SOLUTION STATE AND THERMODYNAMIC STUDIES ON BINARY COMPLEXES OF THE TH(IV) WITH SOME HYDROXY ACIDS

SANGITA SHARMA and K.M. JOSHI

Department of Chemistry, Hemchandracharya North Gujarat University, Patan 384 265, Gujarat, India
sangitamem2000@gmail.com

***Abstract*— A Solution state study on complexation behavior of Th(IV) with hydroxy acids (malic acid, lactic acid, salicylic acid and mandelic acid) has been carried out using the Irving–Rossotti titration technique in aqueous media and mixed media at different temperatures and ionic strengths. The dissociation constant and stability constants (logβ) of the resulting complexes have been calculated with the Fortran IV program BEST using the method of least squares and considering the BESTFIT model. Species distribution curves of complexes have been plotted as function of pH using the SPEPLOT Fortran IV program to visualize various species in equilibrium in the pH range 2–14. Thermodynamic properties were calculated and negative ΔG, ΔH and ΔS values indicated that complex formation is a spontaneous and exothermic process at these temperatures. To understand more about these equilibriums, the stability of these complexes was studied in presence of various systemic errors.**

***Keywords*— Stability constant, Thermodynamic parameters, Hydroxy acids, Systemic error, Dissociation constant.**

I. INTRODUCTION

Aromatic hydroxy acids and their derivatives or constituents are important biologically active compounds and display a range of physiological effects. Malic acid is the source of extreme tartness in confectionery, so it is called as extreme candy. It has also been used with or in place of the less sour citric acid in sour sweets (UKFSA, 2011; USFDA, 2011). Cyclic esters have been derived from L- malic acid and followed by ring opening polymerization (Raybaudi Massilia *et al*., 2009). There are four major areas for the current uses and applications of lactic acid: food, cosmetic, pharmaceutical and chemical industry. It is widely used in almost every segment of the food industry, where it serves in a wide range of functions, such as flavoring, pH regulation, improved microbial quality, and mineral fortification. Moreover, lactic acid is used commercially in the processed meat and poultry industries, to provide products with an increased shelf life, enhanced flavor, and better control of food-borne pathogens. Due to the mild acidic taste of lactic acid, it is also used as an acidulant in salads and dressings, baked goods, pickled vegetables and beverages. Moreover, lactic acid is used in a wide variety of mineral preparations, which include tablets, prostheses, surgical sutures, and controlled drug delivery systems (Datta *et al*., 1995). Salicylic acid is a key ingredient in many skin-care products for the treatment of acne, psoriasis, calluses, corns, keratosis pilaris, warts and used in acute rheumatism. Salicylic acid is also used to prepare salicylic acid- formaldehyde polymer (Grimes, 1999). It has been a ligand to prepare polymeric chelates since the end of XIX century (Towle, 1876). Mandelic acid has a long history of use in the medical community as an antibacterial, particularly in the treatment of urinary tract infections (Taylor, 1999). It has also been applied as an oral antibiotic and it is an alternative to glycolic acid in skin care products (Ley and Heinz- Jürgen, 2001; Herold *et al*., 2002; Lourens *et al*., 2002). Mandelic acid is also recommended for pre- and post-laser treatment, reducing the amount of redness and irritation caused by laser resurfacing (Su *et al*., 2001). Lanthanone (III) complexes play an important role in various biochemical reactions (Jakusch *et al*. 2002; Garg *et al*., 2003; Calderon and Yatsimirsky, 2004; Mathur *et al*., 2007). Many binary and ternary complexes of these acids with transition and inner transition metals have been studied pH metrically (Crea *et al*., 2007; Shokrollahi *et al*., 2008; Kavosh and Rezaienejad, 2012).

Here, we have studied the relative stabilities of Th(IV)–Hydroxy acid (malic acid, lactic acid, salicylic acid and mandelic acid) complexes at (30 ± 0.1), (40 ±0.1), (50 ± 0.1) °C and at the ionic strengths 0.1-0.4 mol^{-1} ($NaClO_4$). Thermodynamic parameters like ΔG, ΔH and ΔS have been evaluated. Effects of pessimistic errors have also studied considering change in concentration of dissolved carbon dioxide, alkali, acid, ligand and metal content. Species curves were drawn to explain more about these equilibriums.

