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Thermodynamics of potassium diclofenac salt aqueous solutions at various temperatures

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Abstract Solution and dilution enthalpies of aqueous solutions of potassium diclofenac salt (K_DC) were measured by an isoperibolic calorimeter at 298.15 and 318.5 K. Heat capacities of the solutions with concentrations 0.002–0.09 mol kg^{-1} were obtained at the temperature interval of 288.15–318.15 K using a scanning adiabatic microcalorimeter. The virial coefficients were derived from Pitzer's model, and the excess thermodynamic functions of both the solvent and the solute of the solution were calculated. The concentration and temperature dependencies of thermodynamic characteristics of the solution were analyzed and discussed.

Keywords Calorimetry · Solution · Dilution · Pitzer's model · Potassium diclofenac salt · Thermodynamic functions

Introduction

Diclofenac is a compound belonging to non-steroidal anti-inflammatory drugs [1] and has a wide spectrum of applications in medical practice. The drugs of this group are poorly soluble in water [2, 3], and this fact decreases essentially the effectiveness of their use. One of the ways to overcome the problem is administration of salts and solvates in practice [3]. Moreover, such kind of ions as Na^+, K^+, and Ca^{2+} play an important role in vital activity processes and this argument makes using the salts more preferable in comparison with acids. Drug partition processes depend strongly on molecular ionic state [4] and temperature [5]. In this connection investigation of drug molecules in solutions at various concentrations, temperature and ionic strength attract interest, because this information is necessary for receiving optimal conditions of drug application. Unfortunately, the methods described in the literature on diclofenac do not explain the mechanisms of solvent–solute action and the processes taking place in the solution components where the concentration and temperature are changed. The approach proposed by us, which includes studying the fundamental aspects of drug solution thermodynamic properties at different conditions, gives an opportunity to clearly define the problems concerned with the molecular interaction mechanisms in the systems [6].

Thermal decomposition processes of diclofenac and their salts have been studied in detail [7–9]. There is practically no experimental data connected with solution calorimetric measurements on diclofenac in the literature with exception of just several studies [10, 11]. For example, Chadha et al. [10] studied diclofenac–paracetamol molecular interaction in aqueous binary solutions by the solution calorimetric method. Whereas Alves et al. [11] used a heat conduction microcalorimeter to measure the enthalpies of dissolution of sodium diclofenac and paracetamol in phosphate buffer (pH 6.91) and DMSO at 298.15 K. It should be noted that there are several articles devoted to using solution calorimetric experiments for

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studying crystal lattice differences of various polymorphic modifications for: glycine [12], paracetamol [13], and theophylline [14].

This study is a continuation of the study of diclofenac salts aqueous solutions thermodynamic properties, initiated by us earlier [15]. As the object of investigation we chose diclofenac potassium salt (K_DC) presented in Fig. 1. The aim of this study was: to derive the experimental values of the solution enthalpies for K_DC in water at wide concentration and temperature intervals; to calculate the virial coefficients within Pitzer's model and determine the aqueous solutions thermodynamic characteristics of the diclofenac salt on the basis of these parameters.

Material, methods and approaches

DSC experiments

Thermal analysis was carried out employing DSC 204 F1 Phoenix differential scanning heat flux calorimeter (NETZSCH, Germany) with a high sensitivity μ-sensor. The sample was heated at the rate of 10 K min^{-1} from 273.15 to 373.15 K in an argon atmosphere and cooled with gaseous nitrogen. The samples were placed into standard aluminum crucibles with lids. Sample weights were of 5.5 mg. Sapphire 0.25 mm in diameter (11.48 mg) was used as a reference. Temperature calibration of the DSC was performed against six high-purity substances: cyclohexane (99.96%), mercury (99.99+%), biphenyl (99.5%), indium (99.999%), tin (99.999%), and bismuth (99.9995%).

Solution calorimetry

Enthalpies of solution and dilution were measured by using an ampoule type isoperibolic calorimeter with a titanium reaction vessel of volume 50 cm^3 [16]. The signal was transferred to a computer, and the dependences obtained were processed by the computer. The automated control scheme allowed the temperature to be maintained with the accuracy over 6×10^{-4} K. The temperature and thermal sensitivities of the calorimeter measuring cell were 10^{-4} K and 10^{-3} J, respectively. The instrumental errors were 0.6–1%. The accuracy of weight measurements corresponded to $\pm 10^{-5}$ g. Due to small values of solution heat effects a correction on the heat of breaking ampoule and evaporation of solvent in the ampoule free volume (q) was introduced: $q(293.15) = 0.034$ J, $q(303.15) = -0.018$ J, and $q(318.15) = -0.059$ J. Other corrections were negligibly small. The Calorimeter was calibrated using KCl (analysis, grade >99.5%, from Merck) in water in a wide concentration interval with the number of measurements more than 20. The obtained standard value of solution enthalpy was 17240 ± 36 J mol^{-1}. This value was in good agreement with the value 17241 ± 18 J mol^{-1} recommended by the IUPAC [17].

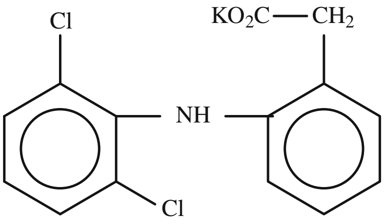

Fig. 1 Structural formula of potassium diclofenac salt

DSC microcalorimetric experiments

Heat capacity values of K_DC aqueous solutions were measured by adiabatic differential scanning microcalorimeter *Scal 1* (Puschino, Russia) at the scanning rate 1 K min^{-1} with 0.1 K step within the temperature interval of 290.15–333.15 K. The volume of the calorimetric vessel was 0.337 cm^3. The maximal noise rating and reproducibility of baseline at the scanning rate were 1 K min^{-1} 0.25 μW and ±2 μW, respectively. The baseline signal was determined for redistillated water. For calculation procedure it was used as the heat capacity [18] and density [19] values for water. The scanning calorimeter was calibrated by using the comparison of heat capacity values for NaCl solution, obtained by us, with the literature data [20] (Fig. 2). As it follows from Fig. 1, the convergence of the received and literature data is over 0.4%.

