Solvent dependence of protonation equilibria for gallic acid in water and different acetonitrile–water cosolvent systems

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ABSTRACT

The stoichiometric dissociation constants (pK) of gallic acid were determined in water and several mixed solvents comprising 10–90% (v/v) acetonitrile in water at a temperature of 24.0 ± 0.5 °C and an ionic strength of 0.10 mol dm^{-3} KCl medium. In this study, the protonation equilibrium values were calculated from potentiometric measurements and the influence of organic solvent composition on the equilibria was correlated with Born electrostatic model and the Kamlet, Abboud and Taft (KAT) solvatochromic parameters of acetonitrile–water mixtures. The pK values obtained increase when the amount of acetonitrile solvent increases in system investigated. The KAT single and multiple correlation analysis suggest that the specific and non-specific solvent interactions including hydrogen-bond donor ability (α), hydrogen-bond acceptor ability (β) and dipolarity/polarizability (π^*) are dominating factors which control the protonation equilibria in system under study.

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1. Introduction

Gallic acid (3,4,5-trihydroxybenzoic acid) is a naturally occurring plant phenol which is derived from certain tannins, gallnuts, lemons and green tea leaves [1]. It is known to have pharmacological properties such as antifungal, antiviral, antiinflammatory and antioxidant activities. Gallic acid also showed selective cytotoxicity against a variety of tumour cells, without harming healthy cells [2,3]. Moreover, gallic acid and its derivations are of considerable industrial importance since they have many applications in photography as well as in pharmaceutical industry [1,4].

Acid dissociation constant is one of the most useful physico-chemical parameters to predict the extent of ionization of weak acids and bases with respect to pH. Pharmacologic properties such as lipophilicity, permeability and solubility are essential for the measurements of pH-dependence. A study of the dissociation equilibria and solvation process of gallic acid in aqueous solutions containing various organic solvents has attracted much attention during the past few years. These properties are important to elucidate the connection between chemical structure and biological activity as well as these alter reactivity, spectral properties, physical behavior, and solubility.

Water has been traditionally considered as a good solvent for a wide range of biological materials so that it has been called "green solvent". However, aquo-organic binary mixtures such as acetonitrile (MeCN)–water, are very valuable media which have a low polar character and a partially aqueous content, as do all biological systems. These cosolvent systems can dissolve a majority of organic acids and bases more effectively than can water, and very often it is a more suitable solvent for

non-aqueous titrimetric analysis and determination of the acidity constants of organic reagents [5].

It should be noticed that relatively few data are available related to the acid dissociation process of gallic acid as a potent antioxidant phenolic acid, in different aquo-organic solvent mixtures and also the solvent dependence of its protonation constants. The main intention of this study, therefore, is to determine aqueous and cosolvent dissociation constant values of gallic acid in water and various aqueous MeCN mixtures (10–90% by v/v) by means of potentiometry technique, and study its equilibria dependence on solvent composition. Potentiometric titration is a high-precision technique for determining the pK values of substances. It is commonly used because of its accuracy, simplicity and speed of operation. Previously, the solvent effect on the protonation process was believed to be guided chiefly by electrostatic solute–solvent interactions (Born model). But recent studies indicate that the change in macroscopic properties such as the dielectric constant of solvent cannot be the sole factor [6]. It is desirable to develop other empirical functions to take into account the complete picture of all intermolecular forces acting between solute and solvent molecules.

2. Experimental

2.1. Materials and apparatus

Gallic acid (GA), Scheme 1, was obtained from Sigma as analytical reagent grade materials and was used without further purification. Sodium hydroxide (Titrisol, 1.00 mol dm^{-3}) and hydrochloride acid (Titrisol, 1.00 mol dm^{-3}) were supplied from Merck Chemical Company. Potassium chloride was purchased from Merck Chemical Co. and was kept at room temperature in a vacuum at least 72 h before use. The
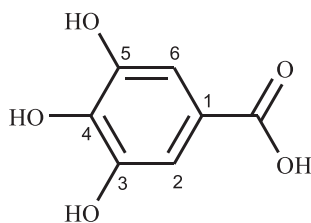
Scheme 1. Sketch of molecular structure of gallic acid.

organic solvent, MeCN (reagent grade) was obtained from Merck and was used without further purification. All dilute solutions were prepared from double-distilled water with a resistance more than 18 MΩ.

To determine the protonation constants of GA, the potential values of the potentiometric cell, E, in potentiometric titrations were measured using a WTW inoLab model 720 pH meter, equipped with a combined glass-pH electrode (model N 6000 A). The electrode response can be read to the third decimal place in terms of pH units with a precision of ± 0.001 and the potential with a precision typically of the order of ± 0.1 mV. The electrode was soaked for 15 to 20 min in each of the MeCN–water mixtures before the potentiometric measurements. All titrations were carried out in a 80 mL commercial double-walled glass vessel and the test solution was stirred magnetically for homogenizing it. To exclude any atmospheric $CO_2(g)$ and $O_2(g)$ traces from the system, a stream of purified $N_2(g)$ was passed through a sodium hydroxide solution and then bubbled slowly during the course of titrations.

