

ВЗАИМОДЕЙСТВИЕ НИКОТИНОВОЙ КИСЛОТЫ С ФЕНИЛАЛАНИНОМ В БУФЕРНЫХ РАСТВОРАХ: ИССЛЕДОВАНИЕ ТЕПЛОЕМКОСТИ И ОБЪЕМНЫХ СВОЙСТВ

Е.Ю. Тюнина, В.Г. Баделин, В.С. Егоркина

Елена Юрьевна Тюнина *, Валентин Георгиевич Баделин

Лаборатория «Термодинамика растворов неэлектролитов и биологически активных веществ», Институт химии растворов им. Г.А. Крестова РАН, ул. Академическая, 1, Иваново, Российская Федерация, 153045
E-mail: tey@isc-ras.ru *, vgb@isc-ras.ru

Валентина Сергеевна Егоркина

Факультет фундаментальной и прикладной химии, Ивановский государственный химико-технологический университет, Шереметевский просп., 10, Иваново, Российская Федерация, 153000
E-mail: valentina-egorkina@mail.ru

Термодинамические и физико-химические свойства многокомпонентных водных растворов, содержащих биологически активные соединения, имеют большое значение в различных областях прикладной химии и особенно важны для понимания химических процессов, происходящих в биологических системах. Детальное изучение движущих сил процессов ассоциации и «молекулярного узнавания» между различными активными центрами белков и лекарственных средств затруднено вследствие сложности и разнообразия существующих взаимодействий в жидких многокомпонентных средах. Методами дифференциальной сканирующей калориметрии и денсиметрии исследованы взаимодействия между модельными соединениями – фенилаланином и никотиновой кислотой в водном фосфатном буферном растворе. Измерения теплоемкости и плотности в системах никотиновая кислота – буфер, фенилаланин – буфер и никотиновая кислота – фенилаланин – буфер выполнены при разных температурах $T = (288,15, 298,15, 308,15 \text{ и } 318,15) \text{ K}$, используя ДСК «SCAL-1» (Pushchino, Russia) и DSA 5000 M (Anton Paar). Оценены значения кажущихся мольных параметров теплоемкости ($^{\circ}C_p$) и объема ($V_{\phi,NA}$) никотиновой кислоты в буферном растворе и в буферном растворе, содержащем 0,0120 моль/кг аминокислоты. Концентрация никотиновой кислоты изменялась в интервале (0,0079 - 0,036) моль/кг. Определены предельные значения ($^{\circ}C_p^0$) и ($V_{\phi,NA}^0$) и их производные по температуре. Показано, что взаимодействие NA с Phe сопровождается комплексообразованием. Молекулы NA в водном буферном растворе проявляют структуроразрушительные свойства, тогда как этот эффект уменьшается в буферном растворе с аминокислотой вследствие взаимодействия NA с молекулами Phe в процессе образования молекулярного комплекса между ними. Полученные результаты обсуждены на основе рассмотрения различных взаимодействий, действующих в исследуемых системах.

Ключевые слова: плотность, теплоемкость, кажущиеся мольные объемы и теплоемкости, L-фенилаланин, никотиновая кислота, образование комплекса

INTERACTION OF NICOTINIC ACID WITH L-PHENYLALANINE IN BUFFER SOLUTIONS: HEAT CAPACITY AND VOLUME PROPERTIES STUDY

E.Yu. Tyunina, V.G. Badelin, V.S. Egorkina

Elena Yu. Tyunina *, Valentin G. Badelin

Laboratory Thermodynamics of Non-Electrolyte Solutions and Active Substances, G.A. Krestov Institute of Solution Chemistry of RAS, Akademicheskaya st., 1, Ivanovo, 153045, Russia

E-mail: tey@isc-ras.ru *, vgb@isc-ras.ru

Valentina S. Egorkina

Department of Fundamental and Applied Chemistry, Ivanovo State University of Chemistry and Technology, Ivanovo, Sheremetievskiy ave., 10, Ivanovo, 153000, Russia

E-mail: valentina-egorkina@mail.ru

Thermodynamic and physicochemical properties of multicomponent aqueous solutions containing biologically active solutes are important in various areas of applied chemistry and are essential for understanding the chemistry of biological systems. Interactions between nicotinic acid (NA) and L-phenylalanine (Phe) were studied in aqueous phosphate buffer solutions (pH=7.35) by differential scanning calorimetry and volume methods. Heat capacities and densities of nicotinic acid-buffer, L-phenylalanine-buffer, and nicotinic acid-L-phenylalanine-buffer mixtures were determined at $T=(288.15, 298.15, 308.15$ and $318.15)$ K using the microdifferential scanning calorimeter SCAL-1 (Pushchino, Russia) and the density meter DSA 5000 M (Anton Paar). The apparent molar heat capacities (ϕC_p) and apparent molar volumes ($V_{\phi,NA}$) of nicotinic acid in buffer solution and in buffer 0.0120 mol kg⁻¹ amino acid solutions were evaluated. The concentration of NA was varied from (0.0079 to 0.036) mol kg⁻¹. The first and second differentials values were determined for NA in an aqueous buffer solution and for NA in an aqueous amino acid buffer solution. The interaction of NA with Phe is accompanied by complex formation. NA molecules in an aqueous buffer solution are water structure breakers, then the structure breaking effects of NA decrease as a result of interactions with Phe molecules during the complex formation in an aqueous amino acid buffer solution. The results were discussed in terms of various interactions taking place in this system.