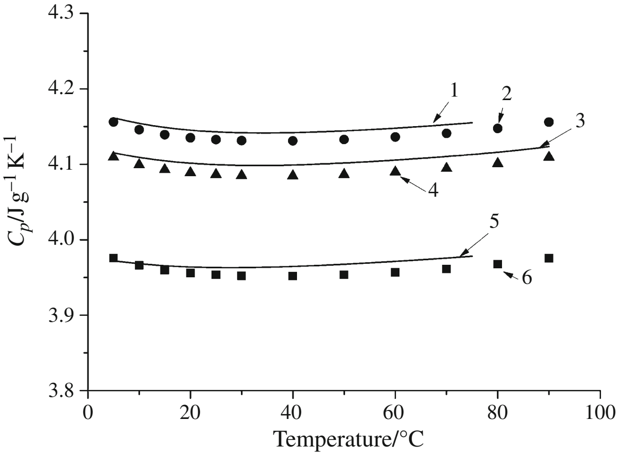

Fig. 2 Temperature dependence of heat capacities of NaCl solutions: experimental (*solid line*, obtained in this study) and literature (points) [20] data (0.2032*m* (1), 0.2*m* (2); 0.3967*m* (3), 0.40*m* (4), 1.0313m (5), 1.0*m* (6))

Density experiments

Density measurements were carried out by the densitometer of vibration type (VIP-2m, Tomsk, Russia) with the density accuracy of ±0.0003 g cm^{-3}. The concentration dependence of density for the aqueous K_DC solution at 293.15 K can be presented as:

$$d/\mathrm{g\,cm}^{-3} = (0.99820 \pm 0.00004) + (0.1290 \pm 0.0016)m \quad (1)$$

$$r = 1.000, s = 0.0001/\mathrm{g\,cm}^{-3}$$

Materials

Potassium diclofenac salt (benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, monopotassium salt; K_DC, pharmaceutical grade) was received as a gift from FARCHEMIA, Bergamo, Italy (>99%). The salt was dried in an oven at 373 K for 3 h. The DSC-curves did not display any heat events corresponding to crystalosolvates in the temperature interval from 298 up to the melting point. Before the calorimetric experiments, the compound was kept in a water-protected desiccator at room temperature with P_2O_5.

For all the experiments it was used redistilled water with specific conductivity $\chi = 1.4/10^{-6}\ \Omega/\mathrm{cm}^{-1}$. In the aqueous K_DC solution, the ratio of hydrolyzed K_DC molecules did not exceed 0.2%; therefore, the hydrolysis processes were negligibly small.

Calculation procedure and approaches:

The dissolution kinetics of K_DC is quite complicated, and this fact leads to an increase in the experimental time, a high probability of rejected experiments and, as a consequence, use of a large amount of the substance. Therefore, the solution enthalpy temperature dependence, within the concentration interval of the salt solubility, was determined on the basis of heat capacities of the solutions for different concentrations and solution enthalpy of the salt in water at 318.15 K:

$$\Delta_{\mathrm{sol}}H^m(T_1) = \Delta_{\mathrm{sol}}H^m(318.15) - \Delta_{\mathrm{sol}}C_p(\mathrm{mid}) \times (318.15 - T_1), \text{at } T_1 < 318.15\,\mathrm{K} \quad (2)$$

where $\Delta_{\mathrm{sol}}H^m(T)$ is the integral solution enthalpy of the solute in water with creating the solution at the concentration m at the temperature T; $\Delta_{\mathrm{sol}}C_p(\mathrm{mid})$ is an average change of molar heat capacity while dissolving the salt with creating the solution at the concentration m:

$$\phi_{C_p} = [(mM + 1000)c_p - 1000c_{p,1}]/m \quad (3)$$

$$\Delta_{\mathrm{sol}}C_p = \phi_{C_p} - Mc_{p,2,\mathrm{cr}} \quad (4)$$

where ϕ_{C_p} is the apparent molar heat capacity of the solute at the concentration m; M is the molecular weight of the salt; c_p, $c_{p,1}$, and $c_{p,2,\mathrm{cr}}$ are specific heat capacity values of the solution, solvent, and crystals of the salt, respectively.

Solution enthalpies of K_DC in water at the concentrations $m > 0.06$ mol kg^{-1} were calculated by Eq. 5 taking into account the molar dilution enthalpies of the salt solutions $\Delta_{\mathrm{dil}}H^{m_i \to m_f}$(where m_i and m_f are the values of initial and final concentrations of the solvent, respectively):

$$\Delta_{\mathrm{sol}}H^{m_i} = \Delta_{\mathrm{sol}}H^{m_f} - \Delta_{\mathrm{dil}}H^{m_i \to m_f} \quad (5)$$

Molar dilution enthalpy of the electrolyte ($\Delta_{\mathrm{dil}}H^{m_i \to m_f}$) can be presented as (6):

$$\Delta_{\mathrm{dil}}H^{m_i \to m_f} = L_\phi(m_f) - L_\phi(m_i) = L_\phi \quad (6)$$

where L_ϕ is the relative partial molar enthalpy of the solution at the concentration m.

On the other hand, L_ϕ-value can be calculated by Eqs. 10–14 [21–23]:

$$L_\phi = |z_M z_X|(2A_H/3b)\ln\left(1 + bI^{1/2}\right) - 2v_M v_X RT^2\left(mB'_{MX} + m^2C'_{MX}\right) \quad (10)$$

where

$$B'_{MX} = \left(\partial\beta^{(0)}_{MX}/\partial T\right)_{I,P} + \left(2/\alpha_1^2 I\right)\left(\partial\beta^{(1)}_{MX}/\partial T\right)_{I,P} \times \left\{1 - \left(1 + \alpha_1 I^{1/2}\right)\exp\left(-\alpha_1 I^{1/2}\right)\right\} + \left(2/\alpha_2^2 I\right)\left(\partial\beta^{(2)}_{MX}/\partial T\right)_{I,P}\left\{1 - \left(1 + \alpha_2 I^{1/2}\right) \times \exp\left(-\alpha_2 I^{1/2}\right)\right\} \quad (11)$$

$$C'_{MX} = 0.5(v_M v_X)^{1/2}(\partial C^\phi_{MX}/\partial T)_{I,P}, \quad (12)$$

$$A_H = -(3/2)vRT^2A_\gamma(1/T + \partial\ln\varepsilon/\partial T - (1/3)\partial\ln d/\partial T) \quad (13)$$

$$A_\gamma = \sqrt{\frac{2\pi N_A e^6 d}{(\varepsilon kT)^3 1000}} = 3A_\phi \quad (14)$$

where A_H is the theoretical slope for the enthalpy (limit Debye-Hückel slope) [24]; v is the number of ions composing the electrolyte; v_M and v_X are the number of cations and anions in the electrolyte molecule (K_DC); ε is the dielectric permeability of the solution; z_M and z_X are the charges of the cation and anion, respectively; d is the density of the solution (Due to a small difference between the densities/dielectric permeabilities of the studied aqueous solutions at various concentrations and in pure water, we used the temperature dependence of water [25] for $\partial\ln d/\partial T$ and $\partial\ln\varepsilon/\partial T$approximation); $I = 0.5\sum_i m_i z_i^2$ is the ionic strength of the solution; N_A is the Avogadro number; k is the Boltzmann constant; R is the universal gas constant; A_γ and A_ϕ are the Debye-Hückel coefficients for the activity and osmotic coefficients, respectively.

