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Effect of Ionic Strength on Deprotonation of Salicylic Acid and its Derivative

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Abstract

The protonation constant values of salicylic and 5-nitrosalicylic acid werestudied by a combination of spectrophotometric and potentiometric methods at 25 °C in wide range of ionic strength. The ionic strength of solutions was kept constant by sodium perchlorate as background electrolyte at 0.10 to 3.0 mol dm^{-3}. Potentiometer was calibrated according to Gran method at each of ionic strength. The pK_a values were calculated using STAR program by multivariate curve fitting of absorbance data. The dependence of deprotonation constants on ionic strength were explained by means of Specific ion Interaction Theory (SIT). Activity coefficients of species were calculated by a modified SIT approach. The specific ion interaction parameters were extracted associated with the thermodynamic protonation constant.

Keywords: pK_a, Salicylic Acid, Ionic Strength,Specific ion Interaction Theory

1.Introduction

The acid dissociation or protonation constant, pK_a, plays an important role in physicochemical behavior of compounds in reaction media. It controls the extent of ionization of the molecules relative to the pH of solution. The determination of pK_a is essential in many different area such as chemistry, geology, biochemistry and medicine. For example, many of drugs have one or more acidic or basic functions in their structure which affect the membrane permeability and solubility of those drugs[1]. In biochemistry, the protein stability and the activity of enzymes are closely related to protonation state of amino acid side chains [2]. In coordination chemistry, the extent of formation of complex is a function of protonation constant of ligands and pH of solution[3-7].

The equilibrium constants, such as protonation equilibrium, are usually determined in constant ionic strength by addition of an excess inert supporting electrolyte to solution to keep activity coefficient of all species constant during measurement process implementation. The equilibrium constants determined in this condition are named as the stoichiometric or conditional equilibrium

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constant. The knowledge of the activity coefficient of the species is needed to compare and predictconditional equilibrium constant in different ionic strength. A quantitative estimation of activity coefficient as a function of ionic strength in a broad range of electrolyte concentration can be provided by the Specific Ion Interaction Theory (SIT) [8]. This model has been successfully used in various studies for description of ionic strength effect on equilibrium constants and for determination of thermodynamics equilibrium constant by extrapolation to infinite dilution in which activity coefficient of species are unity[8-10].

Salicylic acid and some of its derivatives occur naturally in many fruits, plants and vegetables. They are the basic ingredient of a class of non-steroidal anti-inflammatory drugs with anti-pyretic, analgesic and anti-inflammatory effects [11]. The protonation constants of salicylic and 5-nitrosalicylic acid have been determined by some groups in different conditions and by a variety of methods [12-18]. However, to best of our knowledge, no systematic investigation has been done on ionic strength dependence of their protonation constants. In this study the protonation constants of salicylic and 5-nitrosalicylic acid have been determined in wide range of $NaClO_4$ electrolyte concentration. The dependence of protonation constants on ionic strength was studied by the SIT model. The thermodynamics protonation constants were calculated in infinite dilution together with the SIT interaction parameters.

2.Material and Methods

Salicylic acid and its 5-nitro derivativewere supplied from Sigma-Aldrich. Sodium perchlorate as analytical reagent grade and titrasol solutions of NaOH and HCl were obtained of Merck.Water was double-distilled with conductivity of 1.3 ± 0.1 $\mu\Omega^{-1}$ cm^{-1}.

A Jenway potentiometer, model 3520, was used for potentiometric measurements. The *emf* of titration cell was measured by a combined glass electrode. A UV-Vis Shimadzu spectral photometer, model 2100, was used for spectrophotometric measurements. A double-walled reaction vessel was used as measurement cell with temperature thermostatedat 25 °C. Constant ionic strengths of 0.1, 0.5, 1.0, 1.5, 2.0 and 3.0 mol dm^{-3} were maintained by concentrated solution of $NaClO_4$. To avoid CO_2 contamination, a stream of purified nitrogen gas was bubbled through the solution during titration process.