Key words: density, heat capacity, apparent molar volume, heat capacity, L-phenylalanine, nicotinic acid, complex formation

Для цитирования:

Тюнина Е.Ю., Баделин В.Г., Егоркина В.С. Взаимодействие никотиновой кислоты с фенилаланином в буферных растворах: исследование теплоемкости и объемных свойств. *Иzv. вузов. Химия и хим. технология.* 2017. Т. 60. Вып. 4. С. 33–39.

For citation:

Tyunina E.Yu., Badelin V.G., Egorkina V.S. Interaction of nicotinic acid with L-phenylalanine in buffer solutions: heat capacity and volume properties study. *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.* 2017. V. 60. N 4. P. 33–39.

Recent advanced in genetic engineering and other biotechnologies have spurred an increased interest in biochemical processes, with insights into the molecular-level interactions of protein and biological active compounds [1-6]. Fundamental thermodynamic data are critical in describing enzymatic active sites and various forms of molecular recognition. However, the study of driving forces for the association process

is difficult because of the complexity of interactions in such a large molecule. It is well known, that amino acids are building blocks of proteins. Nicotinic acid, also known as pyridine-3-carboxylic acid, is a member of the B-vitamin family. Nicotinic acid has found important pharmacological applications, particularly, as an antihyperlipidemic agent in the reduction the cholesterol level [7]. Drugs are mostly transported in complexes of serum

albumin [1, 8]. It is a protein consisting of aromatic amino acids residues [8, 9]. The complex formation of the aromatic amino acid, L-phenylalanine (Phe), with the nicotinic acid (NA) in aqueous solution ($pH = 7.35$) was earlier described [10-12] by calorimetry and UV-vis spectroscopy. No data are available in literature on the heat capacity and volume properties of nicotinic acid in aqueous buffer and aqueous amino acid buffer solutions. The aim of this work was to study the interaction between the nicotinic acid and L-phenylalanine in aqueous buffer solutions ($pH = 7.35$) through the determination of heat capacity and volume properties.

EXPERIMENTAL SECTION

L-phenylalanine (Phe) (Sigma, ≥ 0.99) and nicotinic acid (NA) (Sigma-Aldrich, ≥ 0.98) were used without further purification after drying for 24 h at 356.15 K in a vacuum until constant weight. All measurements were performed in aqueous phosphate buffer with $pH = 7.35$. Stock phosphate buffer solutions were prepared using doubly distilled water and sodium phosphate monobasic (Sigma, ≥ 0.99) and sodium phosphate dibasic (Sigma, ≥ 0.99) and used within a few days, after checking the actual pH value with a digital pH-meter Mettler Toledo, model Five-Easy. The buffers were used as solvents for the preparation of the measurement solutions by mass (with an accuracy of 1×10^{-5} g) using a Sartorius-ME215S balance.

The density (ρ) of solution was measured using a digital precision vibrating densimeter DMA-5000 M (Anton Paar, Austria). The uncertainty in density measurements was within $\pm 2 \times 10^{-3}$ kg·m⁻³. The temperature inside the densimeter cell was controlled to $\pm 1 \times 10^{-3}$ K by built-in Peltier device. The densimeter was calibrated once a day with twice-distilled freshly degassed water and dry air. The densities of pure water at different temperatures were taken from [13].

The specific heat capacity (C_p) measurements of NA-buffer, Phe-buffer and NA-Phe-buffer mixtures were performed in a differential scanning microcalorimeter SCAL-1 (SCAL Co. Ltd., Pushchino, Russia [14, 15]) in glass cells of 0.337 cm³ capacity relative to buffer solvent at the scanning rate of 1.0 K/min. The temperature was maintained with accuracy ± 0.01 K. The standard uncertainty of the heat capacity was within $\pm 0.03\%$.

The concentration of amino acid was fixed at (0.0120 ± 0.0002) mol·kg⁻¹. The concentration of the solutions of nicotinic acid was varied within the range $(0.0079-0.0364)$ mol·kg⁻¹. The uncertainty in the molality of the solutions was estimated within $\pm 2 \cdot 10^{-4}$ mol·kg⁻¹.

The densities and specific heat capacities of the solutions were determined at $T = (288.15, 298.15, 308.15$ and $318.15)$ K.

RESULTS AND DISCUSSION

The densities obtained decrease with increasing temperature and increase with NA concentration. Values of the specific heat capacities obtained decrease with increasing NA concentration and increase with rise in temperature. The apparent molar heat capacities (${}^\phi C_p$) and volumes ($V_{\phi,NA}$) of the NA were calculated using respectively eq. 1 and eq. 2:

$${}^\phi C_p = M_{NA} c_p + 1000(c_p - c_p^0)/m_{NA}, \quad (1)$$

$$V_{\phi,NA} = M_{NA}/\rho - 1000(\rho - \rho_0)/m_{NA}\rho\rho_0, \quad (2)$$

in which M_{NA} is the molecular mass of nicotinic acid (g·mol⁻¹), m_{NA} is the NA molality (mol·kg⁻¹), c_p and c_p^0 are the specific heat capacities of the solution and the solvent (J·K⁻¹·g⁻¹), ρ and ρ_0 are the densities of the solution and the solvent (g·cm⁻³), respectively.

