ИЗВЕСТИЯ ВЫСШИХ УЧЕБНЫХ ЗАВЕДЕНИЙ.
Т 65 (12) Серия «**ХИМИЯ И ХИМИЧЕСКАЯ ТЕХНОЛОГИЯ**» 2022
V 65 (12) **ChemChemTech** 2022

DOI: 10.6060/ivkkt.20226512.6661

УДК: 541.11:536.7

СТАНДАРТНЫЕ ЭНТАЛЬПИИ ОБРАЗОВАНИЯ ЛОРНОКСИКАМА И ЕГО АНИОНА L^- В ВОДНОМ РАСТВОРЕ

О.Н. Крутова, В.В. Черников, Е.Ю. Тюнина, П.Д. Крутов, Р.А. Романов

Ольга Николаевна Крутова (ORCID 0000-0003-3594-2316)*, Виктор Владимирович Черников (ORCID 0000-0002-1095-1163), Павел Дмитриевич Крутов (ORCID 0000-0002-8110-4818), Руслан Андреевич Романов

Кафедра аналитической химии, Ивановский государственный химико-технологический университет, просп. Шереметевский, 7, Иваново, Российская Федерация, 153000
E-mail: kdvkonkpd@yandex.ru*, chernikov56@mail.ru, r.frnn@mail.ru, evvahxx@gmail.com

Елена Юрьевна Тюнина (ORCID 0000-0002-0530-4375)

Институт химии растворов им. Г.А. Крестова РАН, ул. Академическая, 1, Иваново, Российская Федерация, 153045
E-mail: tey@isc-ras.ru

В качестве объекта исследования нами был выбран лорноксикам. Он представляет собой производное тиенотиазина амид монокарбоновой кислоты. Он играет роль нестероидного противовоспалительного препарата, ненаркотического анальгетика и жаропонижающего средства. Лорноксикам практически не растворим в воде. Измерены теплоты растворения кристаллического лорноксикама в растворах гидроксида калия при 298,15 К прямым калориметрическим методом. Измерения проводились на калориметре с изотермической оболочкой и автоматической записью температурно-временной кривой, в реакционном сосуде объемом 60 см^3 и при T = 298,15 ± 0,01 К и P = 100,5± 0,7 кПа. Относительная погрешность измерения для теплоты растворения стандартного вещества составляла-0,1-0,3%. Работа калориметрической установки была проверена по общепринятому калориметрическому стандарту – теплоте растворения кристаллического хлорида калия в воде. Расчет равновесного состава системы с учетом процессов ступенчатой диссоциации лорноксикама и диссоциации воды проводился по программе KEV. Величина стандартной энтальпии образования лорноксикама была рассчитана по аддитивно групповому методу, основанному на групповой систематике с классификацией фрагментов типа классификации Бенсона, которая учитывает влияние первоначального окружения для атомов. Стандартную энтальпию образования аниона лорноксикама в водном растворе определяли, используя данные по теплоте растворения лорноксикама в растворах щелочи при соотношении эквивалентов не менее 1:2. Рассчитаны стандартные энтальпии образования лорноксикама и продуктов его диссоциации в водном растворе. Значения стандартных энтальпий образования лорноксикама и продуктов его диссоциации в водном растворе получены впервые. Они являются ключевыми величинами в термохимии данного соединения, открывают возможности проведения строгих термодинамических расчетов в системах с лорноксикамом.

Ключевые слова: лорноксикам, биолиганды, калориметрия, энтальпия, растворы

Для цитирования:
Крутова О.Н., Черников В.В., Тюнина Е.Ю., Крутов П.Д., Романов Р.А. Стандартные энтальпии образования лорноксикама и его аниона L^- в водном растворе. *Изв. вузов. Химия и хим. технология*. 2022. Т. 65. Вып. 12. С. 6–11. DOI: 10.6060/ivkkt.20226512.6661.

For citation:
Krutova O.N., Chernikov V.V., Tyunina E.Yu., Krutov P.D., Romanov R.A. Standard enthalpy of formation of lornoxicam and its anion L^- in aqueous solution. *ChemChemTech* [*Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.*]. 2022. V. 65. N 12. P. 6–11. DOI: 10.6060/ivkkt.20226512.6661.