In order to obtain exact concentration of H^+ during spectrophotometric titration, the potentiometric cell was calibrated according to Nernst's equation at each constant ionic strength. Solution of HCl with exact concentration was titrated by standardized NaOH solution. The formal electrode potential, E°_{cell}, and Nernst slope were computed in terms of known concentration of hydrogen ion for solutions at fixed ionic strength. For spectrophotometric titration, 25 mL of solution of salicylic and 5-nitrosalicylic acid was acidified to pH 2.0 and then titrated by stepwise addition of sodium hydroxide solution of 0.1 mol dm^{-3}. After each electrode stabilization, the emf and absorption spectra of solution were recorded in the interval of 200-400 nm. Then absorption data as a function of sample concentration and pH were introduced to STAR program to calculate the pK_a values [19].

3.Resultsand Discussion

Calibration of potentiometric cell in each ionic strength

Glass electrode responses to activity of hydrogen ion rather than its concentration. However, the value of hydrogen ion concentration is needed for calculation of concentration quotients such as protonation constant. Therefore, prior to each spectrophotometric titration, potentiometric cell is needed to be calibrated in terms of H^+ concentration [20]. The response of glass electrode theoretically follows the Nernst equation as [20-22].

$$E_{cell} = E°_{cell} + k\log[H^+] + k\log\gamma_{H^+} + E_{LJ} \quad (1)$$

where$E_{LJ}$and $k$is the liquid junction potential and Nernst slope respectively. In theory,$k$is equal to $2.303RT/F$ with usual meaning for R,T and F.the formal electrode potential and the activity coefficient of hydrogen ion are represented by $E°_{cell}$and γ_{H^+} respectively. In constant ionic strength, parameters of E_{LJ} and γ_{H^+} are approximately constant and can be safely introduced into k_a. Therefore, equation 1 reduces to equation 2.

$$E_{cell} = k_a + k\log[H^+] \quad (2)$$

where $k_a$is equal to $E°_{cell} + k\log\gamma_{H^+} + E_{LJ}$. The exact concentration of hydrogen ion is given by

$$[H^+] = (M_{HCl}V_0 - M_{NaOH}V_1) / (V_0 + V_1) \quad (3)$$

where$M_i$represents the molarities of i, V_0 and V_1denote the initial volume of acid and the added volume of base solution, respectively. Calibration parameters including $k_a$and k were calculated from measured *emf* data using equations of 2 and 3. The experimental *emf* values are depicted as a function of negative logarithm of proton concentration in each ionic strength in figure 1.

In all experiments, the value of k were close to Nernst slop(theoretically equals to 59.167 mV at 25 °C) with correlation coefficients of approximately $r^2 = 0.99$. By having calibration parameters, the negative logarithm of concentration of hydrogen ion, p_cH,can be properly obtained by equation 4.

$$p_cH = (k_a - E_{cell}) / k \quad (4)$$

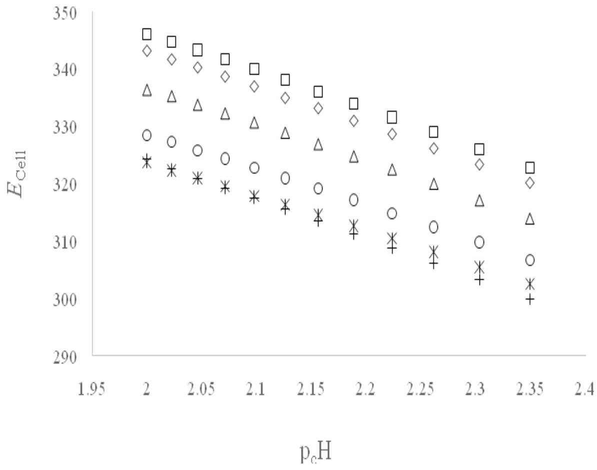

Fig. 1. Experimental emf values versus p_cH in ionic strength of 0.10 (+), 0.50 (ж), 1.00 (O), 1.50 (Δ), 2.00 (◊) and 3.00 (□) mol dm^{-3}NaClO$_4$

Calculation of protonation constants

Spectral change of 5-nitrosalicylic acid is shown typically at varying p_cH values in figure 2. Protonation constants were calculated by spectral data analysis in STAR program [19].