In aqueous solutions at $pH = 7.35$, the amino acid and NA exist as zwitterion and anion, respectively, as described in the literature [7, 10, 11]. The interaction of NA with Phe is accompanied by complex formation. This fact has experimental confirmations. The interactions of Phe with NA in buffer solution have been studied by calorimetric method and UV-spectroscopy at 298.15 K [10-12] which reveals that the aromatic amino acid form 1:2 complex with NA characterized by a binding constant of middle strength ($\lg K_c = 3.68 \pm 0.03$ [10]). The Phe/NA complex formation is an endothermal process [10, 11]. The complex formation between Phe and NA was characterized by positive values of enthalpy and entropy changes. Therefore, the complex is mainly entropically stabilized with a little contribution from the enthalpy factor [11].

The dependences of apparent molar volumes and heat capacities of NA on the NA concentration are represented at different temperatures (Figs. 1-4). As shown in Figs. 2 and 4, the shape of these curves shows that Phe undergoes the binding with NA. The function $V_{\phi,NA} = f(m_{NA})$ has a maximum corresponding to the stoichiometry of complex [16, 17]. The maximal values of $V_{\phi,NA}$ were observed near $m_{NA} = 0.0249$ mol·kg⁻¹ at 298.15 K and near $m_{NA} = 0.0219$ mol·kg⁻¹ at 288.15, 308.15 and 318.15 K (Fig. 2), which correspond to the ~1:2 and 1:1.7 Phe / NA molar ratios, respectively. The maximal values of ${}^\phi C_p$ were observed near $m_{NA} = 0.0199$ mol·kg⁻¹, which correspond to the ~1:1.7 Phe/NA molar ratios at the temperatures studied. Thus, the stoichiometry of the complex obtained was found to weakly depend on temperature.

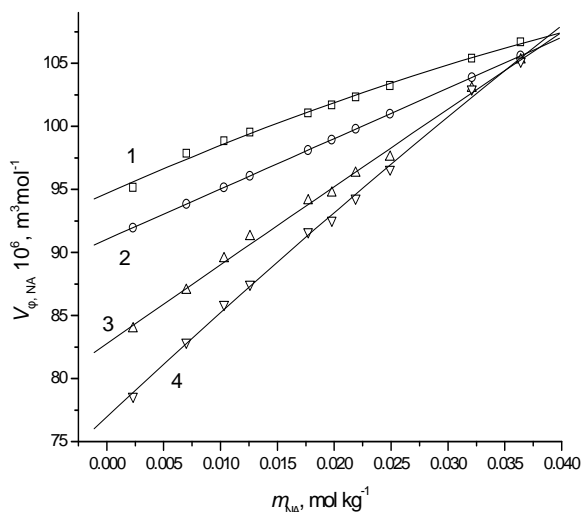


Fig. 1. Apparent molar volumes of nicotinic acid ($V_{\phi,NA}$) in aqueous buffer solutions as a functions of nicotinic acid molality (m_{NA}) at various temperatures, K: 1 – 288.15, 2 – 298.15, 3 – 308.15, 4 – 318.15

Рис. 1. Концентрационные зависимости кажущихся молярных объемов ($V_{\phi,NA}$) никотиновой кислоты в водных буферных растворах при разных температурах, К: 1 – 288,15, 2 – 298,15, 3 – 308,15, 4 – 318,15

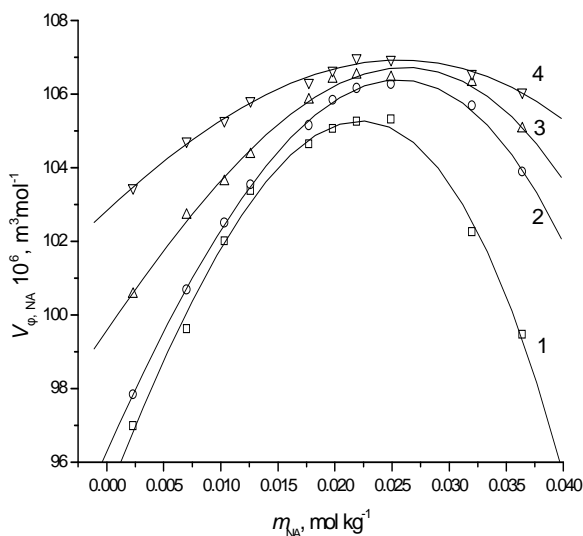


Fig. 2. Apparent molar volumes of nicotinic acid ($V_{\phi,NA}$) in aqueous buffer of L-phenylalanine ($m_{Phe}=0.0120 \text{ mol}\cdot\text{kg}^{-1}$) solutions as a functions of nicotinic acid molality (m_{NA}) at various temperatures, K: 1 – 288.15, 2 – 298.15, 3 – 308.15, 4 – 318.15

Рис. 2. Концентрационные зависимости кажущихся молярных объемов ($V_{\phi,NA}$) никотиновой кислоты в водных буферных растворах, содержащих L-фенилаланин ($m_{NA}=0,0120$ моль/кг), при разных температурах, К: 1 – 288,15, 2 – 298,15, 3 – 308,15, 4 – 318,15

