



Maleic acid complexes in acetonitrile-water mixtures: Speciation Studies

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Abstract: This paper discusses on Speciation Studies of Maleic acid complexes of Ca(II), Mg(II) and Zn(II) in acetonitrile-water mixtures. The speciation study of metal ion complexes is useful to understand the role played by the active site cavities in biological molecules and the bonding behavior of protein residues with the metal ion. The species refined and their relative concentrations under the experimental conditions represent the possible forms of amino acids in bio fluids. Chemical speciation of Maleic acid with Ca(II), Mg(II) and Zn(II) has been investigated pH metrically in acetonitrile-water mixtures 0.0-60.0% v/v at 303.0 K and 0.16 M ionic strength. The predominant species detected for Ca(II), Mg(II) and Zn(II) are ML_2 and ML_3 . Models containing different numbers of species were refined by using the computer program MINQUAD75. The best-fit chemical models were arrived at based on statistical parameters. The trend in variation of complex stability constants with change in the dielectric constant of the medium is explained on the basis of electrostatic and non-electrostatic forces. The major industrial use of maleic acid is its conversion to fumaric acid which is catalysed by a variety of reagents, such as mineral acids and thiourea. Conversion of the cisomer into the Trans isomer is possible by photolysis in the presence of a small amount of bromine. Maleic acid is an industrial raw material for the production of glyoxylic acid by ozonolysis

Key Words: Complex equilibria, Chemical speciation, Maleic acid, Acetonitrile, Metals.

INTRODUCTION

The speciation study of metal ion complexes is useful to understand the role played by the active site cavities in biological molecules and the bonding behavior of protein residues with the metal ion. The species refined and their relative concentrations under the experimental conditions represent the possible forms of amino acids in bio fluids. Due to its numerous uses and high persistence, Calcium was among the first materials known to be essential in the

diet. All foods of vegetable origin contain small but useful amounts of calcium. Serum calcium is maintained within a narrow normal range, chiefly by resorption from the skeleton and alteration of urinary calcium loss and absorption from gut (Brown et al., 1977). Loss of calcium from the body occurs through urine and faeces. The mechanism is thought to be the high phosphate (and perhaps sulphate) content of protein, which complexes calcium in the renal tubule and enhances its excretion (Hegstel et al., 1981; Margen



et al., 1974; Kerstetter et al., 1989). Calcium is used to regulate the permeability and biological membrane (such as cell walls) potentials, which in turn control muscle and blood vessel expansion and contraction, nerve functions, secretion of hormones and enzymes and transmitting impulses throughout the nervous system (NAP, Washington DC, 1997).

Magnesium is the fourth most abundant mineral in the body and is essential for good health. Ribosomes contain large amounts of Mg^{2+} and the stabilization provided is essential to the complexation of this ribo-protein (Sperazza et al., 1983). The Mg^{2+} ion tends to bind only weakly to proteins ($K_d \leq 10$) and this can be exploited by the cell to switch enzymatic activity on and off by changes in the local concentration of Mg^{2+} . Magnesium is a cofactor in hundreds of enzymatic reactions (Grubbs et al., 1987; Wacker et al., 1968; Saris et al., 1996; Beyenbach et al. 1990; Romani et al., 1992) and is important for those enzymes that use nucleotides as cofactors or substrates. Mg is required for protein and nucleic acid synthesis, the cell cycle, cytoskeletal and mitochondrial integrity and for the binding of substances to the plasma membrane (Wacker et al., 1968; Beyenbach et al. 1990). Mg frequently modulates ion transport by pumps, carriers and channels (Beyenbach et al., 1990; Romani et al., 1992; Agus et al., 1991; Flatman et al., 1991) and thereby may modulate signal transduction and the cytosolic concentrations of Ca and potassium. Green vegetables such as spinach are good sources of magnesium because the chlorophyll molecule contains magnesium. Magnesium toxicity and magnesium deficiency both cause

similar symptoms, including diarrhea, nausea, vomiting and appetite loss. Changes in mental status are also possible, including anxiety, irritability and confusion.