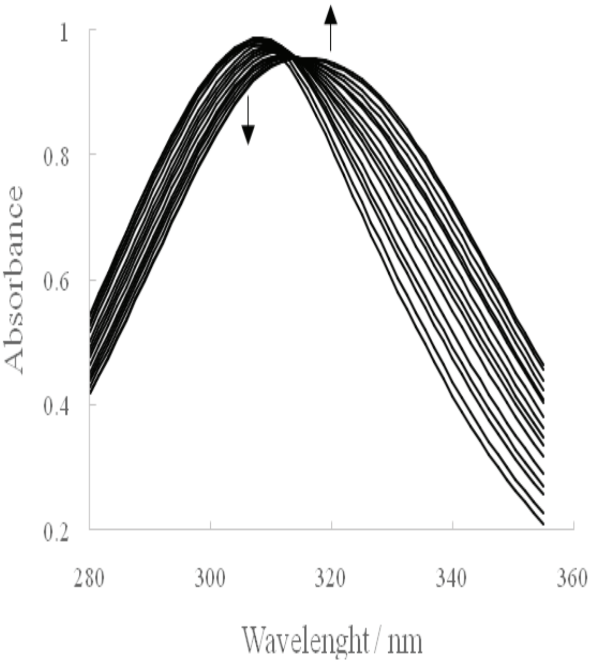

Fig. 2. Spectral change of 5-nitrosalicylic acid with increasing $p_cH$in ionic strength of 0.10 mol dm^{-3} NaClO$_4$

For each spectrophotometric titration, recorded spectra were arranged into a matrix ***R*** with dimension of $m\times n$. In matrix ***R***, m is the number of spectra with different p_cH, and n is the number of wave length in each spectrum at which the absorbance is recorded. According to Beer's law, matrix ***R*** can be represented by the matrix equation of 5

$$\boldsymbol{R} = \boldsymbol{CS} + \boldsymbol{E} \qquad (5)$$

Where $\boldsymbol{C}(m \times p)$, $\boldsymbol{S}(p \times n)$ and $\boldsymbol{E}$ are matrix of pure concentration, pure spectral profiles and optimal residual error respectively. Here p donates the number of absorbing species in the solution. The number of absorbing species was determined from factor analysis[19]. Rank analysis was performed by introducing $\boldsymbol{M}$ as $(1/n)\boldsymbol{RR}^t$, where $\boldsymbol{R}^t$ is transpose of $\boldsymbol{R}$. The rank of $\boldsymbol{M}$, $r_{\boldsymbol{M}}$,is mathematically equal to the number of eigenvectors with corresponding none zero eigenvalues. However, because of experimental error, the number of absorbing species is equal or lower than $r_{\boldsymbol{M}}$.To this problem, in factor analysis, the standard deviation of the absorbance, SD, was calculated as a function of the number of none zero eigenvalues.

$$\mathrm{SD} = \sqrt{\frac{\mathrm{tr}(M) - \sum_{i=1}^{j} a_i}{m - j}} \qquad (6)$$

Where tr($\boldsymbol{M}$) and a_i are the trace and eigenvalue of component i of $\boldsymbol{M}$ matrix. Our results indicate that the spectral change observed during titration is attributed to two absorbing species, and therefore to the first deprotonation of compounds. By this knowledge, equation 5 was solved using hard modeling multivariate curve fitting. By initial estimation of protonation constant, fitting starts by calculation of the concentration profile of two absorbing species, matrix **C**, based on the mass action law constraintin terms ofknown total concentration and p_cH values during titration. At the same time, matrix **S** is solved under non-negative absorptivity constraint for two absorbing species. In the nonlinear least-squares fitting, iterative cycles go on until to find the best set of parameters (protonation constant and molar absorptivities of species) that result in a minimum of $\boldsymbol{E}$. Typically optimized concentration profile and pure spectra for two absorbing species of 5-nitrosalicylic acid is shown in figure 3.

