Journal of Molecular Liquids 248 (2017) 7–12

Contents lists available at ScienceDirect

Journal of Molecular Liquids

journal homepage: www.elsevier.com/locate/molliq

Measurement and thermodynamic analysis of the acid-base equilibria of two bioactive flavanone glycosides in different temperatures and non-aqueous mixtures

Morteza Jabbari *, Zahra Soltanpour, Sayyed Ahmad Nabavi-Amri

School of Chemistry, Damghan University, 36716-41167 Damghan, Iran

ARTICLE INFO

Article history:
Received 30 July 2017
Received in revised form 28 September 2017
Accepted 2 October 2017
Available online 09 October 2017

Keywords:
Protonation equilibria
Naringoside
Hesperidin
Temperature and solvent effect
Thermodynamic quantities

ABSTRACT

In this research, the acid-base properties of two glycosilated flavanones namely naringoside and hesperidin were thermodynamically studied using spectrophotometric and potentiometric techniques at various temperatures (293.15–313.15) K. Because of very low solubility of these flavanones in aqueous solution, the protonation constants were obtained in ethanol-water mixtures (60–90% *v*/*v*) containing 0.10 mol dm^{-3} tetra-n-butylammonium perchlorate (TBAP) as supporting electrolyte for naringoside and DMSO-water mixed solvents (50–95% *v*/*v*) containing 0.10 mol dm^{-3} NaCl for hesperidin. Data process for the calculation of the protonation constants was done using the computer program STAR. The thermodynamic quantities ($\Delta G°$, $\Delta H°$, and $\Delta S°$) of the protonation process were obtained by means of modified van't Hoff equation. It was found that the acid dissociation reaction is exothermic and the entropic contribution is low for both the flavanones. Finally, the influence of solute-solvent interactions on the protonation equilibria in various temperatures was modelled using Kamlet, Abboud and Taft (KAT) solvatochromic parameters and Hildebrand's solubility index.

1. Introduction

The equilibrium dissociation constants (pK_a's) of biologically active molecules in various media provide valuable information to predict the extent of ionization of them as a function of pH and thus are essential in measuring the pH-dependent pharmacologic properties such as solubility, absorption, distribution, metabolism, and excretion of substances [1,2]. Moreover, the data related to pK_a's of a certain compound can be useful for isolation of it with the maximum yield. This is possible by finding the pH range in which the compound shows minimum ionization. Also, the protonation of a newly synthesized substance can give complementary information about its structure characterization [3].

Hesperidin and naringoside are glycosilated flavanones which belong to one of the largest classes of polyphenolic phytochemicals namely flavonoids. These bioflavanones are particularly found at high concentration in citrus fruits such as oranges, grapefruits, etc. [4]. The flavonoid naringoside, with the chemical formula $C_{28}H_{34}O_{15}$ (Fig. 1a) reveals antimicrobial, anticarcinogenic, antioxidant and anti-inflammatory activities [5]. It also inhibits in a small scale bacterial mutagenesis induced by chemical mutagens [6]. Hesperidin with the molecular formula $C_{27}H_{32}O_{14}$ (Fig. 1b) exhibits a variety of beneficial effects on human health such as protecting against the deterioration of bone structure and strength, and it can serve as an alternative for the loss of bone mineral [4]. Hesperidin has also antioxidant, anti-inflammatory activity and can scavenge free radicals involved in cancer [7].

Among the wide range of analytical methods for determining the pK_a's of organic ionizable compounds, an accurate and good-reproducibility technique is a combination of potentiometric titration and spectrophotometric methods which determines the pK_a of each compound that possesses pH-dependent light absorption due to the presence of a chromophore in proximity to ionizable group(s).

This method only requires small amounts of analyte and solubility is not a serious concern [8,9]. The bioflavonoids naringoside and hesperidin are practically insoluble in pure water but they are sufficiently soluble in a water-miscible organic solvent, hence it is possible to determine their acid dissociation constants in co-solvent mixtures pH-metrically. Despite the importance of this family of bioactive compounds as already mentioned above, the information related to acid-base equilibria of them is relatively few or sparse in the literature, in particular in media with high temperatures. Therefore, in the present work we follow a thermodynamic study on the protonation process of two glycosilated flavonoids by using a combination of spectrophotometric and potentiometric methods in different aqueous ethanol and DMSO solutions for naringoside and hesperidin, respectively. During the experiments, the ionic strength of medium was kept constant by 0.10 mol dm^{-3} TBAP and NaCl for naringoside and hesperidin solutions, respectively. From results obtained for these constants in different temperatures, the thermodynamic functions of

* Corresponding author.
E-mail address: m_jabari@du.ac.ir (M. Jabbari).

https://doi.org/10.1016/j.molliq.2017.10.008
0167-7322/

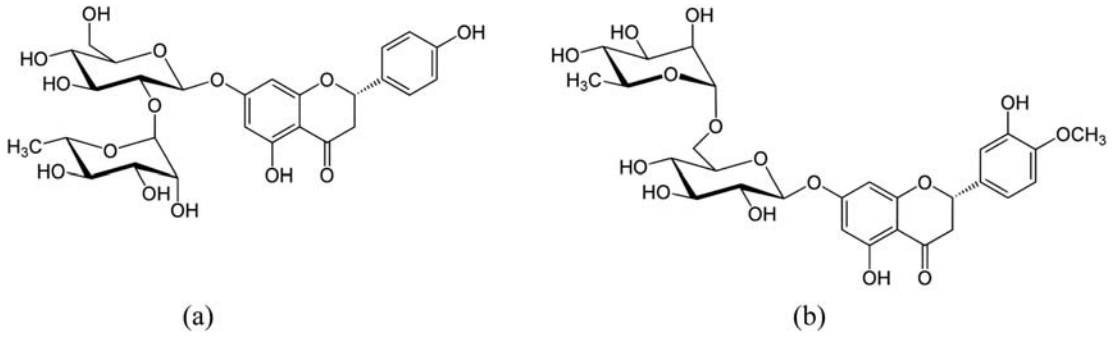

Fig. 1. Scheme of (a) naringoside and (b) hesperidin.

protonation process were determined in non-aqueous mixtures under examination. Finally, the influence of solvent-solute interactions on the acid dissociation constants was also analyzed based on the KAT equations.