STANDARD ENTHALPY OF FORMATION OF LORNOXICAM AND ITS ANION L^- IN AQUEOUS SOLUTION

O.N. Krutova, V.V. Chernikov, E.Yu. Tyunina, P.D. Krutov, R.A. Romanov

Olga N. Krutova (ORCID 0000-0003-3594-2316)*, Viktor V. Chernikov (ORCID 0000-0002-1095-1163), Pavel D. Krutov (ORCID 0000-0002-8110-4818), Ruslan A. Romanov

Department of Analytical Chemistry, Ivanovo State University of Chemistry and Technology, Sheremetevskiy ave., 7, Ivanovo, 153000, Russia
E-mail: kdvkonkpd@yandex.ru *, chernikov56@mail.ru, r.frnn@mail.ru, evvahxx@gmail.com

Elena Yu. Tyunina (ORCID 0000-0002-0530-4375)

G.A. Krestov Institute of Solution Chemistry of the RAS, Academicheskaya st., 1, Ivanovo, 153045, Russia
E-mail: tey@isc-ras.ru

Lornoxicam was chosen as the object of our research. It is a derivative of thienothiazine monocarboxylic acid amide. It plays the role of a nonsteroidal anti-inflammatory drug, a non-narcotic analgesic and an antipyretic. Lornoxicam is practically insoluble in water. The heat of dissolution of crystalline lornoxicam in solutions of potassium hydroxide at 298.15 K was measured by direct calorimetric method. Measurements were carried out on a calorimeter with an isothermal shell and automatic recording of the temperature-time curve, in a reaction vessel with a volume of 60 cm^3 and at $T = 298.15 \pm 0.01$ K and $P = 100.5 \pm 0.7$ kPa. The relative measurement error for the heat of dissolution of the standard substance was 0.1-0.3%. The operation of the calorimetric unit was tested according to the generally accepted calorimetric standard – the heat of dissolution of crystalline potassium chloride in water. The calculation of the equilibrium composition of the system, taking into account the processes of stepwise dissociation of lornoxicam and dissociation of water, was carried out according to the KEV program. The value of the standard enthalpy of lornoxicam formation was calculated using an additive group method based on group systematics with a classification of fragments of the Benson classification type, which takes into account the influence of the initial environment for atoms. The standard enthalpy of lornoxicam anion formation in an aqueous solution was determined using data on the heat of dissolution of lornoxicam in alkali solutions with a ratio of equivalents of at least 1:2. The standard enthalpy of lornoxicam formation and its dissociation products in an aqueous solution are calculated. The values of the standard enthalpy of lornoxicam formation and its dissociation products in an aqueous solution were obtained for the first time. They are key quantities in the thermochemistry of this compound, open up the possibility of conducting rigorous thermodynamic calculations in systems with lornoxicam.

Key words: lornoxicam, bioligands, calorimetry, enthalpy, solutions

Lornoxicam is a thienothiazine derivative of monocarboxylic acid amide. It is used to treat pain, primarily arising from inflammatory diseases of the joints, osteoarthritis, surgical interventions, sciatica and other inflammations. It plays the role of a non-steroidal anti-inflammatory drug, a non-narcotic analgesic and an antipyretic. Lornoxicam is practically insoluble in water. The authors of [1] attempted to improve the solubility of lornoxicam by engineering crystals with different coforms. The behavior of nineteen different coformers was investigated. The prepared cocrystals were evaluated for solubility, powder characteristics, analysis and *in vitro* dissolution study. Multiple approaches have been adopted to improve the solubility of poorly water soluble of active pharmaceutical ingredient [2-6].

The structural formula of lornoxicam ($C_{13}H_{10}ClN_3O_4S_2$; M =371.82) is shown in Fig. 1

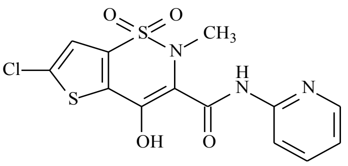

Fig. 1. The structural formula of lornoxicam (4-hydroxy-2-methyl-1,1-dioxo-N-(pyridine-2-yl)-6-chloro-2H-1λ^6-thieno[2,3-e][1,2]thiazine-3-carboxamide)
Рис. 1. Структурная формула лорноксикама (4-Гидрокси-2-метил-1,1-диоксо-N-(пиридин-2-ил)-6-хлор-2H-1λ^6-тиено[2,3-e][1,2]тиазин-3-карбоксамид)

The purpose of this work is to determine the standard enthalpies of lornoxicam formation and its dissociation products in an aqueous solution by the thermal effects of bioligand dissolution in aqueous KOH solutions at 298.15 K. Fig. 2 shows the equilibrium diagram of an aqueous solution of lornoxicam, plotted by calculating the equilibrium composition of solutions of the bioligand at different pH values using the KEV software [7].