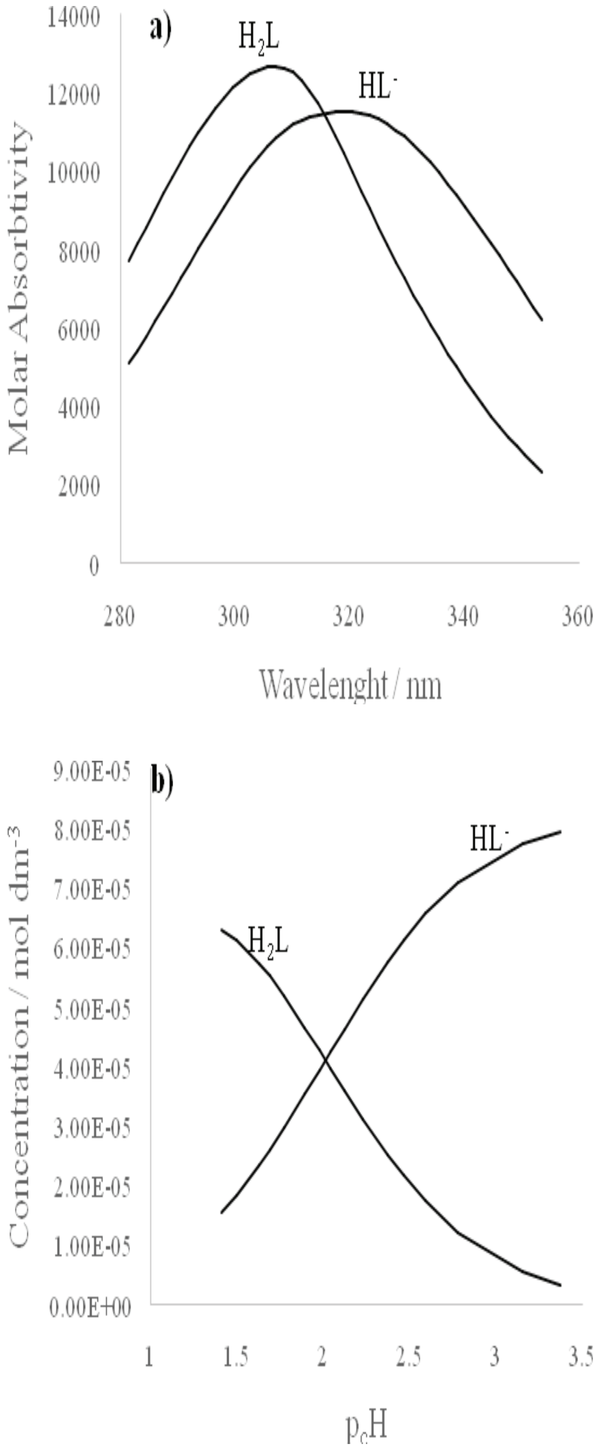

Fig. 3. a) Pure spectra and b) Optimized concentration profile for 5-nitro salicylic acid in ionic strength of 0.10 mol dm^{-3} $NaClO_4$

Table 1. Protonation constants of salicylic acid and 5-nitrosalicylic acid at 25 °C and in different ionic strength of $NaClO_4$