In order to calculate $L_\phi = -\Delta_{\mathrm{dil}}H^{m_i} \rightarrow 0$ by Eq. 10 we used standard values of solution enthalpies ($\Delta_{\mathrm{sol}}H^0$) obtained by Eq. 15 [26]:

$$\Delta_{\mathrm{sol}}H^m - a_H m^{1/2} = \Delta_{\mathrm{sol}}H^0 + bm + cm^{3/2} \tag{15}$$

where a_H is the theoretical slope for the enthalpy (limit Debye-Hückel slope) calculated in the same manner as in the study [26].

The first term of the Eq. 10 corresponds to long-distance electrostatic interactions. The second term takes into account pair ($\beta^{(0)}_{MX}$, $\beta^{(1)}_{MX}$, $\beta^{(2)}_{MX}$) and triple (C^{ϕ}_{MX}) short-range interactions. $\beta^{(0)}_{MX}$-coefficient corresponds to interactions between ion pair with the same charges. $\beta^{(1)}_{MX}$-coefficient corresponds to interactions between ion pair with the opposite charges. $\beta^{(2)}_{MX}$-coefficient corresponds to associative interactions. The b and α_1 values were chosen as 1.2 and 2.0 kg$^{1/2}$ mol$^{-1/2}$, respectively, as recommended by [27]. Whereas α_2 was described by the equation $\alpha_2 = 0.043\ (T - 273.15)$ [27].

The temperature dependence of the coefficients can be described by Eqs. 16–19 [27]:

$$\beta^{(0)}_{MX} = q_1 + q_2\{(T_{\mathrm{R}} - T)/TT_{\mathrm{R}}\} + q_3 \ln(T/T_{\mathrm{R}}) + q_4(T - T_{\mathrm{R}}) + q_5\left(T^2 - T^2_{\mathrm{R}}\right) \tag{16}$$

$$\beta^{(1)}_{MX} = q_6 + q_7(T - T_{\mathrm{R}}) + q_8(T^2 - T^2_{\mathrm{R}}) \tag{17}$$

$$\beta^{(2)}_{MX} = q_9 + q_{10}(T - T_{\mathrm{R}}) + q_{11}(T^2 - T^2_{\mathrm{R}}) \tag{18}$$

$$C^{\phi}_{MX} = q_{12} + q_{13}\{(T_{\mathrm{R}} - T)/TT_{\mathrm{R}}\} + q_{14} \ln(T/T_{\mathrm{R}}) + q_{15}(T - T_{\mathrm{R}}) \tag{19}$$

where $T_{\mathrm{R}} = 298.15$ K. In the Eqs. 16–19 q_{i} are temperature-independent parameters.

The virial enthalpic coefficients $(\partial\beta^{(0)}_{MX}/\partial T)_{I,P}$, $(\partial\beta^{(1)}_{MX}/\partial T)_{I,P}$, $(\partial\beta^{(2)}_{MX}/\partial T)_{I,P}$ and $(\partial C^{\phi}_{MX}/\partial T)_{I,P}$ entering into Eq. 10 can be presented by the temperature-independent parameters q_{i} (20–23):

$$\left(\partial\beta^{(0)}_{MX}/\partial T\right)_{I,P} = -q_2/T^2 + q_3/T + q_4 + 2q_5T \tag{20}$$

$$\left(\partial\beta^{(1)}_{MX}/\partial T\right)_{I,P} = q_7 + 2q_8T \tag{21}$$

$$\left(\partial\beta^{(2)}_{MX}/\partial T\right)_{I,P} = q_{10} + 2q_{11}T \tag{22}$$

Table 1 Coefficients of equation $c_p = a + b \cdot t + c \cdot t^2 + d \cdot t^3 + e \cdot t^4$ for the K_DC aqueous solutions

$m \times 10^2$/ mol kg^{-1}	a/J g^{-1} K^{-1}	$-b \times 10^3$/ J g^{-1} K^{-2}	$c \times 10^5$/ J g^{-1} K^{-3}	$-d \times 10^7$/ J g^{-1} K^{-4}	$e \times 10^8$/ J g^{-1} K^{-5}	r^{2a}	$s_{\mathrm{f}} \times 10^{4b}$/ J g^{-1} K^{-1}	Interval of temperatures/°C
0.207	4.2072 ± 0.0001	2.060 ± 0.008	4.08 ± 0.02	2.31 ± 0.02	–	0.9990	0.5	17–60
0.290	4.2081 ± 0.0001	2.060 ± 0.006	4.08 ± 0.02	2.31 ± 0.01	–	0.9995	0.4	17–60
0.389	4.2077 ± 0.0001	2.080 ± 0.006	4.14 ± 0.02	2.36 ± 0.01	–	0.9995	0.4	17–60
0.509	4.2067 ± 0.0001	2.080 ± 0.007	4.14 ± 0.02	2.37 ± 0.02	–	0.9992	0.5	17–60
0.989	4.2017 ± 0.0001	2.040 ± 0.005	4.03 ± 0.02	2.27 ± 0.01	–	0.9996	0.4	17–60
1.319	4.1997 ± 0.0001	2.010 ± 0.008	3.97 ± 0.02	2.25 ± 0.02	–	0.9990	0.6	17–60
1.338	4.2005 ± 0.0001	2.060 ± 0.005	4.08 ± 0.01	2.32 ± 0.01	–	0.9996	0.4	17–60
1.478	4.1988 ± 0.0001	2.010 ± 0.006	3.94 ± 0.02	2.21 ± 0.01	–	0.9995	0.4	17–60
2.052	4.1942 ± 0.0001	1.970 ± 0.008	3.84 ± 0.02	3.84 ± 0.02	–	0.9992	0.6	17–60
3.067	4.1855 ± 0.0001	1.990 ± 0.005	3.91 ± 0.01	2.19 ± 0.01	–	0.9997	0.3	17–60
3.150	4.1856 ± 0.0001	1.930 ± 0.006	3.75 ± 0.02	2.09 ± 0.01	–	0.9995	0.4	17–60
3.856	4.1794 ± 0.0001	1.940 ± 0.006	3.79 ± 0.02	2.13 ± 0.01	–	0.9992	0.5	17–60
5.112	4.2005 ± 0.0007	5.210 ± 0.008	16.1 ± 0.4	22.1 ± 0.6	1.18 ± 0.04	0.9964	1	17–60
5.163	4.1693 ± 0.0001	1.900 ± 0.006	3.75 ± 0.02	2.11 ± 0.01	–	0.9995	0.4	17–60
5.514	4.335 ± 0.003	17.2 ± 0.3	55 ± 1	77 ± 2	4.0 ± 0.1	0.9936	2	22–60
6.164	4.486 ± 0.006	28.7 ± 0.6	86 ± 2	113 ± 3	5.6 ± 0.2	0.9966	0.9	31–60
7.159	4.273 ± 0.002	8.9 ± 0.1	17.3 ± 0.3	10.7 ± 0.2	–	0.9917	1	33–60
9.108	5.134 ± 0.060	73.4 ± 4.8	195 ± 15	229 ± 20	10 ± 1	0.9937	1	40–60

