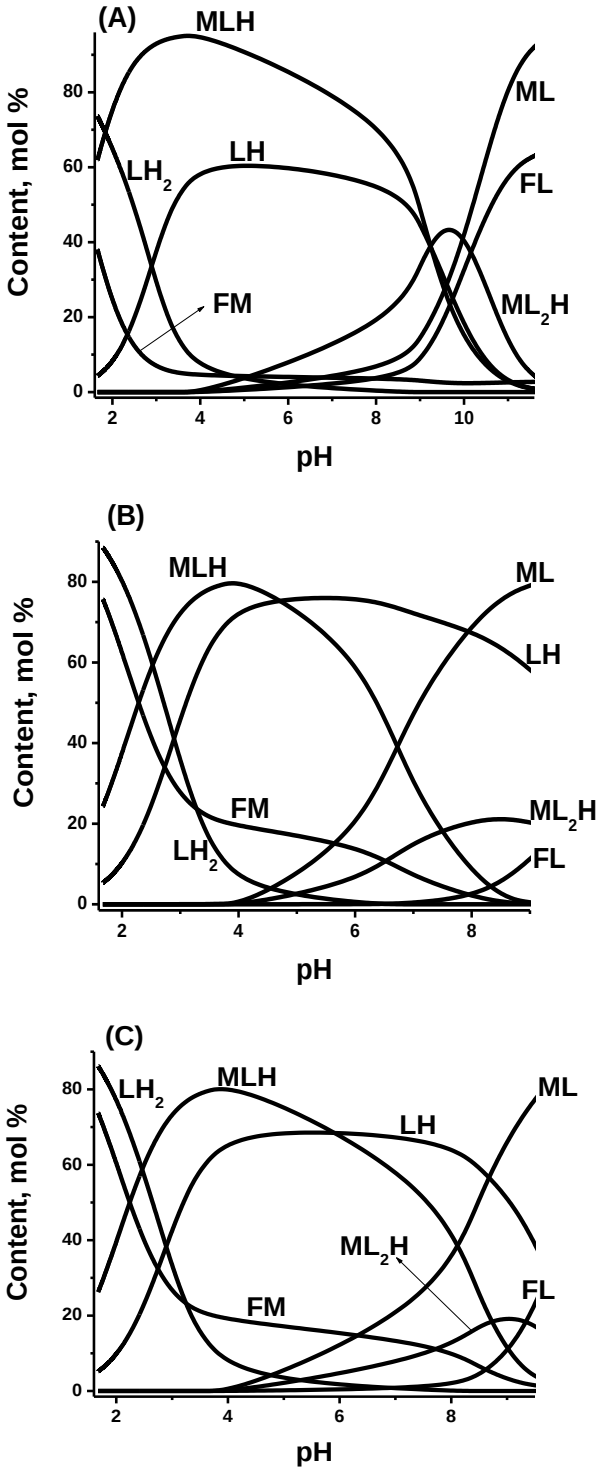

Fig. 2: Formation curves of valine complexes of (A) Ca^{2+}, (B) Zn^{2+} and (C) Mn^{2+} in 30% w/v AN-aqua composition

According to equilibrium studies, equilibria 2 is more outstanding than equilibrium 3, as the strength of free metal (FM) is decreasing, while strength of LH is progressively enhancing. From chemical equilibria 4 and 5, species ML_2H^+ is constructed. Out of these two possible equilibriums, equilibria 4 is more proper than equilibria 5, as the strengths of MLH^{2+} and LH are gradually descending with ascending strength of ML_2H^+. log β of these prime species obeys Mellor-Maley's order[25,26].

Proposed Structures of prime species: There is no structural elucidation of species ML^+, MLH^{2+} and ML_2H^+ from the proposed study. In valine, hetero atom of nitrogen (associate with two hydrogens) and carboxyl oxygen construct bonding with Ca^{2+}, Zn^{2+} and Mn^{2+} ions in physiological pH region. In the study there is a significant competition between hydrogen and metal ions (M) for this donor site resulting in number of equilibria formation of protonated complexes.