II. EXPERIMENTAL

A. Materials:

All chemicals used were analytical reagent grade. Complexing reagents like malic acid (99.05 % purity), lactic acid (99.15 % purity), salicylic acid (99.35 % purity) and mandelic acid (99.00) % purity) were purchased from Sun Pharmaceuticals, Vadodara, India). Thorium nitrate (99.3 % purity, Sigma-Aldrich, USA) was used without further purification. The Thorium nitrate solutions were acidified with accurately known amounts of $HClO_4$ (99.0 % purity, E. Merck Ltd., Mumbai, India) to prevent hydrolysis. The exact concentrations of the solutions of the Thorium nitrates were determined by complex metric titration with the disodium salt of EDTA (99.2 % purity, E. Merck Ltd., Mum-

bai, India), using EBT (98.5 %purity, E. Merck Ltd., Mumbai, India) as the indicator. All solutions were prepared in doubly distilled CO_2-free water. Perchloric acid was standardized with standard NaOH (99.0 % purity by HPLC, E. Merck Ltd., Mumbai, India), and constant ionic strength of solutions were maintained with the inert electrolyte sodium perchlorate ($NaClO_4$) (99.0 % purity, E. Merck Ltd., Mumbai, India).

B. Apparatus.

Potentiometric titrations were carried out with a Systronics µ-pH meter 361 having a combined glass electrode with readability of ±0.01 and temperature probe. The temperature was controlled with a High Precision Water Bath (Cat. No. MSW-274) with readability ±0.1ºC. Titrations were carried out in a specially designed glass cell with magnetic stirrer, in a nitrogen atmosphere to avoid any side reactions from atmospheric CO_2.

C. Preparation of titration sets.

The following three sets were prepared for titrations:

- Acid [40 mmol L^{-1}]
- Acid [40 mmol L^{-1}] + Hydroxy acid [10 mmol L^{-1}]
- Acid [40 mmol L^{-1}] +Hydroxy acid [10 mmol L^{-1}] + Thorium nitrate [1 mmol L^{-1}].

Total volume used in the cell was 50 ml, ionic strength was maintained at 0.1, 0.2, 0.3 or 0.4 mol L^{-1} [$NaClO_4$] and temperature was maintained at 30±0.1ºC, 40±0.1ºC, 50±0.1ºC in all sets. Titrations were carried out with carbonate free standardized 0.2 mol L^{-1} NaOH solutions. A representative titration graph for Th(IV)- Salicylic acid binary system has been given in Fig. 1.

III. RESULTS AND DISCUSSION

A. Selection of Model.

An appropriate equilibrium model from among many feasible models was selected to establish whether or not, this equilibrium model adequately represents the data. So as to establish the criteria to select the "best" model, one or more of the following tests were performed:

(a) The lowest sum of squares of residuals that is the difference between experimental and calculated values.

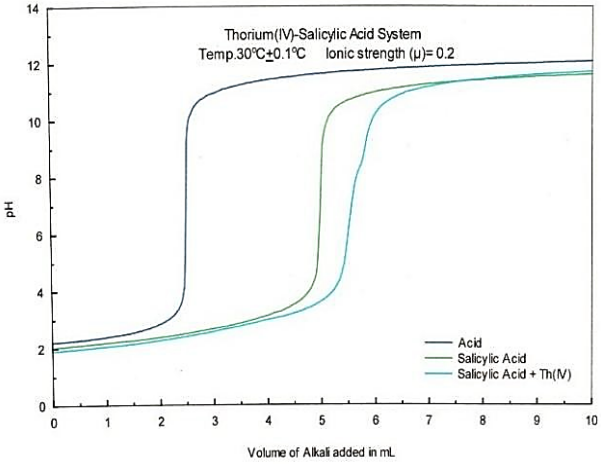

Figure 1. pH metric titration curves for the Th(IV)-Salicylic acid binary system

(b) The minimum variance of the dependent variable, σ^2

(c) A statistical examination of the set of residuals.