[a] r is correlation coefficient

[b] s_{f} is standard deviation: $s_{\mathrm{f}} = \{\Sigma(c^m_p - c^m_{p\,\mathrm{calc}})^2/(N - N_p)\}^{0.5}$, where c^m_p and $c^m_{p\,\mathrm{calc}}$ are specific heat capacities of the solutions obtained by experiment and calculation, respectively; N and N_{p} are number of points and number of parameters of approximating equation, respectively

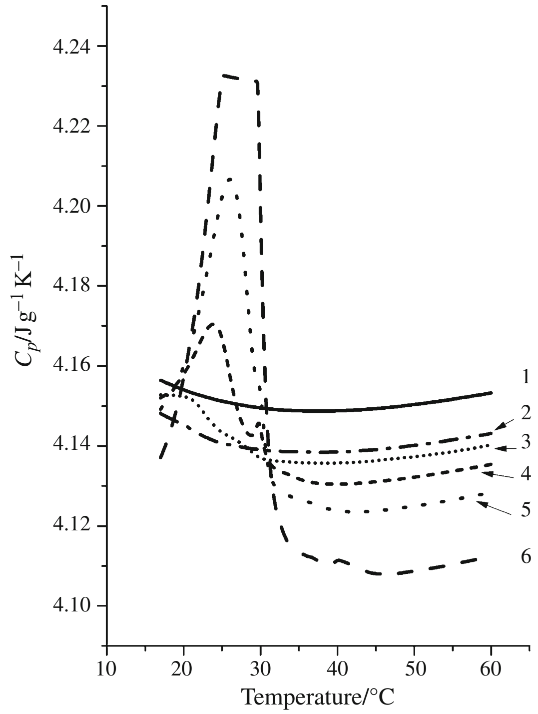

Fig. 3 Temperature dependence of specific heat capacity of the K_DC aqueous solution: 0.0386*m* (1), 0.0511*m* (2), 0.0551*m* (3), 0.0616*m* (4), 0.0716*m* (5), 0.0911*m* (6)

$$\left(\partial C^{\phi}_{MX}/\partial T\right)_{I,P} = -q_{13}/T^2 + q_{14}/T + q_{15} \tag{23}$$

Thus, the temperature-independent parameters and virial enthalpic coefficients can be derived from the data of thermochemical experiments and Eqs. 10, 20–23).

The equations describing the excess solution thermodynamic functions can be presented as [24, 27, 28]:

$$H^E \equiv L_\phi = -\Delta_{\text{dil}}H^{m\to 0} \tag{24}$$

$$\bar{L}_1 = -0.5m^{3/2}M_1\left(\partial L_\phi/\partial m^{1/2}\right) \tag{25}$$

Table 3 Dilution enthalpies ($\Delta_{\text{dil}}H^{m_i\to m_f}$) of K_DC in water at 298.15 and 318.15 K

m_i/mol kg^{-1}	m_f/mol kg^{-1}	$-\Delta_{\text{dil}}H^{m_i\to m_f}$/kJ mol^{-1}
$T = 298.15$ K		
0.06295	0.000730	0.412
0.09226	0.000859	1.531
$T = 318.15$ K		
0.06295	0.000685	−0.089
0.09226	0.000916	0.390
0.1190	0.000878	0.376

$$\bar{L}_2 = L_\phi + 0.5m^{1/2}\left(\partial L_\phi/\partial m^{1/2}\right) \tag{26}$$

$$\phi(T_2) - \phi(T_1) = \left(m^{1/2}/2\nu R\right)\int_{T_1}^{T_2}\left(\partial L_\phi/\partial m^{1/2}\right)d(1/T) \tag{27}$$

$$\ln\left[\gamma_\pm(T_2)/\gamma_\pm(T_1)\right] = (1/\nu R)\int_{T_1}^{T_2}\left[L_\phi + (m^{1/2}/2)(\partial L_\phi/\partial m^{1/2})\right]d(1/T) \tag{28}$$

$$\bar{C}_{p,2} = \phi_{C_p} + 0.5\,m^{0.5}\left(\partial\phi_{C_p}/\partial m^{0.5}\right) \tag{29}$$

$$\partial L_1/\partial T = \bar{C}_{p,1} - \bar{C}^0_{p,1} \tag{30}$$

$$\partial\bar{L}_2/\partial T = \overline{C}_{p,2} - \overline{C}^0_{p,2} = \overline{C}_{p,2} - \phi^0_{C_p} \tag{31}$$

where ϕ and γ are osmotic and activity coefficients, respectively; $\bar{L}_1$ and $\bar{L}_2$ are the partial molar enthalpies of the solvent and solute of the studied solution; ν is the number of ions of K_DC ($\nu = 2$); M_1 is the molar weight of the water; $\overline{C}_{p,1}$ and $\overline{C}_{p,2}$ are the partial molar heat capacities of the water and K_DC in the solution at the

Table 2 Solution enthalpies, $\Delta_{\text{sol}}H^m$, of K_DC in water at 298.15 and 318.15 K

m/mol kg^{-1}	$\Delta_{\text{sol}}H^m$/kJ mol^{-1}	*m*/mol kg^{-1}	$\Delta_{\text{sol}}H^m$/kJ mol^{-1}	*m*/mol kg^{-1}	$\Delta_{\text{sol}}H^m$/kJ mol^{-1}	*m*/mol kg^{-1}	$\Delta_{\text{sol}}H^m$/kJ mol^{-1}
$T = 298.15$ K							
0.00093	11.10	0.00290	10.63	0.00722	11.08	0.03426	10.95
0.00129	10.80	0.00331	10.02	0.00989	10.70	0.05163	11.00
0.00184	11.02	0.00419	10.52	0.01346	11.06	0.06295	11.51[a]
0.00254	11.35	0.00463	10.79	0.01760	11.30	0.09226	12.63[a]
$T = 318.15$ K							
0.00025	16.79	0.00191	18.09	0.01299	18.34	0.06295	17.72[a]
0.00069	17.81	0.00306	17.91	0.01954	17.36	0.09226	18.20[a]
0.00147	18.06	0.00378	17.76	0.03200	17.83	0.1190	18.18[a]
0.00185	17.41	0.00853	18.64	0.05600	17.66		

[a] $\Delta_{\text{sol}}H^m$obtained by recalculation of data from the dilution experiments

Table 4 Coefficients of Eq. 15 for the K_DC aqueous solutions at various temperatures