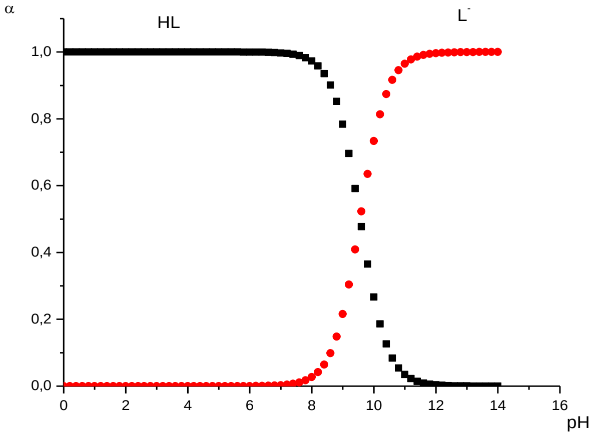

Fig. 2. Diagram of the equilibrium in an aqueous solution of lornoxicam (I = 0.0 and T = 298.15 K)

Рис. 2. Диаграмма равновесия в водном растворе лорноксикама (I = 0,0 и T = 298,15 K)

EXPERIMENTAL PART

Measurements were carried out in a calorimeter with an isothermal shell equipped with a 60 cm^3 reaction vessel, and electrical calibration at T = (293.15-308.15) ± 0.01 K and P = 100.5 ± 0.7 kPa and automatic recording of the temperature curve-time [8-10]. A KMT-14 thermistor was used as a temperature sensor. Thermostatic calorimetric cell was carried out in a thermostat equipped with a PID controller with an accuracy of 0.002 K. The thermostat's temperature sensor was a platinum resistance thermometer. Calorimeter current was calibrated. The volume of the calorimetric liquid was 42.83 ml. The working volume of the ampoule is 1-1.6 cm^3, the maximum thermometric sensitivity of the calorimetric installation was (0.5-2)·10^{-2} J/mm of the recorder scale. The relative measurement error for the heats of dissolution of the standard substance is 0.1-0.3%. The installation was tested by the integral enthalpies of dissolution of crystalline potassium chloride in water and was considered suitable for measuring if the value determined in it $\Delta_{sol}H^{o}_{298.15}(KCl\infty H_2O)$ differed from the standard by no >0.3%. As the standard, the most reliable value currently used was $\Delta_{sol}H^{o}_{298.15}$ $(KCl\infty H_2O) = -17.234 \pm 0.018$ kJ/mol, corresponding to the SRM 1655NBS standard. The calorimeter thermal value for water was 87 ± 12 J/K [11]. Experimental data are presented in Table 2. The results of graphic processing of experimental data are presented in (Fig. 3). The confidence interval of the average ΔH value was calculated with a probability of 0.95. The equilibrium composition of the particles in solution was calculated using the «KEV» program [7].

RESULTS AND DISCUSSION

The values of the standard enthalpies of combustion and lornoxicam formation were calculated using the additive group method [12-14] based on group systematics with a classification of fragments of the Benson classification type, which takes into account the influence of the initial environment for atoms. The calculation of the enthalpy of combustion and formation of the studied compound was carried out according to the formula:

$$\Delta_{c(f)}H^{\circ}(cr.) = \sum A_{\,i}\, \Delta_{c(f)}\, H_i^{\circ},\ i = 1,2,3\ldots n \quad (1)$$

where Δ c(f)Hi° is the energy contribution to the heat of combustion and the formation of a certain atomic group, and i is the number of such atomic groups in the molecule, n is the number of types of atomic groups in the molecule. Initial data for the calculation of $\Delta_fH^{\circ}(cr.)(C_{13}H_{10}ClN_3O_4S_2)$ = - 145.2 ±1.9 kJ/mol are presented in Table 1.