The concentration dependences of the $V_{\phi,NA}$ in aqueous buffer solutions (Fig. 1) were modeled by linear equations of the form:

$$V_{\phi,NA} = V_{\phi,NA}^0 + S_v m_{NA}, \quad (3)$$

where $V_{\phi,NA}^0$ corresponds to the apparent molar volume

extrapolated to infinite dilution and S_v is a parameter

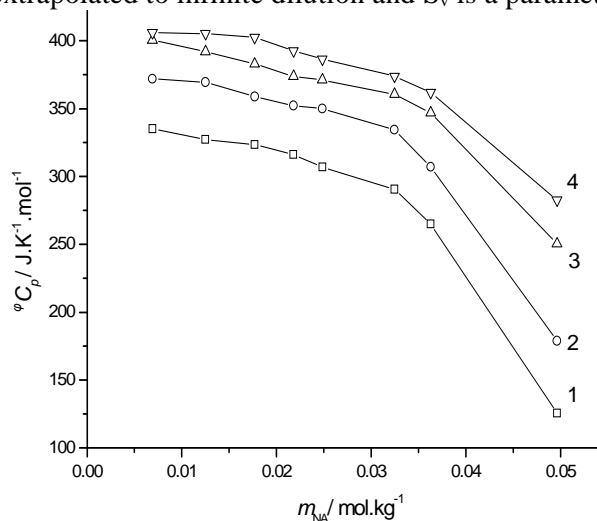


Fig. 3. Apparent molar heat capacity of nicotinic acid (${}^{\phi}C_p$) in aqueous buffer solutions as a function of nicotinic acid molality (m_{NA}) at various temperatures, K: 1 – 288.15, 2 – 298.15, 3 – 308.15, 4 – 318.15

Рис. 3. Концентрационные зависимости кажущихся молярных теплоемкостей (${}^{\phi}C_p$) никотиновой кислоты в водных буферных растворах при разных температурах, К: 1 – 288,15, 2 – 298,15, 3 – 308,15, 4 – 318,15

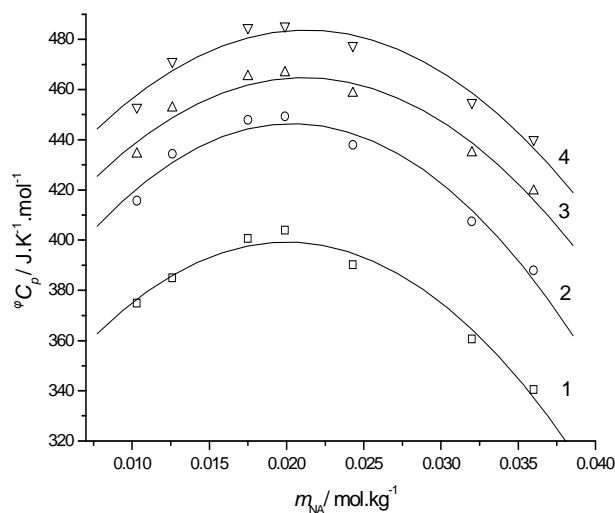


Fig. 4. Apparent molar heat capacity of nicotinic acid (${}^{\phi}C_p$) in an aqueous buffer of L-phenylalanine ($m_{Phe}=0.0120 \text{ mol}\cdot\text{kg}^{-1}$) solutions as a function of nicotinic acid molality (m_{NA}) at various temperatures, K: 1 – 288.15, 2 – 298.15, 3 – 308.15, 4 – 318.15

Рис. 4. Концентрационные зависимости кажущихся молярных теплоемкостей (${}^{\phi}C_p$) никотиновой кислоты в водных буферных растворах, содержащих L-фенилаланин ($m_{NA}=0,0120$ моль/кг), при разных температурах, К: 1 – 288,15, 2 – 298,15, 3 – 308,15, 4 – 318,15

characterizing the solute–solute interactions. The data on the apparent molar volume of NA in buffer Phe solution (Fig. 2) was fitted to an equation of the form:

$$V_{\phi,NA} = V_{\phi,NA}^0 + A m_{NA} + B m_{NA}^2. \quad (4)$$

Here, $V_{\phi,NA}^0$ is the limiting value of apparent

molar volume, which is equal to the partial molar volume at infinite dilution, and A and B are the fitting coefficients. The values of $V_{\phi,NA}^0$ together with standard errors derived by least squares fitting of the $V_{\phi,NA}$ values to Eqs. 3-4 are reported in Table 1. The values of $V_{\phi,NA}^0$ of NA in the buffer amino acid solutions are positive and increases with increase in the temperature, whereas a some decrease has been observed in case of the buffer solutions of NA. Since the formation of complex between Phe and NA involves changes in the hydration water of both amino acid and NA molecules, it must be reflected in the volume property. The increase in the values of $V_{\phi,NA}^0$ with increase of temperature can be explained in terms of the desolvation and the overlap of hydration co-spheres of the solutes during the binding [18, 19]. The water molecules from the solvation shells of Phe zwitterions and NA molecules are released into the bulk aqueous solution, resulting in the expansion of the volume of solution at higher temperature.