I		$pK_{a\text{'Salicylic Acid}}$		$pK_{a\text{'5-nitrosalicylic Acid}}$		Reference
mol dm^{-3}	mol kg^{-1}	mol dm^{-3}	mol kg^{-1}	mol dm^{-3}	mol kg^{-1}	
0.10	0.10	2.92 ± 0.01	2.91	2.02 ± 0.01	2.02	This work
0.50	0.51	2.72 ± 0.02	2.71	1.90 ± 0.01	1.89	-
1.00	1.05	2.83 ± 0.01	2.81	1.86 ± 0.02	1.84	-
1.50	1.62	2.84 ± 0.01	2.81	1.99 ± 0.01	1.96	-
2.00	2.21	3.01 ± 0.01	2.97	2.17 ± 0.01	2.13	-
3.00	3.50	3.18 ± 0.03	3.12	2.39 ± 0.02	2.32	-
0.20	-	2.75	-	-	-	[12]
0.10	-	2.90	-	-	-	[13]
0	-	2.97	-	-	-	[14]
0	-	3.02	-	-	-	[15]
0.10	-	2.81	-	2.20	-	[16]
0.10	-	2.77	-	1.92	-	[17]
0.10	-	2.83	-	-	-	[18]

The protonation constants determined by STAR program in different ionic strength are listed in Table 1 together with literature values. A disagreement between the values, obtained at the same ionic strength, may be attributed to the difference in experimental conditions involving the type of ionic media and the instrumental techniques.

Results indicate that the pK_a value of 5-nitro is lower than salicylic acid. It may be due to electron withdrawing effect of nitro group which makes deprotonated species more stable. Upon first deprotonation, molecules of salicylic acid and 5-nitorsalicylic acid take negative charge on their carboxylic group. However, the presence of electron withdrawing group of nitro on the structure of 5-nitor, results in inductive effect which stabilizes negative carboxylic group more effective than salicylic acid.

Ionic Strength Effect

As shown in Table 1, at first, the pK_a values of salicylic acid and 5-nitrosalicylic acid decreases with increasing ionic strength to 0.5 mol dm^{-3} and then increases with further increasing of ionic strength. This behavior is attributed to change of activity coefficient of species with increasing of ionic strength. Activity coefficient of species are influenced by the type of interactions between ions. At low ionic strength, interactions between ions are of attractive type; resulting in activity coefficient lower than unity. However, as the ionic strength increases, the ionic atmosphere becomes more compressed and screens the ionic charges more effectively, so repulsive interactions become more important; resulting in activity coefficient higher than unity.

The deprotonation equilibrium of two hydroxybenzoic acids can be represented by equation 7.

$$H_2 \rightleftharpoons H^+ + HA^- \qquad (7)$$

According to equation 7, the deprotonation constant can be given by

$$K_a^T = \frac{[H^+][HA^-]}{[H_2A]} \frac{\gamma_{H^+}\gamma_{HA^-}}{\gamma_{H_2A}} = K_a \frac{\gamma_{H^+}\gamma_{HA^-}}{\gamma_{H_2A}} \qquad (8)$$

Where γ_i is activity coefficient of species i; K_a^T represent thermodynamic deprotonation constant, and K_a stands for stoichiometric constant determined at each ionic strength. By taking negative logarithm on equation 8

$$\mathrm{p}K_a = \mathrm{p}K_a^T + \log\gamma_{\mathrm{H^+}} + \log\gamma_{\mathrm{HA^-}} - \log\gamma_{\mathrm{H_2A}} \quad (9)$$

The dependence of pK_a values on ionic strength may be analyzed by considering well known Specific ion Interaction Theory (SIT) [8-10]. In original SIT model, activity coefficient of ion i with charge z_i can be expressed by equation 10 in the solution of ionic strength I (in molal scale) at 25 °C.

$$\log\gamma_i = -z_i^2 \frac{0.51\sqrt{I}}{1+1.5\sqrt{I}} + \sum_j \varepsilon_{ij}\mathrm{m}_j \quad (10)$$

The ion interaction coefficient ε_ij, usually called SIT parameter, interprets the specific short range interactions of ion i with ion j in its molal concentration m_j. SIT model assumes that interaction coefficient is zero for two electrically like sign ions or neutral species.