2.2. Procedure for potentiometric titration

The emf measurements to evaluate the pH of the solution based on the concentration scale were performed at ambient temperature $(24.0 \pm 0.5)°C$ and an 0.10 mol dm^{-3} ionic strength of KCl. All working solutions were prepared freshly for each experiment, and the container was covered with foil to protect the solution from light. Before the potentiometric titration, the glass electrode system calibration was performed in each of the MeCN–water mixtures examined according to the Gran's method [7]. For this purpose, a measured amount of an acidic solution (total volume of 20 mL) was placed in the double-wall glass vessel. The electrode was immersed in the solution in the titration vessel and the acidic solution was titrated potentiometrically with a strong base (0.20 mol dm^{-3} NaOH) both at the same conditions of temperature, ionic strength and composition of MeCN organic solvent [(0 to 90) % by v/v] to be used in later experiments. Sufficient time (normally 2–3 min) was allowed to reach a reasonably stable E reading before the next titrant addition and the recorded E values were then used to obtain calibration constants. Usually, 10 or 12 additions of sodium hydroxide solution were enough for these constants to be accurately determined.

In the next step, a suitable amount of GA (0.0038 g) was added to the pre-titrated background solution. By continuing the titration, from the emf values and volume added of sodium hydroxide solution, the protonation constants were evaluated. Each experiment which includes the glass electrode calibration and the potentiometric titration steps was repeated at least three times under carefully controlled experimental conditions and the average values and corresponding deviations from the average are shown in the text and tables. The total time taken for each experiment was around 3 h. The experimental data for the combined glass electrode calibration and potentiometric titration are listed in Table 1 for 60% (v/v) MeCN as an instance.

The calibration constants were computed from the Nernst equation knowing the exact concentration of H$^+$ in each titration point [8].

Table 1
Experimentally measured emf, E, as a function of the added volume of sodium hydroxide, V_{NaOH}, for the combined glass electrode calibration and protonation titration at 24.0 ± 0.5 °C, an 0.10 mol dm^{-3} ionic strength of KCl and in 60% (v/v) MeCN.

V (mL)	E (mV)	V (mL)	E (mV)	V (mL)	E (mV)	V (mL)	E (mV)
Combined glass electrode calibration titration							
0.00	264.7	0.15	261.2	0.30	255.9	0.45	249.0
0.05	263.7	0.20	259.6	0.35	253.8	0.50	246.2
0.10	262.6	0.25	257.8	0.40	251.6		
Protonation titration							
0.00	246.0	0.70	−164.9	2.40	−315.5	7.40	−341.9
0.05	242.9	0.73	−180.9	2.60	−318.4	7.50	−342.1
0.10	239.3	0.76	−196.2	2.80	−320.5	7.60	−342.3
0.20	229.9	0.79	−211.2	3.00	−322.5	7.70	−342.5
0.25	223.8	0.82	−225.0	3.30	−325.1	7.80	−342.7
0.30	215.9	0.85	−236.5	3.60	−327.3	7.90	−342.8
0.35	205.1	0.9	−250.4	3.90	−329.4	8.00	−343.0
0.40	184.2	0.95	−259.3	4.20	−331.1	8.10	−343.2
0.43	157.4	1.00	−265.9	4.60	−333.1	8.20	−343.4
0.45	123.9	1.10	−276.2	5.00	−334.9	8.30	−343.6
0.47	98.2	1.20	−283.5	5.50	−336.9	8.40	−343.8
0.49	86.8	1.30	−289.0	6.00	−338.5	8.50	−343.9
0.52	65.9	1.40	−293.6	6.20	−339.1	8.60	−344.0
0.55	47.0	1.50	−297.4	6.40	−339.6	8.70	−344.2
0.58	23.8	1.60	−300.6	6.60	−340.1	8.80	−344.4
0.60	0.2	1.70	−303.3	6.80	−340.5	8.90	−344.5
0.62	−54.4	1.80	−305.7	7.00	−341.0	9.00	−344.6
0.64	−118.1	1.90	−307.8	7.10	−341.2		
0.66	−140.2	2.00	−309.8	7.20	−341.5		
0.68	−154.5	2.20	−313.0	7.30	−341.7		

According to the Nernst equation, the potential of a potentiometric cell equipped with a glass electrode can be written as

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

where E_{LJ} is the liquid junction potential, k (the Nernstian slope) = $2.303RT/F$ in which R, T and F have the usual meaning and γ_{H^+} is the activity coefficient of hydrogen ion. Because the ionic strength of the solution is kept constant for each experiment; the activity coefficient of hydrogen ion is constant too. The non-ideality of solutions is then included in E_a (the pseudo-Nernstian standard potential), and thus

$$E_{cell} = E_a + k\log\left[H^+\right] \tag{2}$$

where E_a being $E°_{cell} + k\log \gamma_{H^+} + E_{LJ}$. The hydrogen ion concentration can be easily calculated by

$$\left[H^+\right] = (M_{HCl}V_0 - M_{NaOH}V_{ad})/(V_0 + V_{ad}) \tag{3}$$

where M_{HCl} and M_{NaOH} are the molarities of acid and base, V_0 and V_{ad} are the initial volume of acid and the added volume of sodium hydroxide solution, respectively. The E_a values were calculated from the recorded emf and known concentration of solvated proton in every titration point by linear regression analysis. For each experiment at constant ionic strength, the slopes obtained from least square analysis were close to the theoretical Nernst value (59.167 mV at 25.0 °C) with correlation coefficients greater than 0.99. The calibration constants (E_a and k) obtained for the combined glass electrode at working mixtures are given in Table 2. The calibration constants were used to correct the recorded values in millivolt (E) during titration into the pH scale, pH $\equiv -\log$ [H$^+$], as follows:

$$pH = (E_a - E_{cell})/k. \tag{4}$$