Table 1

Limiting apparent molar volumes, $V_{\phi,NA}^0$, of nicotinic acid and $(\partial V_{\phi}^0/\partial T)_p$ values in aqueous buffer solutions and in aqueous buffer solutions of L-phenylalanine at different temperatures

Таблица 1. Значения предельных кажущихся молярных объемов ($V_{\phi,NA}^0$) никотиновой кислоты и их производных $(\partial V_{\phi}^0/\partial T)_p$ в водных буферных растворах и в водных буферных растворах, содержащих L-фенилаланин, при разных температурах

T, K	$V_{\phi,NA}^0, \text{cm}^3 \cdot \text{mol}^{-1}$	$(\partial V_{\phi}^0/\partial T)_p^b, \text{cm}^3 \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$
NA-buffer solution		
288.15	94.8±0.2	-0.47±0.10
298.15	91.0±0.3	-0.58±0.11
308.15	82.7±0.3	-0.67±0.15
318.15	76.9±0.4	-0.79±0.21
NA- Phe ^a - buffer solution		
288.15	95.5±0.2	0.11±0.10
298.15	96.9±0.2	0.22±0.12
308.15	99.6±0.3	0.32±0.14
318.15	102.9±0.3	0.43±0.18

Notes: ^a $m_{\text{Phe}} = 0.0120 \text{ mol} \cdot \text{kg}^{-1}$, ^b $(\partial V_{\phi}^0/\partial T)_p$ was calculated by equation: $(\partial V_{\phi}^0/\partial T)_p = \beta + 2T\gamma$, where β and γ are constants from Eq. (6)
Примечания: ^a $m_{\text{Phe}} = 0,0120 \text{ моль} \cdot \text{кг}^{-1}$, ^b $(\partial V_{\phi}^0/\partial T)_p$ вычислена по уравнению: $(\partial V_{\phi}^0/\partial T)_p = \beta + 2T\gamma$, где β и γ - коэффициенты ур. (6)

The concentration dependences of the reported apparent molar heat capacities (Figs. 3, 4) were modeled using equations of the general form:

$$\phi C_p = \phi C_p^0 + A m_{\text{NA}} + B m_{\text{NA}}^2. \quad (5)$$

Here, ϕC_p^0 is the limiting value of apparent molar heat capacity, which is equal to the partial molar heat capacity at infinite dilution, and A, B are the fitting coefficients. The estimated values for ϕC_p^0 and

their associated uncertainties are reported in Table 2. The values of ϕC_p^0 for the NA in the binary (NA – buffer) and the ternary (NA – Phe – buffer) systems are positive and increase with increase in the temperature from 288.15 to 318.15 K. This behavior is indicative of hydrophilic character of the solutes molecules as described in the literature [20]. The increase of ϕC_p^0 with increase in temperature indicates that interactions between solutes molecules are stronger than intermolecular hydrogen bonding between water molecules. The higher positive ϕC_p^0 values for NA in $0.0120 \text{ mol} \cdot \text{kg}^{-1}$ Phe compared to the aqueous buffer solution at each temperature generally suggest that the interactions between Phe zwitterions and NA molecules are predominant.

Table 2

Limiting apparent molar heat capacities, ϕC_p^0 , of nicotinic acid and $(\partial \phi C_p^0/\partial T)_p$ values in aqueous buffer solutions and in an aqueous buffer of L-phenylalanine at different temperatures

Таблица 2. Значения предельных кажущихся молярных теплоемкостей (ϕC_p^0) никотиновой кислоты и их производных $(\partial \phi C_p^0/\partial T)_p$ в водных буферных растворах и в водных буферных растворах, содержащих L-фенилаланин, при разных температурах

T, K	$\phi C_p^0, \text{J} \cdot \text{K}^{-1} \cdot \text{mol}^{-1}$	$(\partial \phi C_p^0/\partial T)_p^b, \text{J} \cdot \text{K}^{-2} \cdot \text{mol}^{-1}$
NA – buffer solution		
288.15	292±5	4.85±0.10
298.15	331±5	3.75±0.11
308.15	363±4	2.65±0.15
318.15	386±4	1.15±0.21
NA – Phe ^a – buffer solution		
288.15	330±3	5.21±0.03
298.15	374±4	4.26±0.06
308.15	414±4	3.31±0.15
318.15	439±4	2.36±0.18

Notes: ^a $m_{\text{Phe}} = 0.0120 \text{ mol} \cdot \text{kg}^{-1}$, ^b $(\partial \phi C_p^0/\partial T)_p$ was calculated by equation: $(\partial \phi C_p^0/\partial T)_p = \beta + 2T\gamma$, where β and γ are constants from Eq. (6)

Примечания: ^a $m_{\text{Phe}} = 0,0120 \text{ моль} \cdot \text{кг}^{-1}$, ^b $(\partial \phi C_p^0/\partial T)_p$ вычислена по уравнению: $(\partial \phi C_p^0/\partial T)_p = \beta + 2T\gamma$, где β и γ - коэффициенты ур. (6)