Table 1

Numerical values of energy contributions to the values of enthalpy of formation according to the Benson classification

Таблица 1. **Численные значения энергетических вкладов в значения энтальпии образования по классификации Бенсона**

Group	Number of groups (n)	$-\Delta_fH^0_{(cr.)i}$, kJ/mol
$(C)_3$-N	1	-102.0±64.3
$(C)_3$-CH	5	-19.9±29.3
$(C)_4$-C	1	-9.4±0.2
$(C)_2$-NH	1	-28.9±38.1
(C)(N)-CO	1	182.3±20.6
(C)-OH	1	206.7±11.4
$(O)(C)_3$-C	1	16.5±8.8
$(C)(N)_3$-C	1	-318.0*
(C)-Cl	1	15.9*
$(C)_2$-SO_2	1	288.7*
$(C)_2$-S	1	48.1*
$(C)_3$(S)-C	2	2.3*
(S)$(C)_2$-N	1	-115.5*
(N)-CH_3	1	42.3*
(N)$(C)_3$-C	1	13.4*

Notation: n is the number of types of atomic groups in a molecule. * -the values are presented by the authors without error

Обозначения: n - количество типов атомных групп в молекуле. * - значения представлены авторами без ошибок

The errors of the values were calculated by the formula:

$$S = t_{p,f} \times [\Sigma\Delta^2/n(n-1)]^{1/2} \quad (2)$$

where $t_{p,f}$ is the Student's criterion with a confidence probability of 0.95 and the number of degrees of freedom f = 5.

The standard enthalpy of L^- particle formation in an aqueous solution was determined using data on the heat of dissolution of lornoxicam in alkali solutions with a ratio of equivalents of at least 1:2 (Table 2).

Table 2

Enthalpy of dissolution of lornoxicam in solution KOH at various concentrations and T= 298.15 K (kJ/mol)

***Таблица 2.* Энтальпия растворения лорноксикама в растворе KOH при различных концентрациях и T= 298,15 K (кДж/моль)**

Weight, g	C_{KOH}, mol/l	$-\Delta_{sol}H$ kJ/mol
0.0201 0.0202 0.0201	0.002486	62.03±0.28 62.15±0.29 61.89±0.28
0.0402 0.0403 0.0401	0.004985	62.99 ±0.26 62.88 ±0.29 63.04 ±0.28
0.0601 0.0601 0.0610	0.007459	63. 97±0.29 63.98±0.27 63.95±0.26

The process of dissolution of lornoxicam in KOH solution can be represented by the scheme:

$$HL(cr) + OH^- (sol, nH_2O) =$$
$$= L^-(sol, (n+1)\ H_2O) + H_2O(liq) \quad (3)$$

The calculation showed that the completeness of the reaction (3) was at least 99.9%.

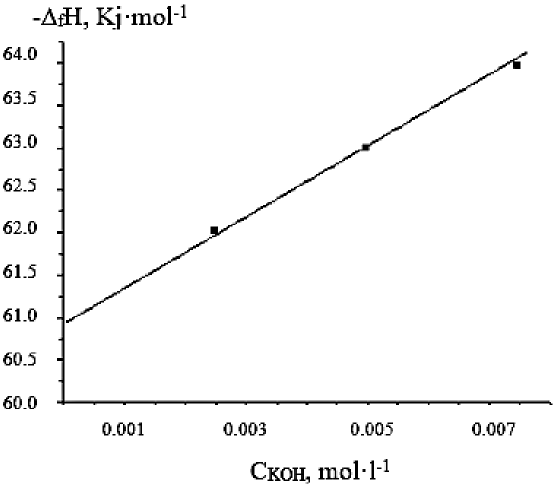

Fig. 3. Dependence of the enthalpy of dissolution of lornoxicam on the concentration of KOH

Рис. 3. Зависимость энтальпии растворения лорноксикама от концентрации KOH

The enthalpies in a standard solution were found by extrapolating the enthalpies of stepwise dissociation at fixed values of ionic strength to the zero ionic strength using the equation introduced in [15]:

$$\Delta rHi - \Delta Z^2\Psi(I) = \Delta rH^0 + bI, \quad (4)$$

where ΔrHi, are the changes in enthalpy at the ultimate value of ionic strength and at I = 0, respectively; Ψ(I) is the function of ionic strength, calculated theoretically; Δz^2 is difference between the squares of charges of reaction products and initial components; and b is an empirical coefficient.