2. Experimental

2.1. Chemicals and apparatus

Naringoside and hesperidin as analytical reagent grade material were obtained from Sigma-Aldrich and were used without further purification. The NaOH and hydrochloric acid solutions (Titrisol, 1.00 mol dm^{-3}), Sodium chloride (NaCl) and tetra-n-butylammonium perchlorate (TBAP) in order to fix the ionic strength in each experiment, and the organic solvents, ethanol (EtOH) and DMSO as pro-analysis grade, were all purchased from Merck. Throughout experiments, dilute solutions were freshly prepared from twice-distilled water with the conductivity lower than 1.2 ± 0.01 μS cm^{-1}.

In potentiometry experiments, the potential values of the potentiometric cell, E_{cell}, were measured using a WTW inoLab (model 720) research pH meter, equipped with a combined glass-pH electrode (model N 6000 A). The estimated precision was typically of the order of ±0.1 mV and ±0.001 mL for E_{cell} and titrant volume readings, respectively. The spectra of solutions in different steps of the titration were measured on a Perkin Elmer (model LAMBDA 25) diode array UV–Vis spectrophotometer in conjunction with a Peltier temperature controller, using quartz cells of path 10 mm.

2.2. Measurements and procedure

All potentiometric/spectroscopic titrations to determine the pK_a values of the selected flavanones naringoside and hesperidin were done in a 80 mL thermostatted commercial double-walled glass vessel. The working solutions were prepared freshly for each experiment.

All experimental measurements were performed at a constant ionic strength 0.10 mol dm^{-3} (NaCl or TBAP) and temperatures ranging from 293.15 to 313.15 K with intervals 5.0 °C. It is noteworthy that this temperature range covers different room conditions and also the normal human body temperature. Before the potentiometric titration, first the electrode was soaked for 10 to 15 min in the solvent mixtures under study and then the calibration of electrode system was done in each of the temperatures and mixed solvents according to the Gran's procedure [10]. Based on this method, a known amount of the acidic solution 0.01 mol dm^{-3} HCl with total volume of 20 mL was placed in the double-wall glass vessel. The electrode was immersed into the titration vessel and the acidic solution was titrated potentiometrically with a 0.10 mol dm^{-3} NaOH solution both at the same conditions of temperature, solvent composition and ionic strength to be used in later experiments. Sufficient time (normally 2–3 min) was allowed to reach a reasonably stable E_{cell} reading before the next titrant addition. The calibration constants were computed from the Nernst equation by using the exact concentration of H^+ in each titration point and the recorded E_{cell} data [11]. According to the Nernst equation, the potential of a potentiometric cell equipped by a glass electrode can be written as

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

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, C_{H+} and γ^{+}_{H} are the molar concentration and activity coefficient of hydrogen ion, respectively. Since 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' as the pseudo-Nernstian standard potential, so

$$E_{cell} = E' + k \log C_{H^+} \quad (2)$$

where E' being $E^{\circ}_{cell} + k \log \gamma^{+}_{H} + E_{LJ}$ and C^{+}_{H} can be easily obtained by means of Eq. (3)

$$C_{H^+} = (C_{HCl}V_0 - C_{NaOH}V_{ad})/(V_0 + V_{ad}) \quad (3)$$

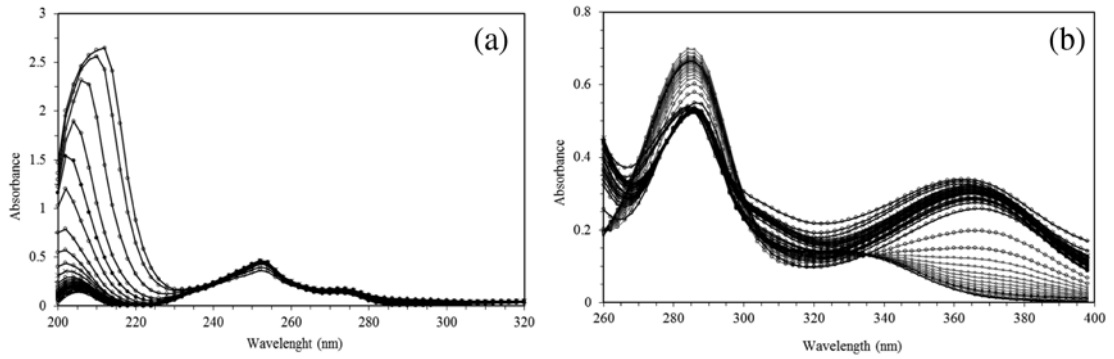

Fig. 2. UV–Vis spectral changes of glycosides (a) naringoside and (b) hesperidin during potentiometric titration at temperature 25.0 °C and aqueous mixture of 80% co-solvent.