The $Y_{\phi,NA}^0$ values for the NA studied in the aqueous buffer solutions and in the aqueous Phe buffer solutions at different temperatures were fitted by the method of least squares using the equation:

$$Y_{\phi}^0 = \alpha + \beta T + \gamma T^2, \quad (6)$$

where $Y \equiv V_{\phi}^0$ or ϕC_p^0 ; α , β and γ are constants and T is the temperature. The $(\partial Y_{\phi}^0/\partial T)_p$ and $(\partial^2 Y_{\phi}^0/\partial T^2)_p$ parameters were then determined from the above Eq. 6. The calculated values of $(\partial V_{\phi}^0/\partial T)_p$ for NA are given in Table 1 at different temperatures. The values of $(\partial V_{\phi}^0/\partial T)_p$ decrease with increase in temperature in

case of NA – buffer solutions whereas in case of NA – Phe – buffer solutions the values of $(\partial V_{\phi}^{\circ}/\partial T)_p$ increase with increase in temperature. The positive values of $(\partial V_{\phi}^{\circ}/\partial T)_p$ indicate the release of electrostricted water from the solvation layers of NA and Phe and hence favoring amino acid – nicotinic acid interactions.

The second differential, $(\partial^2 V_{\phi}^{\circ}/\partial T^2)_p$ has been used to classify solutes on the basis of their effect on water – water interactions as described in the literature [21]. According to Hepler [21], the structure-breaking solutes possess negative $(\partial^2 V_{\phi}^{\circ}/\partial T^2)_p$ values. The positive values of $(\partial^2 V_{\phi}^{\circ}/\partial T^2)_p$ should be associated with the structure-making solutes. In our case, the values of $(\partial^2 V_{\phi}^{\circ}/\partial T^2)_p$ are $-0.0099 \text{ cm}^6 \cdot \text{mol}^{-2} \cdot \text{K}^{-2}$ for NA in aqueous buffer solution and $0.0107 \text{ cm}^6 \cdot \text{mol}^{-2} \cdot \text{K}^{-2}$ for NA in aqueous amino acid buffer solution. Thus, the negative value of $(\partial^2 V_{\phi}^{\circ}/\partial T^2)_p$ suggests that NA in aqueous buffer solution is structure breaker. The positive value of the term can be indicated an obvious structure-making tendency of NA in aqueous Phe buffer solutions.

The $(\partial^{\phi} C_p^{\circ}/\partial T)_p$ and $(\partial^2 C_p^{\circ}/\partial T^2)_p$ parameters were determined for NA in aqueous buffer solution and for NA in aqueous amino acid buffer solution using Eq. 6.

The values of $(\partial^{\phi} C_p^{\circ}/\partial T)_p$ at different temperatures are given in Table 2. The values of $(\partial^2 C_p^{\circ}/\partial T^2)_p$ are $-0.11 \text{ J} \cdot \text{K}^{-3} \cdot \text{mol}^{-1}$ for NA in aqueous buffer solution and $-0.08 \text{ J} \cdot \text{K}^{-3} \cdot \text{mol}^{-1}$ for NA in aqueous amino acid buffer solution. If one identifies NA molecules in aqueous buffer solution as water structure breakers [22, 23], then the structure breaking effects of NA decrease as a result of interactions with Phe molecules during the complex formation in aqueous amino acid buffer solution.

CONCLUSIONS

The heat capacities and densities measurements of nicotinic acid in aqueous buffer solutions and aqueous $0.0120 \text{ mol} \cdot \text{kg}^{-1}$ L-phenylalanine buffer solutions have been carried out at various temperatures. Apparent molar heat capacities (${}^{\phi}C_p$) and volumes ($V_{\phi, \text{NA}}$) and partial molar heat capacities (${}^{\phi}C_p^{\circ}$) and volumes ($V_{\phi, \text{NA}}^{\circ}$) at infinite dilution have been calculated from the experimental data. The results obtained in this work, along with the data reported earlier [10-12], support that the hydrophilic–hydrophilic interactions of the zwitterionic centers ($\text{COO}^-/\text{NH}_3^+$) of Phe with the charged carboxyl group of NA molecule are predominant.

ЛИТЕРАТУРА

1. **Jha N.S., Kishore N.** Thermodynamic studies on the interaction of folic acid with bovine serum albumin. *J. Chem. Thermodynamics*. 2011. V. 43. P. 814-821.
2. **Bhuiyan M.M.H., Hakin A.W., Liu J.L.** Densities, specific heat capacities, apparent and partial molar volumes and heat capacities of glycine in aqueous solutions of formamid, acetamide, and N,N-dimethylacetamide at $T=298.15 \text{ K}$ and ambient pressure. *J. Solution Chem.* 2010. V. 39. P. 877-896.
3. **Banik I., Roy M.N.** Study of solute-solvent interaction of some bio-active solutes prevailing in aqueous ascorbic acid solution. *J. Mol. Liq.* 2012. V. 169. P. 8-14.
4. **Makrlík E., Selucký P., Vaňura P.** Complexation of some protonated α -amino acid methyl esters with benzo-18-crown-6 in nitrobenzene saturated with water. *J. Mol. Liq.* 2013. V. 180. P. 221-224.
5. **EI-Dossoki F.I.** Volumetric and solvation properties of glycyl-glycine and glycyl-L-leucine in aqueous acetate solutions. *J. Solution Chem.* 2015. V. 44. P. 264-279.
6. **Xu H.** Spectroscopic studies on the interaction of vitamin C with bovine serum albumin. *J. Solution Chem.* 2009. V. 38. P. 15-25.
7. **Gonçalves E.M., Joseph A., Conceição A.C.L., Minas da Piedade M.E.** Potentiometric titration study of the temperature and ionic strength dependence of the of the acidity constants of nicotinic acid (niacin). *J. Chem. Eng. Data*. 2011. V. 56. P. 2964-2970.
8. **Koch-Weser J., Sellers E.M.** Drug therapy: Binding of drugs to serum albumin. *N. Engl. J. Med.* 1976. V. 294. P. 311-316.
9. **Bakkialakshmi S., Chandrakala D.** A spectroscopic investigations of anticancer drugs binding to bovine serum albumin. *Spectrochim. ACTA. Part A*. 2012. V. 88. P. 2-9.