Red meats, especially beef, lamb, and shell fish have highest concentration of zinc in food (Berdanier et al., 2007). Zinc is also present in low concentrations in potatoes, wheat (20-60 ppm), sweet corn (about 20 ppm) apples and oranges (1ppm). Zinc is also found in beans, nuts, almonds, whole grains, pumpkin seeds and sun flower seeds. Symptoms of chronic zinc deficiency are stunted growth and retarded sexual development. Zinc deficiency during gestation causes a variety of advance effects in the foetus including abortion, malformations and growth failure. Higher concentrations of zinc in human body suppress copper and iron absorption. The free zinc ions in solution are highly toxic to invertebrate and vertebrate fish. Free zinc ions react with hydrochloric acid of gastric juice to form corrosive zinc chloride, which can cause damage to the stomach lining (Klevay et al., 1994).

Maleic acid (Ma) is a dicarboxylic acid and more soluble in water, than its isomer fumaric acid. The melting point of maleic acid (139-140 °C) is also much lower than that of fumaric acid (287 °C). Both properties of maleic acid can be explained on account of the intramolecular hydrogen bonding that takes place in maleic acid at the expense of intermolecular interactions and that are not possible in fumaric acid for geometric reasons. The major industrial use of maleic acid is its conversion to fumaric acid which is catalysed by a variety of reagents, such as mineral acids



and thiourea. Conversion of the cis isomer into the trans isomer is possible by photolysis in the presence of a small amount of bromine. Maleic acid is an industrial raw material for the production of glyoxylic acid by ozonolysis (Kurt et al., 2000).

Acetonitrile (AN) is a colorless polar aprotic solvent (Loudon, 2002). It behaves as a weaker base (Laubengayer et al., 1945) and as a much weaker acid (Fritz et al., 1955) than water. It has a dielectric constant of 36 and autoprotolysis constant of 33.6 . AN also acts as a strongly differentiating solvent with a modest solvating power for many polar ionic solutes (Aktas et al., 2006).

Hence Mal is selected for speciation studies of its complexes with Ca(II), Mg(II) and Zn(II) in AN-water mixtures. The protonation constants of Phe and Mal in EG- and AN- water mixtures were reported earlier. (Sreevaram et al., 2015a and Sreevaram et al., 2015b).

EXPERIMENTAL

Materials: Acetonitrile (Merck, Mumbai) was used as received. Aqueous solutions of Maleic acid and sodium chloride (E-Merck, Germany) were prepared. Metal solutions of Ca(II), Mg(II), and Zn(II) chlorides were prepared. To increase the solubility of Mal and to suppress the hydrolysis of metal salts, the mineral acid concentration in the above solutions was maintained at 0.05 M. To assess the errors that might have crept into the determination of the concentrations, the data have been subjected to analysis of variance of one way classification (ANOVA). The strength (concentration)

of alkali has been determined using the Gran plot method (Gran, 1952, 1988).

Apparatus: The titrimetric data were obtained with a calibrated ELICO (Model L1-120) pH-meter (readability 0.01) which can monitor the changes in H^+ concentration. The pH meter was calibrated with 0.05 M potassium hydrogen phthalate in acidic region and 0.01 M borax solution in basic region. The glass electrode was equilibrated in a well-stirred AN-water mixture containing inert electrolyte. All the titrations were carried out in the medium containing varying concentrations of AN ($0-60.0$ % v/v) maintaining an ionic strength of 0.16 M with sodium chloride at 303.0 ± 0.1 K. The effect of variations in asymmetry potential, liquid junction potential, activity coefficient, sodium ion error and dissolved carbon dioxide on the response of glass electrode were accounted for in the form of correction factor (Sailaja et al., 2004).

Procedure: For the determination of stability constants of metal-ligand binary species, initially titrations of strong acid with alkali were carried out at regular intervals to check whether complete equilibration was achieved. Then the calomel electrode was refilled with AN-water mixture of equivalent composition as that of titrand. In each of the titrations, the titrand consisted of approximately 1 mmol mineral acid in a total volume of 50 mL. Titrations with different ratios ($1 : 2.5$, $1 : 3.75$ and $1 : 5.0$ in Ca(II), Mg(II) and Zn(II)) of metal-to-ligand were carried out with 0.4 mol L^{-1} sodium hydroxide. Other experimental details are given elsewhere (Raju et al., 2012).