The evaluation of dissociation constants and stability constants was done by including the refinement of initial estimates through inclusion of neighboring overlapping reactions. The most common determination of dissociation constants was widely employed in accepted computer programs which had been originally designed for the refinement of metal – ligand stability constants. The minimization values of $S_{min}= \Sigma (\upsilon_{obs}-\upsilon_{cal})$ where υ is the volume of titrant added at each point and $(\upsilon_{obs}-\upsilon_{cal})$ is the difference between the calculated and observed values. Internal consistency and a good sigma fit are rather easy to achieve because the curve fitting algorithm is set up to do just that. A poor or incorrect model is either incomplete or an incorrect statement of species present.

A BESTFIT model was developed after considering a set of experimental conditions for calculating dissociation and stability constants. This model was used for various calculations and the σ_{fit} was calculated by using BEST FORTRAN VI program (Motekaitis and Martell, 1982; Ramunas and Martell, 1982) .

B. Dissociation Constants.

The results from Table 1 show that the values of dissociation constants of four selected hydroxy acids are constant. The results are comparable with literature values.

C. Stability Constants.

BESTFIT model was developed considering S_{min}<1 and repeating each titration three times between pH 2 and 10 with 60-70 titration data points. The stability constants of the binary complexes formed due to interaction of tetravalent Th(IV) ion with hydroxyl acids like Malic acid, Lactic acid, Salicylic acid and Mandelic acid were calculated by measuring the protons liberated during the titration of the ligand in absence and in presence of metal against standard sodium hydroxide solution i.e. from separation of curves obtained from titration sets (ii) and (iii). The metal ligand stability constant values have been presented in the Table 2. The stability of complexes so formed is governed by properties of both metal and ligand, considering other factors like, temperature, pressure, kinetic effect, thermodynamic effects. The inner transition metals are typical hard acids. The low stability of inner transition metals complexes can be increased by the chelating effect. Inner transition metals are also hard acceptors and have high degree of ionic bonding. The most stable oxidation state of Th(IV) in their complexes is +4 and formation of stable complexes requires coordination numbers of 6 to 12. The coordination number changes as the ligand and experimental conditions change.

In case of hydroxyl acids, the two proton dissociation constants are apart. The hydrogen bonded to –COOH gets dissociated at lower pH and hence it is the region where complexation is possible. So the metal-ligand stability constant is dependent on the first dissociation constant of ligand. All the hydroxy acids are bi-

dentate ligands and coordination can take place from one –OH and one –COOH group except in case DL-Malic acids which is tridentate in nature. The order of stability of binary complexes on the basis of the hydroxy acid as a ligand is as given below: Malic acid> Lactic acid> Salicylic acid >Mandelic acid.

Salicylic acid has the lowest basicity but the stability of its binary complexes is higher than the stability of the complexes with Mandelic acid. It might be due to the ring structure of salicylic acid which has led to ring stabilization when complexed. DL- lactic acid has the highest value for dissociation constant (K_1^H) but log K_2 value for binary complexes of DL- Malic acid is higher than log K_2 of DL- Lactic acid. DL- Malic acid is a tridentate ligand with one –OH group and two -COOH groups. Two stability constant values (log K_1 and log K_2) are obtained in case of DL- Malic acid showing the participation of both –COOH groups during complexation with Thorium(IV).

D. Effect of ionic strength.

The log B_n values decreased with increase in ionic strength in all selected complexes. The values of dissociation constants and metal ligand stability constants decreased with increase of ionic strength of medium which is in agreement with Debye Hückel treatment. The thermodynamic stability constant (log K_0) is obtained by extra plotting the linear plot of log K vs $\sqrt{\mu}$ to zero ionic strength is given in Table 3.

E. Effect of Temperature.

The values of stability constants in Table 2 revealed that stability constants decreased with increase in temperature along with the pK_H values. The high temperatures have not favored the formation of stable complexes.

F. Effect of systemic error on the best fit model.

In order to rely upon the best fit chemical model for critical evolution of stability constants in the present set of experimental conditions, an investigation was made by introducing pessimistic error in calculation in the form of change in concentration of dissolved carbon dioxide, alkali, acid, ligand and metal content. BEST does not have direct option for calculation of systematic error on stability constants but pessimistic small changes in various components can be explained as change in stability constants. These has been reported as percentage error for the representative Th(IV)-Salicyclic acid complexes in Table 4. The order of systematic error for these complexes has been as: dissolved carbon dioxide > alkali > acid > ligand > metal. It is observed that when the error is high, the percentage of species ML and ML_2 get changed (decrease or increase) and hydroxy species become predominant.

