Investigation of the Specific Ion Interactions and Determining Protonation Constant of 3,5-Dihydroxy-2-(3,4,5-trihydroxybenzoyl)oxy-6-[(3,4,5-trihydroxybenzoyl)oxymethyl] oxan-4-yl] 3,4,5-trihydroxybenzoate at Different Ionic Strength

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ABSTRACT: *In this research, the protonation constant value of tannic acid was determined at 25 °C and different ionic strengths (0.1 to 0.7 mol dm^{-3} NaCl) using potentiometric titration technique. The dependence of protonation constant on ionic strength was modeled and discussed by a Debye-Hückel type equation. Then, based on the obtained data from experiments, the minimizing sum of squares error (SSE) was done by Microsoft's Excel solver program and the most suitable model was chosen. After optimization, the protonation constant of tannic acid at different ionic strengths was calculated and curves of log K_{cal} and log K_{exp} were compared. Finally, Daniele constants of C and D were measured and the Specific Ion interaction Theory (SIT) was assessed for this weak acid. The obtained results show that the protonation constants of tannic acid decrease with increasing ionic strength.*

KEYWORDS: *Tannic acid; Potentiometric titration; Debye-Hückel equation; Ionic strength effect; SIT.*

INTRODUCTION

3,5-dihydroxy -2- (3,4,5- trihydroxybenzoyl)oxy -6-[(3,4,5-trihydroxybenzoyl)oxymethyl]oxan-4-yl] 3,4,5-trihydroxybenzoate (tannic acid) is a light, shapeless, and odorless powder belongs to a big group of chemical compounds called tannin [1]. In other words, it is a special form of tannin that is considered a kind of polyphenol compounds [2]. Tannic acid belongs to the class of hydrolysable tannins and is comprised of a pentagalloylglucose core esterified at all functional hydroxyl groups with gallic acid molecules [3]. Also, this acid is a specific commercial form of tannin, and has weak acidity due to the numerous phenol groups in its structure. Tannic acid owing to the pK_a value between 7 and 8, as a function of the degree of dissociation, partially gets hydrolyzed into glucose and digallic acid moieties under mild acidic/basic conditions [4-6]. At its natural

acidic pH, tannic acid behaves as a weak reducing agent which can induce growth of only seeds to nanoparticles at room temperature [7-9]. Generally, its structure is as a polymer which has composed of gallic acid molecule, glucose, etc [10]. Tannin is used commercially in industry and also is considered as the best primary matter of pure tannic acid in acorn which exists in some types of oak trees and this acid is soluble in water, glycerin and alcohol and is not soluble in pure ether and greasy oils. It can be also used as an anticancer agent for breast and prostate cancer cell treatments [11]. Tannic acid and tannin are similar but they are sometimes wrongly used instead of each other, so it should be mentioned that tannic acid has tannin but it is not tannin itself [12].

In Debye-Hückel theory, a variable was introduced which is called ionic strength, *I*, and it has great importance in justifying the activity of ions in solution. Also, ionic strength which is a scale of average electrostatic interaction between ions in electrolyte, is equal to half the sum of sentences obtained from multiplying the concentration of each ionic species in the solution and the square of the charge on that [13].

In other words, the ionic strength of a solution is a function of the concentration of all the ions present in a solution as the following equation:

$$I = \frac{1}{2}\sum_i C_i Z_i^2 \tag{1}$$

Where C_i and Z_i are the molar concentration and the charge of ion *i*, respectively [14].

Measuring the potential of the floating electrode in a solution compared to a testifier electrode (electrode with constant potential and not in the experimented compound), is called potentiometric. Potentiometric is a method that used in measuring differences of potential between two indicator electrodes and reference electrodes and it is an electrochemical method. In this way, the amount of matter in solution is measured by direct and indirect measurement of electromotive force (*emf*) between two electrodes [15].