T/K	$\Delta_{sol}H^0$/kJ mol^{-1}	a_H/kJ mol^{-1}	b/kJ kg mol^{-2}	$-c$/kJ kg$^{3/2}$ mol$^{-5/2}$	r	s_f^a/kJ mol^{-1}
293.15	8.063 ± 0.002	1.753	20.53 ± 0.37	18.9 ± 1.6	1.000	0.003
298.15	9.998 ± 0.002	1.931	16.62 ± 0.30	15.5 ± 1.3	1.000	0.002
303.15	11.888 ± 0.001	2.119	12.41 ± 0.22	11.06 ± 0.90	1.000	0.002
308.15	13.797 ± 0.002	2.321	8.07 ± 0.13	6.21 ± 0.48	1.000	0.002
310.15	14.560 ± 0.001	2.390	6.60 ± 0.11	5.23 ± 0.41	1.000	0.001
313.15	15.685 ± 0.001	2.533	3.955 ± 0.056	2.59 ± 0.19	1.000	0.001
315.15	16.424 ± 0.001	2.614	2.440 ± 0.036	1.66 ± 0.12	1.000	0.001

[a] Standard deviation $s_f = \{\Sigma(\Delta_p H_i^m - \Delta_p H_{calc,i}^m)^2/(N - N_p)\}^{0.5}$, where $\Delta_p H_i^m$ and $\Delta_p H_{calc,i}^m$ are solution enthalpies calculated from heat capacity of solution and calculated from approximated dependence, respectively. N and N_p are number of points and number of parameters of approximating equation, respectively

concentration m, respectively; $\overline{C}_{p,1}^0$ and $\overline{C}_{p,2}^0$ are the partial molar heat capacities at infinite dilution of the solution (equal to water heat capacity) and K_DC, respectively; $\phi_{C_p}^0$ is the apparent molar heat capacity of the electrolyte at $m = 0$.

Results and discussion

The experimental heat capacity values for (water-K_DC) system were obtained by Eq. 32. The coefficients of the equation are presented in Table 1.

$$c_p = a + bt + ct^2 + dt^3 + et^4 \tag{32}$$

where t is the temperature in °C.

The temperature dependence of specific heat capacity of K_DC aqueous solution is shown in Fig. 3. As it follows from the specific heat capacity values, the solution homogeneity is broken at $m > 0.05$ and at low temperatures and there appears a heterogeneity region, which with a concentration increase shifts to the interval of higher temperatures.

The specific heat capacity values of K_DC, obtained by using DSC 204 F1 Phoenix (NETZSCH, Germany), can be presented by the equation (where t is in °C):

$$c_{p,2,cr}(\mathrm{J\,g^{-1}\,K^{-1}}) = (0.7066 \pm 0.0005) + (1.958 \pm 0.008) \times 10^{-3}\,t \tag{33}$$

$r^2 = 0.998, s_f = 0.002\ \mathrm{J\,g^{-1}K^{-1}}$

The experimental values of solution and dilution enthalpies of K_DC in water at 298.15 and 318.15 K are presented in Tables 2 and 3, respectively.

The coefficients of Eq. 15 are summarized in Table 4. The solution enthalpies of K_DC in water at 298.15 K obtained through the calorimetric experiments and the calculation procedure using the heat capacity values are shown in Fig. 4. The calculation employed the solution enthalpies of K_DC in water received at 318.15 K and smoothed by the expression with $s_f = 0.47$ J mol^{-1}:

$$\Delta_{sol}H^m = (17.49 \pm 0.12) + 2.759m^{1/2} \tag{34}$$

where $a_H = 2.759$ (kJ kg$^{1/2}$ mol$^{-3/2}$) corresponds to the theoretical slope for the enthalpy (limit Debye-Hückel slope) at 318.15 K [26].

It is not difficult to see that the experimental and calculated data are in good agreement. The accuracy of solution enthalpies estimation by the expression is ±0.5 kJ mol^{-1}.

In order to estimate the excess thermodynamic functions q_i parameters were calculated (Table 5). The results of calculating the temperature derivatives of $(\partial\beta_{MX}^{(0)}/\partial T)_{I,P}$, $(\partial\beta_{MX}^{(1)}/\partial T)_{I,P}$, $(\partial\beta_{MX}^{(2)}/\partial T)_{I,P}$ and $(\partial C_{MX}^{\phi}/\partial T)_{I,P}$ for the

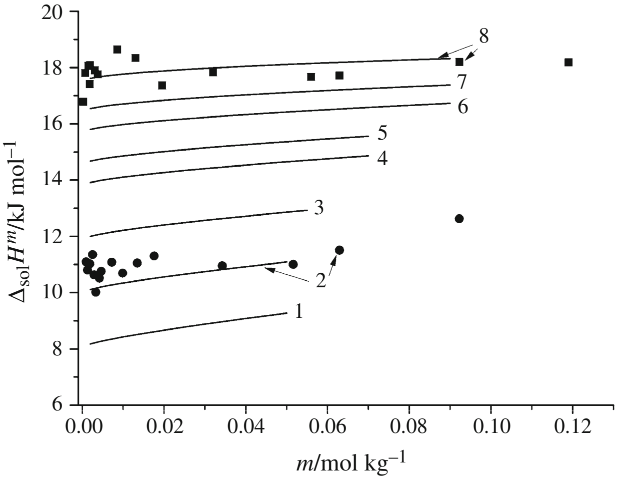

Fig. 4 Concentration dependence of solution enthalpies of K_DC in water: 293.15 (1), 298.15 (2), 303.15 (3), 308.15 (4), 310.15 (5), 313.15 (6), 315.15 (7), 318.15 (8). Solid line corresponds to calculated values obtained by the heat capacity of the solution. Points correspond to the experimental values

models, with and without taking into account the ion association, are summarized in Table 6. It should be noted that the calculations with a correction for ion association follow from the expression $(\partial\beta_{MX}^{(2)}/\partial T)_{I,P} \neq 0 = \text{const}$. The description accuracy of the solution by means of the model with a correction for ion association is higher in comparison with the model without such a correction. But the difference between the models is not essential. This fact makes it possible to use in future only the model without this correction.

The thermodynamic characteristics of the diclofenac potassium salt aqueous solution are presented in Table 7.