RESULTS AND DISCUSSION

Alkalimetric titration curves in AN-water mixtures revealed that the acido-basic equilibria of Mal (LH_2 , LH and L^-) were active in the pH range 2.0-3.0, 3.0-7.0 and 7.0-12.0, respectively. Based on the active forms of the ligands in this pH range, models containing various numbers and combination of complex species were fed to MINIQAD75 along with the alkalimetric titration data. The models indicated better statistics as the number of species was increased, confirming better fit. There was no further improvement in the fit on inclusion of some more species in the model containing CaL , CaL_2 and CaL_3 . This indicates that the final model appropriately fits the experimental data. Such exhaustive modeling was performed for all the systems. The best-fit model was selected using the statistical parameters (Rao et al., 1991) of the least squares residuals. A very low standard deviation in $\log \beta$ values indicates the precision of these parameters. The small values of U_{over} (sum of squares of deviations in the concentrations of ingredients at all experimental points corrected for degrees of freedom) indicate that the experimental data can be represented by the model. Small values of mean, standard deviation and mean deviation for the systems corroborate that the residuals are around a zero mean with little dispersion. For an ideal normal distribution, the values of kurtosis and skewness should be three and zero, respectively. Kurtosis is a measure of the peakedness of the error distribution near a modal value. For an ideal normal

distribution kurtosis value should be three (mesokurtic). If the calculated kurtosis is less than three, the peak of the error distribution curve is flat (platykurtic) and if the kurtosis is greater than three, the distribution shall have sharp peak (leptokurtic). The kurtosis values in the present study indicate that the residuals form leptokurtic as well as platykurtic patterns. The values of skewness recorded in the tables are between -2.30 and 3.82. These data evince that the residuals form part of a normal distribution. Hence, the least-squares method can be applied to the present data. The sufficiency of the model is further evident from the low crystallographic R-value recorded. These statistical parameters thus show that the best-fit models portray the metal-ligand species in AN-water mixture.

Effect of systematic errors on best-fit model

In order to rely upon the best chemical model for critical evaluation and application under varied experimental conditions with different accuracies of data acquisition, an investigation was made by introducing pessimistic errors in the influential parameters (Latha et al., 2007) like concentrations of alkali, mineral acid, ligand and metal (Table 3). The order of the ingredients that influence the magnitudes of stability constants due to incorporation of errors is alkali > acid > ligand > metal. Some species are even rejected when errors are introduced in the concentrations. This study confirms the appropriateness of the chosen best-fit models. This study also indicates the relative sensitivities of model parameters.



Table 1: Effect of errors in influential parameters on the Ca(II) Maleic acid complex stability constants in 20% v/v AN-water mixture.

Ingredient	% Error	log β (SD)		
		110	120	130
Alkali	0	3.89(8)	7.92(8)	19.04(9)
	-5	Rejected	Rejected	Rejected
	-2	3.95(26)	Rejected	19.63(32)
	+2	3.94(24)	8.19(65)	19.66(29)
	+5	Rejected	Rejected	Rejected
Acid	-5	Rejected	Rejected	Rejected
	-2	3.76(34)	8.29(59)	19.87(19)
	+2	3.78(32)	Rejected	19.65(21)
	+5	Rejected	Rejected	Rejected
Ligand	-5	3.89(54)	8.11(61)	19.75(26)
	-2	3.62(37)	7.84(22)	19.23(15)
	+2	3.58(33)	7.93(15)	19.42(14)
	+5	3.99(65)	8.12(52)	19.38(21)
Metal	-5	3.67(37)	7.93(29)	19.72(16)
	-2	3.96(12)	7.81(29)	19.12(11)
	+2	3.64(26)	7.79(26)	19.25(13)
	+5	3.72(32)	7.96(31)	19.75(17)

CONCLUSIONS

The present biomimetic studies of metal ion complexes with Maleic acid in AN-water mixtures indicated that the complexes were non protonated in acidic pH values. The species detected were ML , ML_2 and ML_3 to Ca(II), Mg(II) and Zn(II) ions. The log β values non-linearly increased with 1/D of the medium, indicating the dominance of non-

electrostatic forces over electrostatic forces, in Ca(II), Mg(II) and Zn(II). The order of ingredients influencing the magnitudes of stability constants due to incorporation of errors in their concentrations was alkali > acid > ligand > metal. The stability constants of binary complexes were found to follow the trend Mg(II) < Zn(II) < Ca(II).



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