In this research, based on *Daniele* equation [16], the effect of ionic strength on protonation constant is calculated and also, Daniele experimental parameters, *C* and *D*, which is unknown in this equation, can be calculated. Also log K_{cal} and log K_{exp} of equilibrium

reaction were compared. The deprotonation equilibrium of tannic acid can be represented by Eq. (2).

$$HL \leftrightarrow H^+ + L^- \tag{2}$$

According to the Eq. (2), the deprotonation constant of tannic acid can be given by:

$$K_a^T = \frac{\left[H^+\right]\left[L^-\right]}{\left[HL\right]} \cdot \frac{\gamma_{H^+}\gamma_{L^-}}{\gamma_{HL}} = K_a \frac{\gamma_{H^+}\gamma_{L^-}}{\gamma_{HL}} \tag{3}$$

Where K_a^T is the thermodynamic deprotonation constant; K_a is the deprotonation constant of tannic acid which determined at each ionic strength; HL and L^- are the different species of the tannic acid in the deprotonation equilibria and γ_i is the activity coefficient of species i [17].

The carboxyl hydrogen in the digallic acid molecule is the source of the acidic properties of tannic acid. The substance is in effect a monoprotic acid, inasmuch as the OH groups attached to the benzene rings do not readily yield protons. The anion that results from the dissociation of tannic acid is $C_6H_2(OH)_3COOC_6H_2(OH)_2COO^-$ which can be abbreviated for present purposes to the symbol L^-.

Different interactions exist between species in the solution, including interactions between soluble molecules, between solvent species and between solution-soluble species and they can be classified into two groups: short-range interactions and long-range interactions [18]. Parker has also classified solvents based on specific interactions into two groups: polar protic and polar aprotic solvents [19]. In this research, the electrostatic specific ion interactions of tannic acid in aqueous media were investigated.

EXPERIMENTAL SECTION
Materials
Tannic acid with $C_{76}H_{52}O_{46}$ chemical formula, Scheme 1 [20], was purchased from Sigma-Aldrich Company with purity higher than 99%. Hydrochloric acid solution was prepared from Merck and used as supplied. Sodium hydroxide solution of 0.1 mol dm^{-3} was prepared from a titrisol solution (Merck), and its concentration was determined with a standard HCl solution. Sodium chloride was supplied from Merck as analytical reagent grade materials and without further purification. All diluted solutions were prepared using double distilled water with a conductivity of 1.5 ± 0.1 μS/cm.
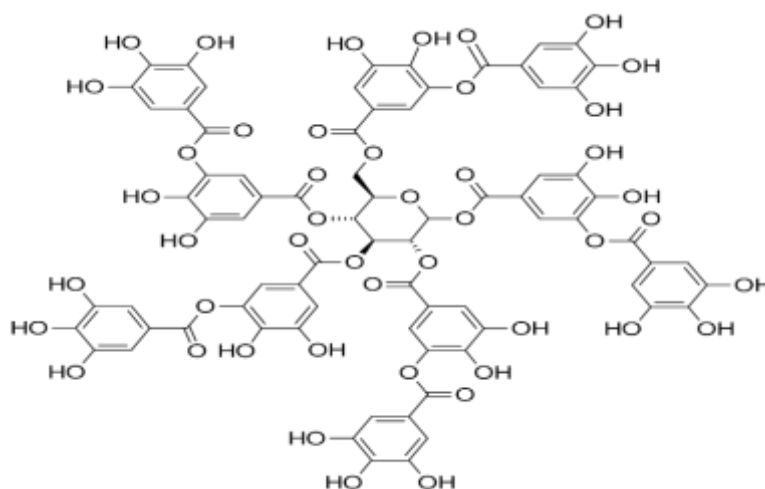
Scheme 1: Molecular structure of tannic acid.

Instrumentation

A Jenway potentiometer, model 3310, was used for potentiometric measurements. A combined glass electrode was used for electromotive force measurements. An analytical balance, Sartorius mark, model CP 124S, was used for weighing the materials needed with an accuracy of 0.1 mg. A variable sampler, Boeco mark, with usage range (100-1000) μL manufactured by German Company, was used for sampling of solutions. All titrations were carried out in a 50 ml double-wall glass vessel which combined with Optima model 740 thermostat equipment. Pure nitrogen was bubbled through the solutions in titration cells to remove O_2 and CO_2 from solutions and the solutions were stirred magnetically.