By considering the SIT model for calculation of activity coefficients of species, equation 8 can be reformulated as following

$$\mathrm{p}K_a = \mathrm{p}K_a^T - z^* \frac{0.51\sqrt{I}}{1+\sqrt{I}} + \Delta\varepsilon I \quad (11)$$

Where

$$z^* = \sum(\mathrm{charges})^2_{\mathrm{products}} - \sum(\mathrm{charges})^2_{\mathrm{reactants}} \quad (12)$$

$$\Delta\varepsilon = \varepsilon_{\mathrm{HL^-,Na^+}} + \varepsilon_{\mathrm{H^+,ClO_4^-}} \quad (13)$$

It should be noted that pK_a and I values are in molal concentration scale.

Experimental p$K_\mathrm{a}$values form Table 1 were fitted into equation 11 as a function of ionic strength by least squares regression analysis. The following expressions were obtained in accordance with SIT model where equations 14 and 15 are obtainedfor salicylic acid and 5-nitrosalicylic acid respectively.

$$\mathrm{p}K_a = (3.04 \pm 0.04) - 2\frac{0.51\sqrt{I}}{1+\sqrt{I}} + (0.16 \pm 0.02)I \quad (14)$$

$$\mathrm{p}K_a = (2.14 \pm 0.04) - 2\frac{0.51\sqrt{I}}{1+\sqrt{I}} + (0.19 \pm 0.02)I \quad (15)$$

The goodness of fit of SIT model was judged by excellent square correlation coefficients (r^2 is 0.936 and 0.939 for equation 14 and 15 respectively), associated with low values of standard deviation obtained for each of regression coefficients. The specific interaction coefficient of $\mathrm{HClO_4}$ is 0.146 [23], therefore according to equation 13, the specific interaction coefficient between $\mathrm{HA^-}$ and $\mathrm{Na^+}$ are calculated to be 0.014 and 0.044 for salicylic acid and 5-nitrosalicylic acid respectively.

4.Conclusion

The protonation constant of salicylic acid and 5-nitrosalicylic acid were investigated by an accurate spectroscopic method in wide range of ionic strength supplied by sodium perchlorate at 25 °C. The pK_a values assigned for first deprotonation equilibrium were calculated by multivariate curve fitting implemented in STAR program. Results show that in a regular trend, at first the pK_a decreases to a minimum value at around 0.5 mol kg^{-1} of ionic strength; then increases with a relatively linear manner along the curve. The SIT theory was applied successfully to describe the ionic strength dependency of pK_a values. The thermodynamic deporotonation constant of salicylic acid and 5-nitrosalicylic acid were calculated as 3.04 and 2.14 respectively. Alsothe specific interaction coefficient between deprotonated form of salicylic acid and 5-nitrosalicylic acidwith $\mathrm{Na^+}$are calculated as 0.014 and 0.044 respectively. The SIT models obtained can be used for estimation of protonation constants of salicylic acid and

5-nitrosalicylic acid in each ionic strength in the range of 0.0 to 3.0 mol $dm^{-3}$of $NaClO_4$.

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References

[1] H.V.D.Waterbeemd, B.Testa,. Drug bioavailability: estimation of solubility, permeability, absorption and bioavailability, Wiley-VCH: Weinheim, Germany, 2008.

[2] O. Holmes,.Human acid-base physiology: a student text, Chapman & Hall Medical, London, UK, 1993.

[3] A. E. Martell, R. M. Smith,Critical stability constants, Plenum, New York, USA, 1974.

4. S. K. Sahoo, B. K. Kanungo, M. Baral,Complexation of a tripodal amine-catechol ligand tris((2,3-dihydroxybenzylamino)ethyl)amine towards Al(III), Ga(III), and In(III), Monatsh Chem.140 (2009) 139-145.

[5] A. Farajtabar, F. Gharib, P. Jamaat, N. Safari,Complexation of 5,10,15,20-Tetrakis(4-sulfonatophenyl)porphyrin with Zinc(II) Ions in Aqueous Solution. J. Chem. Eng. Data 53 (2008) 350-354.

[6] F. Gharib, M. Jabbari, A. Farajtabar, Interaction of dioxouranium(VI) ion with EDTA at different ionic strengths, J. Mol. Liq. 144 (2009) 5-8.