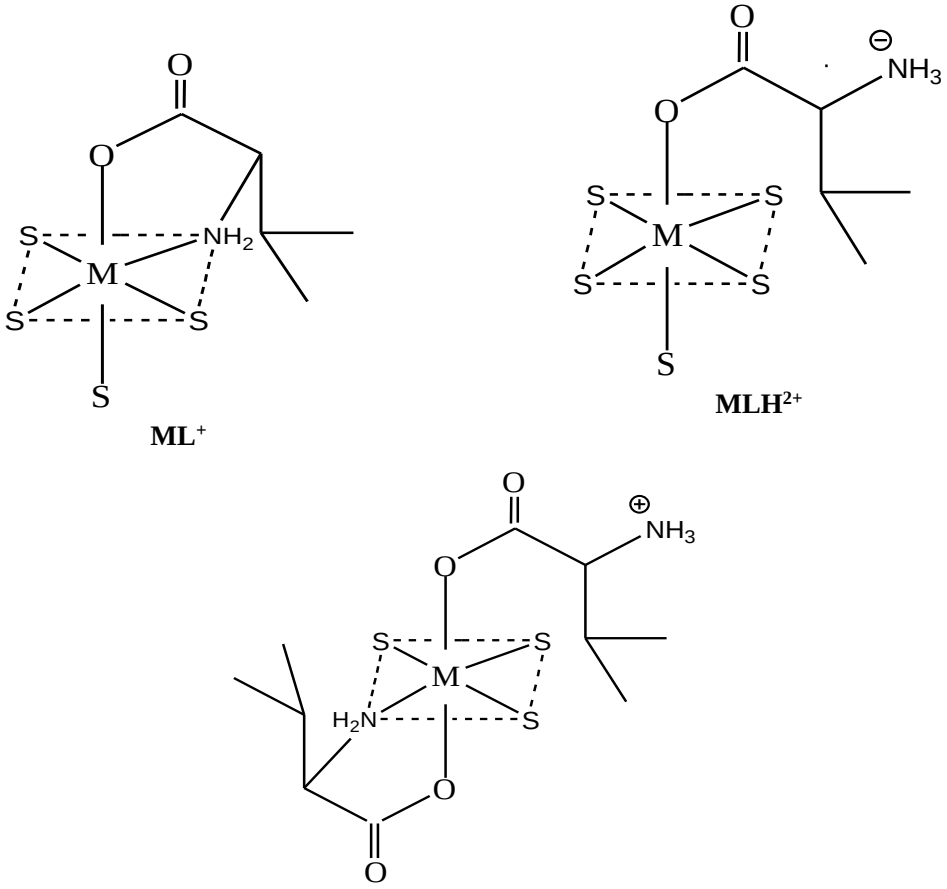

Fig. 3: Proposed structures of prime species

The aqueous solutions of Ca(II), Zn(II) and Mn(II) ions with L-valine complex structures are postulated based on comparison with known structures for related complexes and literature results showed octahedral complexes[17, 24]. Based on reported results, the prime species may have octahedral structures as proposed in figs. 3.

Conclusion

1. The chemical species are ML^+, MLH^{2+} and ML_2H^+ for Ca^{2+}, Zn^{2+} and Mn^{2+} ions with L-valine in acetonitrile solvent at pH 1.5-11.6.
2. The linear escalation in log β of the complexes with 1/D of the acetonitrile confirms the more electric attraction in the proposed structures.
3. These prime species may exist in octahedral structures for getting more stability.
4. The strength of influential components on log β is NaOH > HCl > valine > M (Ca^{2+}, Zn^{2+} and Mn^{2+}) > log *F*.

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(Received 10th December 2019, accepted 03rd March 2020)