RESULTS AND DISCUSSION

Procedure

In this research, the protonation constant of tannic acid was calculated at a different ionic strength of 0.1, 0.3, 0.5 and 0.7 mol dm^{-3} NaCl. It was determined by the fitting method in Excel software and entering the logarithmic form of protonation constant of tannic acid for ionic strength which was mentioned in the program. Also, by defining an error function as (log K_{exp} - log K_{cal})^2 and its minimization, Daniele experimental parameters, *C* and *D* were calculated [17].

The relationship between logarithmic form of protonation constants and ionic strength for a specific reaction is defined as the following equation:

$$\log K = \log K_o - AZ^* \frac{\sqrt{I}}{1 + Ba\sqrt{I}} \tag{4}$$

Where K_0 is the protonation constant at infinite dilution and Z^* can be expressed by the following equation:

$$Z^* = \Sigma \left(\text{charges}\right)^2_{\text{products}} - \Sigma \left(\text{charges}\right)^2_{\text{reactants}} \tag{5}$$

The Eq. (4), can be resulted by inserting the activity coefficient of the species from the extended Debye-Hückel equation as the following equation:

$$\log \gamma_i = -AZ_i^2 \frac{\sqrt{I}}{1 + Ba\sqrt{I}} \tag{6}$$

Where γ_i is the activity coefficient of the species involved in the dissociation equilibria. The parameters of *A* and *Ba* are the temperature-dependent constants which at 25 °C they are equal to, 0.5 and $1.5\sqrt{\text{kg/mol}}$, respectively [20].

The Eq. (4) can be written for two ionic strength *I* and I_1, and then subtracted them into the following term:

$$\log K\left(I\right) = \log K\left(I_1\right) - AZ^* \left[\frac{\sqrt{I}}{1 + Ba\sqrt{I}} - \frac{\sqrt{I}}{1 + Ba\sqrt{I_1}}\right] \tag{7}$$

Where *I* and I_1 are intended ionic strength and reference ionic strength, respectively. By the use of experimental results, *Daniele* and *Colleagues* came to the conclusion that, adding $C(I-I_1)$ and $D(I^{1.5}-I_1^{1.5})$

expressions, cause better agreement between Eq. (7) and experimental results [21]. Thus the extended equation was introduced as the following term:

$$\log K(I) = \log K(I_1) - Z^* \left[\frac{0.51 I^{\frac{1}{2}}}{1 + 1.5 I^{\frac{1}{2}}} - \frac{0.51 I_1^{\frac{1}{2}}}{1 + 1.5 I_1^{\frac{1}{2}}} \right] + \quad (8)$$

$$C(I - I_1) + D(I^{1.5} - I_1^{1.5})$$

Where the constants of *C* and *D* are calculable by using Eq. (8).

Daniele parameters can be found from decreasing error function in identifying the amount of log *K*, and can be used to make convergent the applied experimental data in Excel program [17, 18]. The parameters *C* and *D* were calculated by the non-linear regression method and their values are given in this work.

The specific ion interaction theory is a way that is used for estimating the coefficient of unit ion activity by considering the interactions between different ions in electrolyte solution [21]. The coefficients of interaction are determined from obtained equilibrium constant at a different ionic strength of the solution. Also, the specific ion interaction theory uses an advanced Debye-Hückel equation which is far more complicated than Davies equation [22]. Also, it should be considered that SIT model is based on the Debye-Hückel equation. SIT model defines the coefficient of activity in molality unit as the following formula:

$$\log \gamma_i = -\frac{A Z_i^2 \sqrt{I_m}}{1 + Ba \sqrt{I_m}} + \sum \varepsilon_{(i,k)} m_k \quad (9)$$

Where *A* and *Ba* have the usual meaning, $\varepsilon_{(i,k)}$ is a parameter of specific ion interaction between *k* and *i* ions and, m_k is the molality of the ion *k* [23].

The basic hypothesis about SIT model is that, $\varepsilon_{(i,k)}$ is equal to zero based on Brösnted principle regarding the specific interactions between ions which have the same charges. Generally, $\varepsilon_{(i,k)}$ is considered to be concentration-independent [24, 25]. Excel software is used for theoretical calculations of the specific ion interactions and after doing required calculations in this software, the specific interaction coefficient between Na^+ and non-proton form of tannic acid, L^-, was calculated.