[7] F. Gharib, A. Farajtabar,Complexation of Dioxovanadium(V) with Cysteine in Different Ionic Media: Salt Effects and Formation Constant, Rev.Inorg. Chem. 29 (2009) 37-48.

[8] B. Allard, S. A.Banwart, J. Bruno, J. H. Ephraim, R.Grauer, I.Grenthe, J.Hadermann, W. Hummel, A.Jakob, T.Karapiperis, A. V.Plyasunov, I.Puigdomenech, J. A.Rard, S.Saxena, K.Spahiu, Modelling in Aquatic Chemistry, OCDE,France, 1997.

[9] F. Gharib, A. Farajtabar, Interaction of dioxouranium(VI) ion with serine at different ionic strength,J. Mol. Liq. 135 (2007) 27-31.

[10] C. Bretti, F. Crea, C. De Stefano, C. Foti, S. Materazzi, G. Vianelli, Thermodynamic Properties of Dopamine in Aqueous Solution. Acid–Base Properties, Distribution, and Activity Coefficients in NaCl Aqueous Solutions at Different Ionic Strengths and Temperatures, J. Chem. Eng. Data, 58 (2013) 2835-2847.

[11] R. K. Madan, J. Levitt, A review of toxicity from topical salicylic acid preparations, J. Am. Acad. Dermatol. 70 (2014) 788–92.

[12] M. Jezowska-Bojczuk, H. Kozłowski, A. Zubor, T. Kiss, M. Branca, G. Micera, A. Dessi, Potentiometric and Spectroscopic Studies on Oxovanadium(iv) Complexes of Salicylic Acid and Catechol and Some Derivatives, J. Chem. Soc., Dalton Trans. (1990) 2903-2907.

[13] G. Kortum, W. Vogel, K. Andrussow, Dissociation Constants of Organic Acids in Aqueous Solution, Butterworths (IUPAC), London, 1961.

[14] R.Ruiz, M. Roses, C. Rafols, E. Bosch, Critical validation of a new simpler approach to estimate aqueous pK_a of drugs sparingly soluble in water, Anal. Chim. Acta 550 (2005) 210–221.

[15] Z. Jia, Physicochemical profiling by capillary electrophoresis. Curr. Pharm. Anal. 1 (2005) 41–56.

[16] A. E. Martell, R. J. Motekaitis, R. M. Smith, Aluminium complexes of hydroxyaliphatic and hydroxyaromatic ligands in aqueous systems—some problems and solutions, Polyhedron, 9 (1990) 171-187.

[17] M. S. AKSOY, U. OZER, Equilibrium Studies on Chromium(III) Complexes of Salicylic Acid andSalicylic Acid Derivatives in Aqueous Solution, Chem. Pharm. Bull. 52 (2004) 1280—1284.

[18] R. Tauler, I. Marques, E. Casassas, Multivariate curve resolution applied to three-way trilinear data: Study of a spectrofluorimetric acid–base titration of salicylic acid at three excitation wavelengths, J. Chemom. 12 (1998) 55-75.

[19] J. L. Beltran, R. Codony, M. D. Prat, Evaluation of stability constants from multi-wavelength absorbance data: program STAR, Anal. Chim. Acta 276 (1993) 441-454.

[20] R.J. Motekaitis, A.E. Martell, The Determination and Use of Stability Constants, VCH, New York, 1988.

[21] G. Gran, H. Dahlenborg, S. Laurell, M. Rottenberg, Determination of the Equivalent Point in Potentiometric Titrations, Acta Chem. Scand. 4 (1950) 559-577.

[22] G. Gran, Determination of the equivalence point in potentiometric titrations, Analyst 77 (1952) 661-671.

[23] C. Bretti, C. Foti, N. Porcino, S. Sammartano, SIT Parameters for 1:1 Electrolytes and Correlation with Pitzer Coefficients, J. Solution Chem. 35 (2006) 1401-1415.