The specific heat capacity of the solution (K_DC-water) decreases with increasing the solution concentration. Whereas the mentioned value with a temperature increase shows the same tendency as pure water (Table 1). In electrolyte solutions the solution heat capacity comes under two types of influence. On the one hand, affected by the ion field, hydrogen bonds between the solvent molecules are broken. On the other hand, the effects of the ion field result

Table 5 Temperature-independent parameters q_i for calculation of L_Φ-values of K_DC

Parameters	Model taking into account association	Model without association
q_2	$(4.999 \pm 0.186)\ 10^3$	$(1.980 \pm 0.134)\ 10^4$
q_3	–	160.0 ± 12.4
q_4	$(4.752 \pm 0.175)\ 10^{-2}$	-0.3088 ± 0.0264
q_7	$-(4.996 \pm 0.340)\ 10^{-2}$	-0.2387 ± 0.0153
q_8	$(3.486 \pm 0.593)\ 10^{-5}$	$(3.759 \pm 0.245)\ 10^{-4}$
q_{10}	$(2.877 \pm 0.198)\ 10^{-2}$	–
q_{14}	-58.5 ± 16.0	$-(1.390 \pm 0.240)\ 10^2$
q_{15}	0.1873 ± 0.0514	0.4407 ± 0.0766
s_f/J mol^{-1}[a]	1.4	1.5
r[b]	1.0000	1.0000

[a] s_f is standard deviation; $s_f = \{\Sigma(L_\phi - L_{\Phi,\text{calc}})^2/(N - N_p)\}^{0.5}$

[b] r is correlation coefficient

Table 6 The $(\partial\beta_{MX}^{(0)}/\partial T)_{I,P}$, $(\partial\beta_{MX}^{(1)}/\partial T)_{I,P}$, $(\partial\beta_{MX}^{(2)}/\partial T)_{I,P}$ and $(\partial C_{MX}^{\phi}/\partial T)_{I,P}$ values to calculate L_Φ-values of K_DC in water at various temperatures (I—model taking into account association, II—model without association)

T/K	Model	$\left(\partial\beta_{MX}^{(0)}/\partial T\right)_{I,P}$ 10^{-3}/ kg mol^{-1} K^{-1}	$-\left(\partial\beta_{MX}^{(1)}/\partial T\right)_{I,P}$ 10^{-2}/ kg mol^{-1} K^{-1}	$\left(\partial\beta_{MX}^{(2)}/\partial T\right)_{I,P}$ 10^{-2}/ kg mol^{-1} K^{-1}	$-\left(\partial C_{MX}^{\phi}/\partial T\right)_{I,P}$ 10^{-3}/ kg^2 mol^{-2} K^{-1}	s_f/J mol^{-1}
293.15	I	-10.649 ± 0.417	2.9525 ± 0.0079	2.877 ± 0.198	12.19 ± 3.27	3
	II	6.792 ± 0.669	1.826 ± 0.093	–	33.66 ± 5.22	3
298.15	I	-8.714 ± 0.345	2.918 ± 0.014	2.877 ± 0.198	8.84 ± 2.35	2
	II	5.298 ± 0.465	1.450 ± 0.069	–	25.70 ± 3.85	2
303.15	I	-6.874 ± 0.276	2.883 ± 0.020	2.877 ± 0.198	5.61 ± 1.47	2
	II	3.729 ± 0.259	1.074 ± 0.044	–	18.01 ± 2.53	2
308.15	I	-5.124 ± 0.211	2.848 ± 0.026	2.877 ± 0.198	2.479 ± 0.609	2
	II	2.097 ± 0.053	0.698 ± 0.020	–	10.57 ± 1.24	2
310.15	I	-4.447 ± 0.186	2.834 ± 0.028	2.877 ± 0.198	1.255 ± 0.273	2
	II	1.427 ± 0.030	0.548 ± 0.010	–	7.656 ± 0.741	2
313.15	I	-3.456 ± 0.149	2.813 ± 0.032	2.877 ± 0.198	0.552 ± 0.223	1
	II	0.408 ± 0.154	0.322 ± 0.005	–	3.360 ± 0.001	1
315.15	I	-2.811 ± 0.125	2.799 ± 0.034	2.877 ± 0.198	1.737 ± 0.548	1
	II	-0.281 ± 0.237	0.172 ± 0.015	–	0.542 ± 0.486	1
318.15	I	-1.866 ± 0.090	2.778 ± 0.038	2.877 ± 0.198	3.49 ± 1.03	0.5
	II	-1.329 ± 0.361	-0.054 ± 0.030	–	3.62 ± 1.20	1

Table 7 Molar thermodynamic properties of K_DC aqueous solutions at 293.15–318.15 K

m/mol kg^{-1}	L_ϕ/J mol^{-1}	$\bar{L}_2$/J mol^{-1}	$\Delta_{\text{sol}}C_p$/ J mol^{-1} K^{-1}	γ^{a}	ϕ^{a}
$T = 293.15$ K, $A_H = 1315$ J kg$^{1/2}$ mol$^{-3/2}$					
0.0005	46	73	395	0.990	0.997
0.001	70	111	395	0.986	0.995
0.005	190	313	393	0.971	0.991
0.010	300	499	391	0.961	0.988
0.015	393	658	388	0.955	0.986
0.020	478	802	386	0.950	0.985
0.025	556	936	383	0.946	0.984
0.030	630	1061	381	0.942	0.984
0.035	700	1182	378	0.939	0.983
0.040	768	1297	376	0.937	0.982
0.045	833	1410	373	0.934	0.982
0.050	896	1520	371	0.932	0.982
$T = 298.15$ K, $A_H = 1448$ J kg$^{1/2}$ mol$^{-3/2}$					
0.0005	49	76	381	0.989	0.996
0.001	73	114	381	0.985	0.995
0.005	190	308	379	0.970	0.990
0.010	294	481	376	0.960	0.988
0.015	381	627	373	0.953	0.986
0.020	459	757	371	0.947	0.984
0.025	531	878	368	0.943	0.983
0.030	598	991	366	0.939	0.982
0.035	662	1098	363	0.935	0.981
0.040	723	1201	361	0.933	0.981
0.045	782	1301	358	0.930	0.980
0.050	838	1397	356	0.928	0.980
$T = 303.15$ K, $A_H = 1590$ J kg$^{1/2}$ mol$^{-3/2}$					
0.0005	52	80	377	0.989	0.996
0.001	76	118	377	0.985	0.995
0.005	190	303	375	0.969	0.990
0.010	288	463	372	0.958	0.987
0.015	369	596	370	0.951	0.985
0.020	441	713	367	0.945	0.983
0.025	506	821	365	0.940	0.982
0.030	567	921	362	0.936	0.981
0.035	625	1016	360	0.932	0.980
0.040	679	1106	357	0.929	0.979
0.045	731	1193	355	0.926	0.979
0.050	782	1277	352	0.923	0.978
0.055	831	1359	349	0.921	0.978
$T = 308.15$ K, $A_H = 1740$ J kg$^{1/2}$ mol$^{-3/2}$					
0.0005	55	84	389	0.991	0.997
0.001	79	122	388	0.988	0.997
0.005	191	299	386	0.979	0.994
0.010	283	446	384	0.971	0.991
0.015	358	566	381	0.963	0.987
0.020	423	670	379	0.955	0.983
0.025	482	765	376	0.948	0.980
0.030	537	853	374	0.943	0.978
0.035	588	935	372	0.939	0.978
0.040	636	1013	369	0.937	0.978
0.045	682	1088	367	0.936	0.980
0.050	726	1160	364	0.938	0.984
0.055	769	1229	362	0.942	0.989
0.060	810	1297	359	0.948	0.997
0.070	889	1427	354	0.910	0.974
$T = 310.15$ K, $A_H = 1793$ J kg$^{1/2}$ mol$^{-3/2}$					
0.0005	56	85	376	0.989	0.996
0.001	80	123	376	0.984	0.995
0.005	191	296	374	0.968	0.990
0.010	280	437	372	0.956	0.986
0.015	352	551	369	0.948	0.984
0.020	415	650	367	0.942	0.982
0.025	471	740	364	0.937	0.981
0.030	523	822	362	0.932	0.980
0.035	571	900	359	0.928	0.978
0.040	617	973	357	0.925	0.978
0.045	660	1042	354	0.922	0.977
0.050	702	1109	352	0.918	0.976
0.055	742	1173	349	0.916	0.975
0.060	780	1236	346	0.913	0.975
0.070	854	1356	341	0.909	0.974
$T = 313.15$ K, $A_H = 1900$ J kg$^{1/2}$ mol$^{-3/2}$					
0.0005	58	88	377	0.989	0.996
0.001	83	126	376	0.984	0.995
0.005	193	295	374	0.967	0.989
0.010	279	429	372	0.955	0.986
0.015	347	535	369	0.947	0.984
0.020	406	627	367	0.941	0.982
0.025	458	709	364	0.935	0.980
0.030	507	785	362	0.931	0.979
0.035	551	855	359	0.927	0.978
0.040	594	921	357	0.923	0.977
0.045	633	983	354	0.920	0.976
0.050	671	1043	352	0.917	0.975
0.055	708	1100	349	0.914	0.974
0.060	743	1156	347	0.911	0.974
0.070	809	1261	342	0.906	0.973
0.080	872	1360	337	0.902	0.972
0.090	932	1455	332	0.898	0.971
$T = 315.15$ K, $A_H = 1961$ J kg$^{1/2}$ mol$^{-3/2}$					
0.0005	59	89	365	0.989	0.996
0.001	84	127	365	0.984	0.995
0.005	193	293	363	0.967	0.989
0.010	276	421	360	0.955	0.986