Measurements

All measurements were done at 25 ± 0.1 °C and variable ionic strength (0.1 to 0.7 mol dm⁻³ sodium chloride). In the first step, calibration of the glass electrode was performed using a titration of an exact amount of HCl solution with NaOH solution. For this purpose, 20 cm³ of acidic solution at the same temperature and ionic strength was placed in a double-wall thermostated glass vessel. Then, the acidic solution was titrated by stepwise addition of NaOH solution of 0.1 mol dm⁻³ (in the interval 0.0-0.5 cm³) at the same ionic strength. After each addition of titrant, the potential was allowed to establish and emf recorded to obtain standard electrode potential according to the Nernst's equation:

$$E_{cell} = k_1 + k \log C_{H^+} + k \log \gamma_{H^+}^+ \quad (10)$$

Where k_1 is Emprise standard potential of the cell, E_{cell}°, and the liquid junction potential, E_{LJ}, and *k* is equal to 2.303*RT/F* in which *R*, *T*, and *F* are the gas constant, temperature, and the Faraday constant, respectively [26]. As the ionic strength is kept constant in each run, so the activity coefficient of hydrogen ion and the liquid junction potential are constant too. Thus the equation 10 can be written as the following formula:

$$E_{cell} = k' + k \log C_{H^+} \quad (11)$$

Where k' is the specific constant of potentiometer cell. The Nernst's parameters, *k,* and *k'*, were obtained from the slope and the intercept E_{cell} versus log C_{H+} at each ionic strength, respectively.

The experimental E_{cell} values are shown as a function of the logarithm of proton concentration in each ionic strength of NaCl in Fig. 1.

In the second step, when the total volume of solution in the vessel reaches up to 20.5 cm³, 0.3 g of tannic acid (7.76 × 10⁻³ mol/dm³) and 2 cm³ of HCl solution of 0.1 mol/dm³ was added into the vessel and titration with NaOH of 0.1 mol dm⁻³ in the same of ionic strength was continued to reach lower potentials. In the Excel software, obtained potentials are entered according to the volume of titrant. Then, by minimizing the sum of squares errors, the protonation constant of tannic acid is calculated. All measurements are repeated at the different ionic strengths (0.1, 0.3, 0.5 and 0.7 mol dm⁻³ NaCl) and based on the amount of protonation constant which

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Table 1: The values of protonation constant of tannic acid at 25 ± 0.1 ºC and various ionic strength of NaCl.

I / mol dm^{-3}	K / 10^7
0.1	1.86
0.3	1.58
0.5	1.51
0.7	1.41

Table 2: The values of Daniele coefficients and the effective charge for determining the protonation constants of tannic acid at 25 ± 0.1 ºC.

Z^*	2
C / kg mol^{-1}	-1.42
D / kg$^{1.5}$ mol$^{-1.5}$	1.04
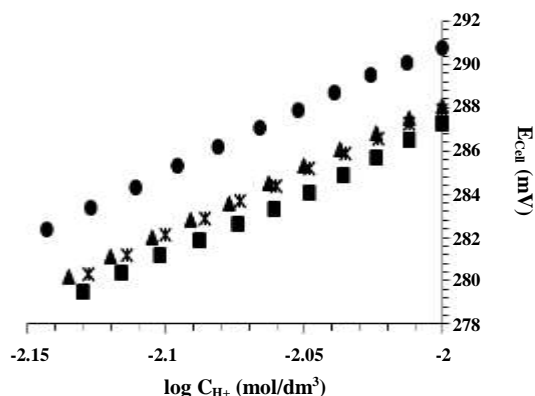
Fig. 1: Plot of E_{Cell} changes vs. log C_{H+} of tannic acid solution in ionic strength of 0.1 (●), 0.3 (▲), 0.5 (ж), and 0.7 (■) mol dm^{-3} of NaCl.

obtained at the different ionic strengths, the specific ion interaction of tannic acid was evaluated [27].

The values of calculated protonation constant at 25 ± 0.1 ºC and different ionic strengths of NaCl were listed in Table 1. A small decreasing is observed in protonation constant values with increasing ionic strength of solutions, according to Table 1.