REFERENCES

1. **Jha N.S., Kishore N.** Thermodynamic studies on the interaction of folic acid with bovine serum albumin. *J. Chem. Thermodynamics*. 2011. V. 43. P. 814-821.
2. **Bhuiyan M.M.H., Hakin A.W., Liu J.L.** Densities, specific heat capacities, apparent and partial molar volumes and heat capacities of glycine in aqueous solutions of formamid, acetamide, and N,N-dimethylacetamide at $T=298.15 \text{ K}$ and ambient pressure. *J. Solution Chem.* 2010. V. 39. P. 877-896. DOI: 10.1007/s10953-010-9540-y.
3. **Banik I., Roy M.N.** Study of solute-solvent interaction of some bio-active solutes prevailing in aqueous ascorbic acid solution. *J. Mol. Liq.* 2012. V. 169. P. 8-14. DOI: 10.1016/j.molliq.2012.03.006.
4. **Makrlík E., Selucký P., Vaňura P.** Complexation of some protonated α -amino acid methyl esters with benzo-18-crown-6 in nitrobenzene saturated with water. *J. Mol. Liq.* 2013. V. 180. P. 221-224. DOI: 10.1016/j.molliq.2013.01.016.
5. **EI-Dossoki F.I.** Volumetric and solvation properties of glycyl-glycine and glycyl-L-leucine in aqueous acetate solutions. *J. Solution Chem.* 2015. V. 44. P. 264-279. DOI: 10.1007/s10953-015-0314-4.
6. **Xu H.** Spectroscopic studies on the interaction of vitamin C with bovine serum albumin. *J. Solution Chem.* 2009. V. 38. P. 15-25. DOI: 10.1007/s10953-008-9351-6.
7. **Gonçalves E.M., Joseph A., Conceição A.C.L., Minas da Piedade M.E.** Potentiometric titration study of the temperature and ionic strength dependence of the of the acidity constants of nicotinic acid (niacin). *J. Chem. Eng. Data*. 2011. V. 56. P. 2964-2970. DOI: 10.1021/je200263g.
8. **Koch-Weser J., Sellers E.M.** Drug therapy: Binding of drugs to serum albumin. *N. Engl. J. Med.* 1976. V. 294. P. 311-316. DOI: 10.1056/NEJM197602052940605.
9. **Bakkialakshmi S., Chandrakala D.** A spectroscopic investigations of anticancer drugs binding to bovine serum albumin.