G. Thermodynamic Parameters.

Determination of stability constants at different temperatures has been used in the evaluation of thermodynamic parameters accompanying the formation of metal complexes. The enthalpy change (ΔH) reflect the energy changes with the intermolecular bonding whereas free energy factor (ΔG) gives the magnitude of stability of a particular species in equilibrium. The values of overall change in the free energy (ΔG), enthalpy (ΔH) and the entropy (ΔS) for the complexation reaction of metal ions and hydroxyl acids are reported in the Table 2. The enthalpy changes (ΔH) have been calculated from linear plots of log K vs $1/T$ according to equation of isobaric reaction.

$$\frac{d\log(K_1/K_2)}{d(1/T)} = \frac{-\Delta H}{4.57} \qquad (1)$$

The data showed that the dissociation constant of the ligands and their stability constants with metal ions decreased with the increase in the temperature, indi-

Table 1: Dissociation constants of Hydroxy Acids at μ= 0.2M dm^{-3} ($NaClO_4$)

Hidroxy Acids	30±0.1ºC			40±0.1ºC			50±0.1ºC		
	pK_1^H	pK_2^H	pK_3^H	pK_1^H	pK_2^H	pK_3^H	pK_1^H	pK_2^H	pK_3^H
Malic Acid	11.7001	4.7801	3.2100	11.5899	4.6008	3.1978	11.3008	4.3287	3.0861
Lactic Acid	11.410	3.8300	--	11.2987	3.7991	--	11.1438	3.6334	--
Salicylic Acid	11.8000	2.9300	--	11.6987	2.7384	--	11.5849	2.5998	--
Mandelic Acid	11.6000	3.1800	--	11.5384	3.0091	--	11.2489	2.9114	--

Values are calculated from point wise calculation method

Table 2: Stability Constants and Thermodynamic Parameters Th(IV)-Hydroxy Acid complexes

Hydroxy Acids		Stability Constant			ΔG (KCal.mol^{-1})			ΔH (KCal.mol^{-1})		ΔS (KCal.mol^{-1})	
		303K	313K	323K	303K	313K	323K	313K	323K	313K	323K
Malic Acid	logK_1	22.3619	22.1097	21.9873	-31.01	-31.63	-32.46	-10.93	-5.66	-0.0329	-0.0149
	logK_2	24.7812	24.5148	24.3101	-34.36	-35.07	-35.88	-11.55	-9.46	-0.0346	-0.0267
	S_{min}	0.7277	0.5800	0.9799							
LacticAcid	logK_1	11.4619	11.3009	11.1476	-15.89	-16.16	-16.46	-6.98	-7.08	-0.0214	-0.0210
	logK_2	13.8812	13.6120	13.4009	-19.25	-19.47	-19.78	-11.67	-9.75	-0.0366	-0.0292
	S_{min}	0.6355	0.1421	0.7329							
Salicyclic Acid	logK_1	4.3119	4.17091	4.0001	-5.98	-5.97	-5.9	-6.11	-7.89	-0.0196	-0.0246
	logK_2	7.7312	7.6101	7.3429	-10.72	-10.89	-10.84	-5.25	-12.35	-0.0162	-0.0384
	S_{min}	0.7231	0.5834	0.8991							
Mandelic Acid	logK_1	4.0604	3.9114	3.7004	-5.63	-5.59	-5.46	-6.46	-9.75	-0.0207	-0.0306
	logK_2	7.4797	7.2149	6.9018	-10.37	-10.32	-10.19	-11.47	-14.47	-0.0368	-0.0452
	S_{min}	0.2061	0.7390	0.9789							

cating a reaction which is exothermic in nature. This isalso evident from negative values of the enthalpy (ΔH). The negative values of free energy (ΔG) and entropy (ΔS) indicate that these factors are major driving force for the spontaneity of such reactions. The enthalpy changes accompanying the solution are the characteristic properties of the heat of the reaction and measures energy difference between metal ligand (ML) and the metal water [M-H_2O] coordination bonds. The obtained results suggested that the metal-ligand bonds are fairly strong as evidenced by their negative enthalpy changes.

The entropy changes accompanying the formation of metal complexes can be related to the number of reacting species in the system and changes in solvation of the reactant and product species.