In this work, the SIT model was applied to determine the protonation constants of tannic acid. For the simple protonation reaction, one can express the dependence of protonation constant on ionic strength of solution according to equation 8. For determining the protonation constant of tannic acid, the effective charge, Z^*,

must be evaluated. The interaction coefficients of C and D can be found with the fitting of experimental data into equation 8. The values of different parameters in the extended Daniele equation for determining the protonation constants of tannic acid were reported in Table 2 at 25 ± 0.1 ºC.

The small values of C and D coefficients show that the interactions between H$^+$ and L$^-$ is strong. So with the increasing ionic strength of the solution from 0.1 to 0.7 mol/dm^3 NaCl, the logarithmic form of the protonation constants of tannic acid decreases from 7.27 to 7.15. In another word, the proton affinity of Cl$^-$ is higher than L$^-$, then the specific short-range interactions between aqueous species of L$^-$ and Na$^+$ is low [28].

A plot of mole fraction of the different species of tannic acid (HL and L$^-$) *vs.* pH, is shown in Fig. 2 at 0.5 mol/dm^3 ionic strength. According to Fig. 2, the above line is related to HL and its mole fraction is high at first, and then by the increase of pH, its mole fraction decreases, because it loses H$^+$ ion. Also, the below line is related to L$^-$ and its mole fraction is low at first, and then by the increase of pH gradually, its mole fraction increases. According to Fig. 2, lines will reach together in a position, which is called the contact position or the pK_a of tannic acid.

Assessment of the effect of ionic strength on the protonation constant showed that, the log K curve *vs.* $\sqrt{I}$ follows an equation similar to Debye-Hückel equation [29, 30]. The comparison of protonation constants of tannic acid obtained from experimental data and SIT model is shown in Fig. 3.

The summary of calculations related to determining electrostatic specific ion interactions of tannic acid were represented in Table 3.

By considering the SIT model, the following equation can be written for the calculation of $\Delta\varepsilon$ parameter:

$$\log K = \log K_0 - 0.51 Z^* \frac{I_m^{1/2}}{1 + I_m^{1/2}} + (\Delta\varepsilon) I_m \qquad (12)$$

It should be noted that log K and I values are in the molal concentration scale. For tannic acid as the form of HL with a background electrolyte of NaCl, $\Delta\varepsilon$ parameter is defined as:

$$\Delta\varepsilon = \varepsilon\left(H^+, Cl^-\right) + \varepsilon\left(Na^+, L^-\right) \qquad (13)$$

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Table 3: The summary of calculations related to determining the electrostatic specific ion interaction of tannic acid at 25 ± 0.1 °C.

I / mol dm^{-3}	I_m / mol kg^{-1}	*D	$\log (K$ / mol kg$^{-1})$	$\log (K$ / mol kg$^{-1}) + 2D$	$\log (K$ / mol dm$^{-3})$
0.1	0.101	0.11	7.27	7.49	7.26 ± 0.01
0.3	0.305	0.15	7.20	7.51	7.20 ± 0.03
0.5	0.513	0.18	7.18	7.53	7.19 ± 0.02
0.7	0.725	0.19	7.15	7.53	7.14 ± 0.01

$$*D = \left(AI_m^{1/2} \right) \big/ \left(1 + BaI_m^{1/2} \right)$$
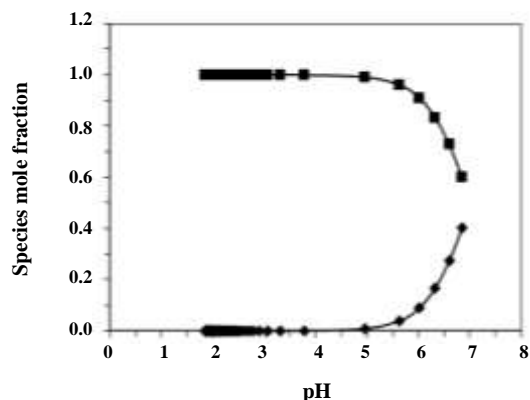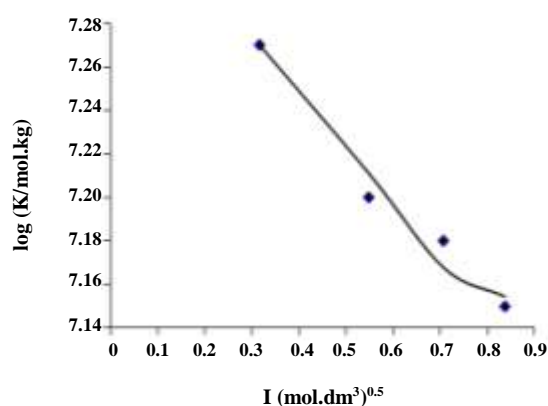