Table 7 continued

m/mol kg^{-1}	L_{ϕ}/J mol^{-1}	$\bar{L}_2$/J mol^{-1}	$\Delta_{\mathrm{sol}}C_p$/ J mol^{-1} K^{-1}	γ^{a}	ϕ^{a}
0.015	342	522	358	0.947	0.983
0.020	398	609	355	0.940	0.981
0.025	448	686	353	0.935	0.980
0.030	494	756	350	0.930	0.979
0.035	536	821	348	0.926	0.978
0.040	575	882	345	0.922	0.976
0.045	613	940	343	0.919	0.976
0.050	648	995	340	0.916	0.975
0.055	682	1047	338	0.913	0.974
0.060	715	1098	335	0.910	0.973
0.070	746	1193	330	0.905	0.972
0.080	834	1282	325	0.901	0.971
0.090	888	1366	320	0.897	0.970
$T = 318.15$ K, $A_H = 2069$ J kg$^{1/2}$ mol$^{-3/2}$					
0.0005	62	92	352	0.988	0.996
0.001	87	130	351	0.984	0.995
0.005	194	291	349	0.966	0.989
0.010	275	412	347	0.954	0.985
0.015	337	505	344	0.946	0.983
0.020	389	584	342	0.939	0.981
0.025	436	654	339	0.934	0.980
0.030	480	717	336	0.929	0.978
0.035	520	775	334	0.924	0.977
0.040	557	829	331	0.921	0.976
0.045	592	880	329	0.917	0.975
0.050	625	928	326	0.914	0.974
0.055	657	973	324	0.911	0.973
0.060	687	1017	321	0.908	0.973
0.070	744	1097	316	0.903	0.972
0.080	797	1172	311	0.899	0.970
0.090	847	1240	305	0.895	0.970

[a] γ and ϕ calculated by Debye-Hückel equation [25]: $\ln\gamma = -Am^{0.5}/\left(1 + Bbm^{0.5}\right)$, where $b = 4.5$ Å and $1 - \phi = \left(Am^{0.5}/3\right)\phi\left(Bbm^{0.5}\right)$, where $\phi(\mathrm{X}) = (3/\mathrm{X}^3)$ $[1 + \mathrm{X}\text{-}2\ln(1 + \mathrm{X})\text{-}1/(1 + \mathrm{X})]$; Å $= 0.5317$ mol$^{-0.5}$ l$^{0.5}$ [25], 10^{-8} $B = 0.3334$ cm^{-1} mol$^{-0.5}$ l$^{0.5}$ [25]

in ordering/orientation of solvent molecules around the ion which decreases the mobility of the solvent molecules and, as a consequence, reduces the solution heat capacity [29]. Thus, within the studied temperature and concentration intervals the structure of the solution is formed by the solvent structure. Nevertheless, electrolyte ions decrease the mobility of solvent molecules due to (solute–solvent) interactions.

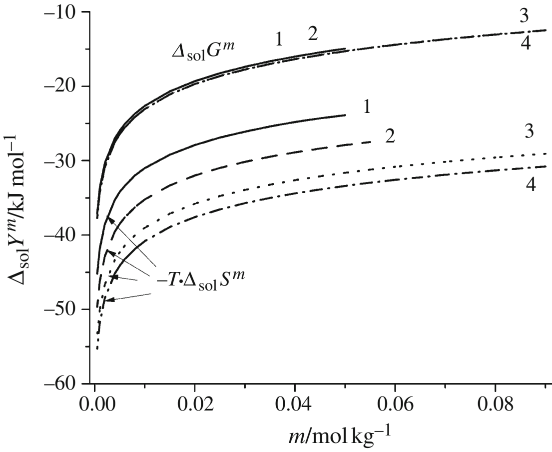

Fig. 5 Concentration dependence of $\Delta_{\mathrm{sol}}G^m$ and $-T\Delta_{\mathrm{sol}}S^m$: 293.15 (1), 303.15 (2), 313.15 (3), 318.15 (4)

The change of the heat capacity value of K_DC in the process of dissolution in water (Table 7) is positive at all studied conditions. This fact indicates an increase of interaction between the electrolyte molecule and water molecules in comparison with the analogous molecules in the crystal lattice. The value $\Delta_{\mathrm{sol}}C_p$ decreases them both with a concentration increase.

The concentration dependence of activity and osmotic coefficients (Table 7) of the solution shows a change in the electrolyte state (activity coefficient) and solvent state (osmotic coefficient) in the solution. These dependencies are not linear. While the concentration and temperature values increase, the $\gamma_{\pm}$ and ϕ values decrease. This observation indicates an ion association of the electrolyte molecules and additional structuredness of water molecules in the solution. Moreover, the structuredness of the solvent molecules (water) in the solution is much higher than their kinetic energy.