During the formation of metal complexes in the solution, the ligand species get coordinated to the solvated metal ions by displacing the water molecules from the aqua complex $[M(H_2O)n]^{4+}$ as shown by the following equation

$$[M^{4+}(H_2O)n] + L(aq) \rightarrow ML^{4+}(aq) + nH_2O.$$

The significance of the thermodynamic quantities can be known by considering the well-known thermodynamic relationship:

$$\Delta G = -2.303RT \log K$$

and

$$\Delta G = \Delta H - T\Delta S \qquad (2)$$

For all the binary complexes studied, the negative ΔH and ΔS values indicate that both enthalpy and entropy factors are favoring the complex formation. The decreases in the log K values with the increase in the temperature show that the reactions are exothermic. This probably results from the covalent interaction between the metal ions and oxygen of the ligand. The positive entropy changes could be due to the displacement of water molecules from hydration shells of interacting ions which accompanies the electrostatic interaction between positively charged metal ions and the electron pair of nitrogen (ligand).

H. Species Distribution.

For development of species distribution plots, the data were pruned for different set of models and for various expected stoichiometric species like HL, H_2L, ML, ML_2 and MLH_{-1}.. Perusal of species diagram revealed that ML_2 species lie in between 92-97% in pH range 8.0-12.0 and 75-80% ML species are formed in pH range of 5.5-6.8. Stability constant values and species distribution diagrams revealed that ML_2 is the most stable type of species formed. Species distribution curves were plotted with the help of SPEPLOT program (Motekaitis and Martell, 1992) and a representative species distribution plot for binary Th(IV) Salicylic systems is presented in Fig. 2.

IV. CONCLUSION

PH-metric studies on interaction of Th(IV) with Hydroxyl acids namely lactic acid, malic acid, salicyclic acid and mandelic acid revealed that hydroxyl acids contain two dissociable sites except in malic acid (three dissociatin constants) at low pH Species distribution curves and calculations using BESTFIT models showed that ML_1 and ML_2 type of binary complexes were formed, with dominance of ML_2 type of complexes. The stability of all the analogous complexes were in order Malic acid> Lactic acid> Salicylic acid >Mandelic acid

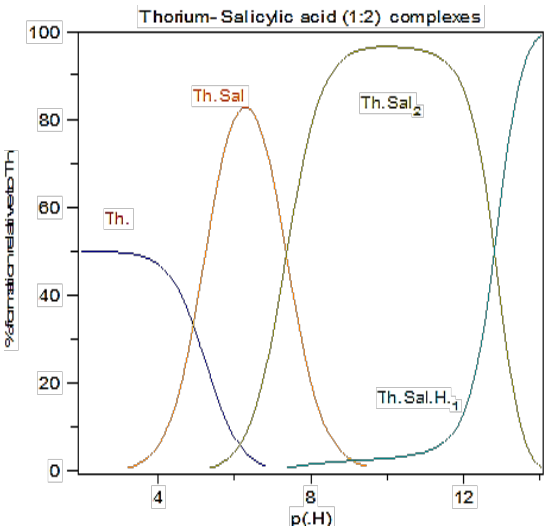

Figure 2. Species distribution curves as function of pH calculated for binary Th(IV)-Salicylic systems in ratio of 1:10 at 30 ± 0.1 °C, μ = 0.2 mol·L^{-1} ($NaClO_4$). Th.Sal=ML, $Th.Sal_2=ML_2$, $Th.Sal.H_{-3}$ =ML(OH).

Table 3: Binary Stability constants of Th(IV)-Hydroxy acids at different ionic strength at temperature 30 ± 0.1ºC. $\log\beta_1 = \log\beta_{ML}$ and $\log\beta_2 = \log\beta_{ML} + \log\beta_{ML2}$