Fig. 2: Distribution diagram of the different species of tannic acid at 25 ± 0.1 °C and in 0.5 mol dm^{-3} ionic strength of NaCl. Symbols (■) and (♦) refer to the mole fraction of HL and L$^-$ species, respectively.

Fig. 3 Comparison of log K_{exp} with log K_{cal} and their changes with the square root of ionic strength ($I^{1/2}$) in NaCl at 25 ± 0.1 °C. Symbols refer to the protonation constants of tannic acid obtained from experimental data, while the solid line represents the values calculated according to the SIT model.

where $\varepsilon(H^+, Cl^-)$ and $\varepsilon(Na^+, L^-)$ are the appropriate specific ion interaction coefficients, which can be determined independently from the slope of the line obtained from plotting of log K+ 2D vs. I_m in terms of molality (Fig. 4).

The following expression was obtained following SIT model for determining of the protonation constant of tannic acid:

$$\log K = \left(7.47 \pm 0.03 \right) - 1.02 \frac{I_m^{1/2}}{1 + I_m^{1/2}} + \left(0.14 \pm 0.01 \right) I_m \quad (14)$$

The goodness of fit using the SIT model was obtained by an acceptable square correlation coefficient (R^2 is equal to 0.984), associated with low values of standard deviation. The specific interaction coefficient of HCl is equal to 0.125 [31]. Accordingly, the slope and intercept of the SIT plot is estimated to be 0.14 kg/mol and 7.47 log unit, respectively. So the specific interaction coefficient of $\varepsilon(Na^+, L^-)$ to be found 0.015 kg/mol.

CONCLUSIONS

The Specific Ion interaction Theory (SIT) has been employed to determine the protonation constants of tannic acid at 25 ± 0.1 °C. Based on the obtained results, it is observed that the SIT model can be applied effectively to determine the protonation constants of tannic acid. According to Fig. 4, SIT plot of tannic acid solution is satisfactorily linear with the excellent square correlation coefficient. The protonation constants of tannic acid decrease with increasing the ionic strength of solutions. The protonation constants obtained from experimental data and SIT model are in good agreement. The values of Daniele coefficients C and D were found -1.42 kg/mol and 1.04 kg$^{1.5}$ mol$^{-1.5}$, respectively. Finally, the specific ion interaction coefficient between Na$^+$ and non-proton form of tannic acid, L$^-$, is recommended value of 0.015 kg/mol. The SIT model obtained can be used for estimation of the protonation constants of tannic acid in each ionic strength in the range of 0.0 to 1.0 mol/kg NaCl.
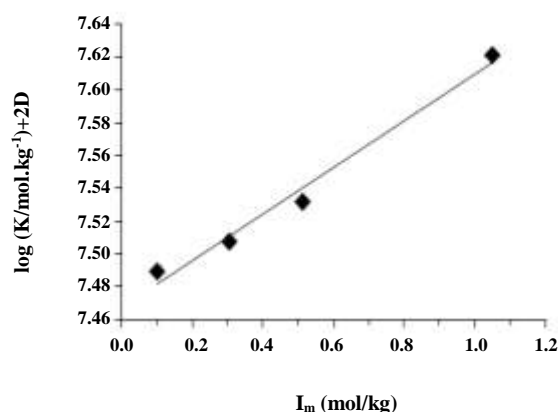
Fig. 4: Plot of log K + 2D changes of tannic acid vs. ionic strength in terms of molality at 25 ± 0.1 ºC. Symbols refer to experimental data and solid lines obtained from linear regression.

SUPPLEMENTARY MATERIAL

Potentiometric titration data and extensive tables and graphs are available electronically from the corresponding author on request.

Acknowledgments

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