As the K_DC concentration increases, a small extension of endothermic behavior of the enthalpic characteristic of the salt dissolution within the temperature interval 293.15–318.15 K is observed (Fig. 4). There is a bigger increase in the endothermic behavior of the dissolution process (around 0.25 kJ mol^{-1} per degree) with a temperature increase. The K_DC dissolution in water is a spontaneous process, because a Gibbs energy change has a negative sign within the considered intervals of the concentrations and temperatures (Fig. 5). The values of $\Delta_{\mathrm{sol}}G^m$ are practically the same within the temperatures studied, but depend on the concentration. The enthalpic factor counteracts the process of the K_DC dissolution in water, whereas the entropic one promotes this process. The entropic term characterizes the dependence of $\Delta_{\mathrm{sol}}G^m$-function on the concentration. Absence of a trend between the entropic term and the temperature is a result of the compensation effect (between enthalpic and entropic terms). The enthalpic and entropic terms work in the opposite directions: with a temperature increase the endothermic effect of the enthalpic term increases as well, whereas for the entropic term an

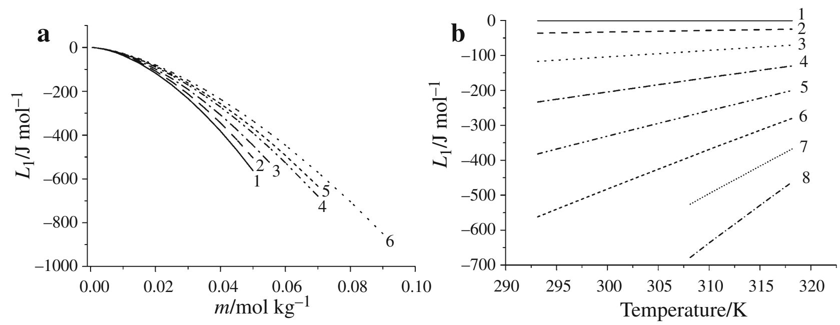

Fig. 6 Dependence of $\bar{L}_1$ of the K_DC aqueous solution versus concentration (**a**) and temperature (**b**): **a** 293.15 (1), 298.15 (2), 303.15 (3), 308.15 (4), 313.15 (5), 318.15 (6); **b** 0.0005m (1), 0.01m (2), 0.02m (3), 0.03m (4) 0.04m (5), 0.05m (6), 0.07m (7), 0.09m (8)

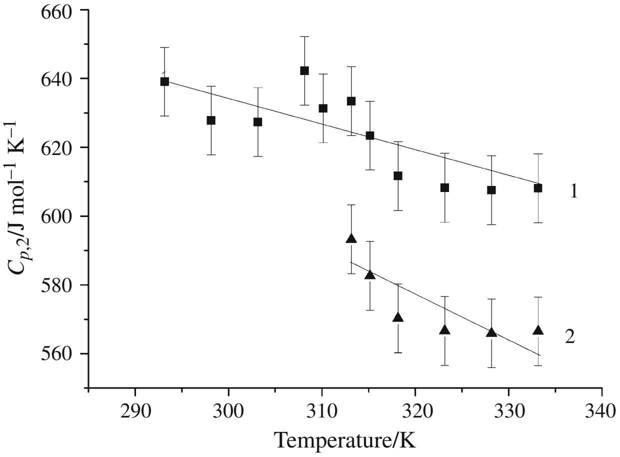

Fig. 7 Temperature dependence of $\bar{C}_{p,2}$ for the K_DC aqueous solution: 0.01m (1), 0.09m (2)

increase of temperature leads to an increase of the dissolution salt exothermic effect.

The impact of temperature and concentration on the hydration process of K_DC is similar to the hydration of organic electrolytes [30, 31]: hydration decreases with an increase of both the concentration and the temperature.

The relative partial molar enthalpies indicate various solution components interactions (Table 7; Fig. 6). The solvent molecules introduced in the solution interact with the solution: e.g., at $m > 0.01$ $\bar{L}_1$-value changes from ~ -50 to -900 J mol^{-1} (Fig. 6a). The water molecules dissolve in K_DC aqueous solution practically without a variation of $\bar{L}_1$-value at $m < 0.01$. This fact indicates weak interactions between the solvent and the dissolved water molecules within the concentration interval.

For K_DC the $\bar{L}_2$-value is positive within the whole intervals of the concentrations and temperatures studied (at $m > 0.01$ $\bar{L}_2$-value changes from 400 to 1500 J mol^{-1}). This observation indicates that the salt being soluble, the cost of destructing solute–solute interactions exceeds the profit from solute–solvent interactions. Increasing the temperature from 293.15 to 318.15 K leads to a decrease of $\bar{L}_2$-value at $m > 0.01$. $\bar{L}_2$-value does not depend on the temperature at $m < 0.01$.

The temperature coefficients $\partial \bar{L}_1 / \partial T$ (Fig. 6b) and $\partial \bar{L}_2 / \partial T$ (Table 7) are equal to zero at $m < 0.01$, whereas at $m > 0.01$ $\partial \bar{L}_1 / \partial T > 0$ and $\partial \bar{L}_2 / \partial T < 0$ within the whole temperature interval studied. If $\partial \bar{L}_2 / \partial T > 0$, then $\overline{C}_{p,1} > \overline{C}^0_{p,1}$. On the other hand, if $\partial \bar{L}_2 / \partial T < 0$, then $\overline{C}_{p,2} < \overline{C}^0_{p,2}$.

As it follows from the observations, at $m > 0.01$ the structuredness (tie-up) of water molecules in the solution increases in comparison with pure water. For the solute at $m > 0.01$ and within the whole temperature interval, the partial molar heat capacity of the electrolyte is lower than the analogous value for the infinitely diluted solution. This observation indicates that the state of K_DC molecules is more "friable" in the aqueous solution at $m > 0.01$ in comparison with the infinitely diluted solution. This tendency intensifies with increasing the temperature.

The dependence of $\overline{C}_{p,2}$-values on the temperature is presented in Fig. 7 at just one arbitrary concentration. It is not difficult to see, that within the whole concentration and temperature intervals $\overline{C}_{p,2} > 0$ and with the concentration and temperature increasing, the $\overline{C}_{p,2}$-value decreases. This fact confirms the "breaking" effect of K_DC on the water structure with increasing both the temperature and the concentration. As $\overline{C}_{p,2}$-value is essentially higher than zero ($\sim$560–640 J mol^{-1} K^{-1}), it can be assumed that the hydrophobic effects of the electrolyte influence the solution.

Conclusions

Interactions between K_DC molecules in the aqueous solution are higher than the analogous interactions in solid state. We have discovered that the enthalpic factor resists to the salt solubility process, whereas the entropic one promotes this process. We also showed that the interaction of water molecules (introduced in the solution) with the components of the solution becomes stronger both with the decrease of the temperature and with the increase of the concentration. The temperature and concentration regularities of the studied functions in the aqueous solutions are determined by the hydrophilic properties of potassium diclofenac molecules.

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