	Stability Constant	Ionic Strength				
		0.1	0.2	0.3	0.4	log K_0
Malic acid	log β_1	22.4809	22.3619	22.0011	21.8901	23.1594
	log β_2	24.9312	24.7812	24.7812	24.2713	25.6713
	S_{min}	0.9831	0.7277	0.5800	0.9799	
Lactic acid	log β_1	11.5902	11.4619	11.4321	11.2141	11.9484
	log β_2	13.9734	13.8812	13.7891	13.3801	11.5844
	S_{min}	0.5841	0.6355	0.1131	0.5321	
Salicylic acid	log β_1	4.7218	4.3119	4.0981	3.9688	5.4382
	log β_2	7.9802	7.7312	7.5821	7.2431	8.7093
	S_{min}	0.1149	0.7231	0.1932	0.6132	
Mandelic acid	log β_1	4.3510	4.0604	3.8431	3.6321	5.0688
	log β_2	7.8611	7.4797	7.1390	6.7328	9.0098
	S_{min}	0.4298	0.2061	0.1141	0.3981	

Table 4: Effect of Systematic Errors on equilibrium of Th(IV)-Salicyclic acid complexes in 10% Ethanol-Water (v/v) Mixture.

Component	% of Error	$\log\beta_{ML}$	$\log\beta_{ML2}$	$\beta_{ML(OH)}$
Dissolved Carbon Di-oxide	10	26.1109	26.0091	-2.3468
	5	24.9981	26.3192	-2.6005
	0	22.3619	24.7812	-2.7031
	-5	23.1121	25.1192	-2.7085
	-10	24.6812	25.9873	-2.4678
Alkali	10	18.1432	16.1214	-2.1650
	5	20.1321	20.1321	-2.5100
	0	22.3619	24.7812	-2.2639
	-5	21.1321	23.1421	-2.1659
	-10	24.1244	25.9802	-2.3990
Acid	10	22.4721	24.9999	-2.1425
	5	22.4009	24.9822	-2.3425
	0	22.3619	24.7812	-2.5415
	-5	22.1149	24.1132	-2.1115
	-10	22.0091	24.0091	-2.8140
Ligand	10	23.9987	25.9973	-2.3415
	5	23.1141	25.8622	-2.4482
	0	22.3619	24.7812	-2.7429
	-5	22.0091	24.0892	-2.1425
	-10	22.0087	24.0013	-2.6107
Metal	10	23.2422	25.8711	-2.5695
	5	23.1421	25.0278	-2.6295
	0	22.3619	24.7812	-2.7012
	-5	22.0987	24.1102	-2.4393
	-10	22.0011	24.0021	-2.7095

$\log\beta_1 = \log\beta_{ML}$ and $\log\beta_2 = \log\beta_{ML} + \log\beta_{ML2}$

as anticipated by the increasing pK values. The order of systematic error effect on stability of complexes was: dissolved carbon dioxide > alkali > acid > ligand > metal. When the error was large, the percentage of species ML and ML_2 change and hydroxy species became predominant. Thermodynamic studies have shown that the reactions for the formation of Th(IV) complexes with selected acids were exothermic in nature and favored by enthalpy change. The values of ΔS indicated that complexation reactions were entropically favored under present experimental conditions.

REFERENCES

Calderon, A. and A.K. Yatsimirsky, "Formation and phosphordiesterolytic activity of lanthanide(III) N,N-bis(2-hydroxy ethyl) glycine hydroxo complexes," *Inorg. Chim. Acta*, **357**, 3483-3492 (2004).

Crea, F. A. De Robertis, C. De Stefano and S. Sammartano, "Dioxouranium (VI) – carboxylate complexes. A calorimetric and potentiometric investigation of interaction with oxalate at infinite dilution and in NaCl aqueous solution at I = 1.0 mol L(-1) and T = 25°C," *Talanta*, **71**, 948-963 (2007).

Datta, R., S.P. Tsai, P. Bonsignore, S.H. Moon, J.R. Frank, " Technological and economic potential of poly(lactic acid) and lactic acid derivatives," *FEMS Microbiol. Rev.*, **16**, 221–231 (1995).

Garg, B.S., B.K Singh, D.N. Kumar and P.K. Singh "Thermodynamic parameters and stability constants of lanthanide(III) complexes of biologically active glutathione (GSH) and their chemical speciation," *Indian Journal of Chemistry*., **42(A)**, 79-83 (2003).

Grimes, P.E., "The safety and efficacy of salicylic acid chemical peels in darker racial-ethnic groups," *Dermatologic Surgery*, **25**, 18-22 (1999).