10. **Баделин В.Г., Тюнина Е.Ю., Межевой И.Н., Тарасова Г.Н.** Термодинамические характеристики взаимодействия никотиновой кислоты и фенилаланина в водном буферном растворе при 298 К. *Журн. физич. химии*. 2013. Т. 87. № 8. С. 1316-1319.
11. **Tyunina E.Yu., Badelin V.G., Mezhevoi I.N., Tarasova G.N.** Thermodynamics of aromatic amino acid interactions with heterocyclic ligands. *J. Mol. Liq.* 2015. V. 211. P. 494-497.
12. **Баделин В.Г., Тарасова Г.Н., Тюнина Е.Ю.** Исследование взаимодействия ароматических аминокислот с никотиновой кислотой и урацилом в водных растворах. *Изв. вузов. Химия и хим. технология*. 2014. Т. 57. Вып. 3. С. 34-36.
13. **Kell G.S.** Density, thermal expansivity, and compressibility of liquid water from 0 to 150°C: Correlations and tables for atmospheric pressure and saturation reviewed and expressed on 1968 temperature scale. *J. Chem. Eng. Data*. 1975. V. 20. P. 97-105.
14. **Senin A.A., Potekhin S.A., Tiktopulo E.I., Filimonov V.V.** Differential scanning microcalorimeter SCAL-1. *J. Therm. Anal. Calorim.* 2000. V. 62. P. 153-160.
15. **Senin A.A., Dzhavadov L.N., Potekhin S.A.** High-pressure differential scanning microcalorimeter. *Rev. Sci. Instrum.* 2016. V. 87. P. 034901-034906.
16. **Zielenkiewicz W., Pietraszkiewicz O., Wszelaka-Rylic M., Pietraszkiewicz M., Royx-Desgranges G., Roux A.H., Grolier J.-P.E.** Molecular interactions of macrocycles with dipeptides in aqueous solutions. Partial molar volumes and heat capacities of transfer of a chiral 18-crown-6 and calyx[4]resorcinarene derivative from water to aqueous dipeptide solutions at 250°C. *J. Solution Chem.* 1998. V. 27. P. 121-134.
17. **Terekhova I.V., Kulikov O.V.** Thermodynamics of the interactions of ascorbic acid with α - and β -cyclodextrins in aqueous solutions. *Mendeleev Comm.* 2002. V. 3. P. 1-2.
18. **Franks F.** Water: A comprehensive treatise. V. 3. New York: Plenum Press. 1973.
19. **Gurney R.W.** Ionic processes in solution. New York: McGraw Hill. 1953.
20. **Hakin A.W., Duke M.M., Groft L.L., Marty J.L., Rushfeldt M.L.** Calorimetric investigations of aqueous amino acid and dipeptide systems from 288.15 to 328.15 K. *Can. J. Chem.* 1995. V. 73. P. 725-734.
21. **Hepler L.G.** Thermal expansion and structure in water and aqueous solutions. *Can. J. Chem.* 1969. V. 47. P. 4613-4617.
22. **Roberts M.J., Bently M.D., Harris J.M.** Chemistry for peptide and protein PEGylation. *Adv. Drug Delivery Rev.* 2002. V. 54. P. 459-476.
23. **Kunda A., Kishore N.** Apparent molar heat capacities and apparent molar volumes of aqueous nicotinamide at different temperatures. *J. Solution Chem.* 2003. V. 32. N 8. P. 703-717.
10. **Badelin V.G., Tyunina E.Yu., Mezhevoi I.N., Tarasova G.N.** Thermodynamic characteristics of the interaction between nicotinic acid and phenylalanine in an aqueous buffer solution at 298 K. *Russ. J. Phys. Chem. A*. 2013. V. 87. P. 1306-1309. DOI: 10.1134/S0036024413070078.
11. **Tyunina E.Yu., Badelin V.G., Mezhevoi I.N., Tarasova G.N.** Thermodynamics of aromatic amino acid interactions with heterocyclic ligands. *J. Mol. Liq.* 2015. V. 211. P. 494-497. DOI: 10.1016/j.molliq.2015.07.024.
12. **Badelin V.G., Tarasova G.N., Tyunina E.Yu.** Investigation of interaction of aromatic amino acids with nicotinic acid and uracil in aqueous solutions. *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.* 2014. V. 57. N 3. P. 34-36 (in Russian).
13. **Kell G.S.** Density, thermal expansivity, and compressibility of liquid water from 0 to 150°C: Correlations and tables for atmospheric pressure and saturation reviewed and expressed on 1968 temperature scale. *J. Chem. Eng. Data*. 1975. V. 20. P. 97-105. DOI: 10.1021/je60064a005.
14. **Senin A.A., Potekhin S.A., Tiktopulo E.I., Filimonov V.V.** Differential scanning microcalorimeter SCAL-1. *J. Therm. Anal. Calorim.* 2000. V. 62. P. 153-160. DOI: 10.1023/A:1010171013669.
15. **Senin A.A., Dzhavadov L.N., Potekhin S.A.** High-pressure differential scanning microcalorimeter. *Rev. Sci. Instrum.* 2016. V. 87. P. 034901-034906. DOI: 10.1063/1.4944859.
16. **Zielenkiewicz W., Pietraszkiewicz O., Wszelaka-Rylic M., Pietraszkiewicz M., Royx-Desgranges G., Roux A.H., Grolier J.-P.E.** Molecular interactions of macrocycles with dipeptides in aqueous solutions. Partial molar volumes and heat capacities of transfer of a chiral 18-crown-6 and calyx[4]resorcinarene derivative from water to aqueous dipeptide solutions at 250°C. *J. Solution Chem.* 1998. V. 27. P. 121-134. DOI: 10.1023/A:1022653222581.
17. **Terekhova I.V., Kulikov O.V.** Thermodynamics of the interactions of ascorbic acid with α - and β -cyclodextrins in aqueous solutions. *Mendeleev Comm.* 2002. V. 3. P. 1-2.
18. **Franks F.** Water: A comprehensive treatise. V. 3. New York: Plenum Press. 1973.
19. **Gurney R.W.** Ionic processes in solution. New York: McGraw Hill. 1953.
20. **Hakin A.W., Duke M.M., Groft L.L., Marty J.L., Rushfeldt M.L.** Calorimetric investigations of aqueous amino acid and dipeptide systems from 288.15 to 328.15 K. *Can. J. Chem.* 1995. V. 73. P. 725-734. DOI: 10.1139/v95-092.
21. **Hepler L.G.** Thermal expansion and structure in water and aqueous solutions. *Can. J. Chem.* 1969. V. 47. P. 4613-4617. DOI: 10.1139/v69-762.
22. **Roberts M.J., Bently M.D., Harris J.M.** Chemistry for peptide and protein PEGylation. *Adv. Drug Delivery Rev.* 2002. V. 54. P. 459-476. DOI: 10.1016/S0169-409X(02)00022-4.
23. **Kunda A., Kishore N.** Apparent molar heat capacities and apparent molar volumes of aqueous nicotinamide at different temperatures. *J. Solution Chem.* 2003. V. 32. N 8. P. 703-717. DOI: 10.1023/B:JOSL.0000002990.73945.c9.

Поступила в редакцию 09.12.2016
Принята к опубликованию 01.03.2017

Received 09.12.2016
Accepted 01.03.2017