Herold, B.C., I. Scordi-Bello, N. Cheshenko, D. Marcellino, M. Dzuzelewski, F. Francois, R Morin, V. Mas Casullo, R.A. Anderson, C. Chany II, D.P. Waller, L.J. Zaneveld and M.E. Klotman, "Mandelic acid condensation polymer: novel candidate microbicide forprevention of human immuno deficiency virus and herpes simplex virus entry," *Journal of Virology*, **76**, 11236-11244 (2002).

Jakusch, T., P. Buglyo, A.I. Tomaz, J. Costa Pessoa and K. Tamas, "Thiolate-S as anchoring donor in the binary and ternary VO(IV) complexes of mercapto propionyl glycine," *Inorg. Chim. Acta*, **339**, 119-128 (2002).

Kavosh, M. and S. Rezaieneja, "Complexation of Dioxovanadium(V) with D- (-)-Quinic Acid at Different Ionic Strengths Using Different Models Based on the Debye-Hückel Theory," *Journal of Solution Chemistry*, **41**, 937-952 (2012).

Ley, J.P and B. Heinz-Jürgen, "Synthesis of polyhydroxylated aromatic mandelic acid amides and their antioxidative potential," *Tetrahedron*, **57**, 1277–1282 (2001).

Lourens, J.D, R. Zaneveld, A. Anderson, X.-H. Diao, D.P. Waller, C. Chany II, K. Feathergill, G. Doncel, M.D. Cooper and B. Herold, "Use of mandelic acid condensation polymer (SAMMA), a new antimicrobial contraceptive agent, for vaginal prophylaxis," *Fertility and Sterility*, **78**, 1107-1115 (2002).

Mathur, J.N., K. Cernochova and G.R Choppin, "Thermodynamics and laser luminescence spectroscopy of binary and ternary complexation of Am(III), Cm(III) and Eu(III) with citric acid, and citric acid + EDTA at high ionic strength," *Inorg. Chim. Acta*, **360**, 1785-1791 (2007).

Motekaitis, R.J. and A.E Martell, "BEST — A new program for rigorous calculation of equilibrium parameters of complex multicomponent systems", *Can. J. Chem.*, **60**, 2403-2409 (1982).

Motekaitis, R.J. and A.E. Martell, *Determination and Use of Stability Constants*, VCH, New York (1992).

Ramunas, J.M. and A.E Martell, "Program PKAS: a novel algorithm for the computation of successive protonation constants," *Can. J. Chem.*, **60**, 168-173 (1982).

Raybaudi-Massilia R.M., J. Mosqueda-Melgar, O. Martín-Belloso, "Antimicrobial activity of malic acid against Listeria monocyto genes, Salmonella Enteritidis and Escherichia coli O157:H7 in apple, pear and melon juices," *Food Control*, **20**, 105–112 (2009).

Shokrollahi, A., M. Ghaedi, R. Hamid Reza and N. Marzieyeh Sadat, "Potentiometric study of binary

complexes of methyl 2-pyridyl ketone oxime, phenyl 2- pyridyl ketone oxime and diacetylmonooxime with some transition and heavy metal ions in aqueous solution," *Spectrosc. Acta Part A: Mole. and Biomole. Spectrosc*.,**71,** 655-662 (2008).

Su, T., Y. Wu, B. Doughan, K. Kane-Maguire, C.K Marlowe, J.P. Kanter, J. Woolfrey, B. Huang, P. Wong, U. Sinha, G. Park, J. Malinowski, S. Hollenbach, R.M. Scarborough and B.-Y. Zhu, "Design and synthesis of glycolic and mandelic acid derivatives as factor Xa inhibitors," *Bioorganic and medicinal chemistry letters*, **11**, 2279–2282 (2001).

Taylor, MB, "Summary of mandelic acid for the improvement of skin conditions," *Cosmetic Dermatology*, **21**, 26–28 (1999).

Towle, S.K., "Salicylic acid in Acute Rheumatism", *The Boston Medical and Surgical Journal*, **5**, 593-595 (1876).

UKFSA, *Current EU approved additives and their E Numbers*, U.K. Food Standards Agency, October (2011).

USFDA, *Listing of Food Additives Status. Part II*, U.S. Food and Drug Administration, October (2011).

Received: September 26, 2014.
Accepted: July 7, 2015.
Recommended by Subject Editor: María Luján Ferreira.