Since in the reaction (2) $\Delta z^2 = 0$, the thermal effects of the dissolution of the peptide at zero ionic strength were calculated by the equation:

$$\Delta_rH_{(3)} = \Delta_rH^0_{(3)} + bI \quad (5)$$

where $\Delta_rH_{(3)}$ and $\Delta_rH^0_{(3)}$ are the thermal effects of the process (2) at finite and zero values of ionic strength. Well-proven for similar systems [15].

Using the obtained values of $\Delta_rH°$ reaction (3) and the values of $\Delta_fH°$ (OH^-, sol. n H_2O, stand. s., 298.15 К), $\Delta_fH°(H_2O$, liq., 298.15 К), calculated the standard enthalpy of formation of the deprotonated anion:

$$\Delta_fH^0(L^-,sol,\ H_2O,\ stand.\ s.,\ 298.15\ К) =$$
$$= \Delta_fH^0(HL,\ cr,\ 298.15\ К) +$$
$$+ \Delta_fH^0(OH^-,\ sol.\ H_2O,\ stand.\ s.,\ 298.15\ К) +$$
$$+ \Delta_rH°_{(2)} - \Delta_fH^0(H_2O,\ liq.,\ 298.15\ К) =$$
$$= -145.2-230.04 + (-60.99) + 285.83 =$$
$$= -150.4 \pm 1.9\ kJ/mol \quad (6)$$

The standard enthalpy of formation of the HL particle in the standard hypothetical undissociated state was also calculated by the equation:

$$\Delta_fH^0(HL,\ sol,\ H_2O,\ stand.\ s.,\ hyp.\ nediss.,\ 298.15\ К) =$$
$$= \Delta_fH^0(L^-,\ sol,\ H_2O,\ stand.\ s.,\ 298.15\ К) -$$
$$- \Delta_{dis}H^0(HL,\ 298.15\ К) = -150.4-(-34.2) =$$
$$= -116.2 \pm 1.9\ kJ/mol \quad (7)$$

$\Delta_{dis}H°$(*HL*, 298.15 K) were calculated by using the «HEAT» computer program [16]. The calorimetric data were processed using experimental dependences of ΔH on the initial concentration ratio of the reagents. The values of thermodynamic parameters have been calculated by the program HEAT developed to simultaneously calculate the binding constants and the enthalpy of complex formation reaction for systems with any stoichiometry [17]. The «HEAT» use and application were more described in previous publications for the treatment of calorimetric data on the molecular complex formation of amino acids with heterocyclic compounds in aqueous solutions [18]. The algorithm for the calculation of $\lg K_r$ and Δ_rH used by «HEAT» program package [17] consists in the numerical minimization of function *F* for various models of binding stoichiometry:

$$F = \sum_{i=1}^{N} w_i(\Delta_rH_{i,\exp} - \Delta_rH_{i,\mathrm{calc}})^2 \quad (8)$$

where $\Delta_rH_{i,\exp}$ and $\Delta_rH_{i,\mathrm{calc}}$ are the experimental and calculated enthalpy effects from the *i*-th reaction, respectively, *N* is the number of experiments and w_i is a weighed factor.

The use of calorimetry as a method that is the main source of thermodynamic information in the physiochemistry of solutions is very relevant today [19-25].

The values of the standard enthalpies of the formation of lornoxicam and its dissociation products in an aqueous solution (Table 3) received for the first time. They are key quantities in the thermochemistry of the lornoxicam, open up the possibility of conducting rigorous thermodynamic calculations in systems with lornoxicam.

Table 3

Standard enthalpy formation of lornoxicam and its anion L^- in aqueous solution

Таблица 3. **Стандартная энтальпия образования лорноксикама и его аниона L^- в водном растворе**

Particle	Condition	$\Delta_fH°$(298.15K), kJ/mol
HL	Crystal.	-145.2 ± 1.9
	solution, H_2O, standard state, hypothetically non-dissociated.	-150.4 ± 1.9
L^-	solution, H_2O, standard state.	-116.2 ± 1.9

The work was carried out at the Research Institute of Thermodynamics and Kinetics of Chemical Processes of the Ivanovo State University of Chemical Technology within the framework of the State Assignment (basic part) project no. FZZW-2020-0009. The study was conducted using the resources of the ISUCT Center for the Sharing of Scientific Equipment (with the support of the Ministry of Science and Higher Education of Russia, grant no. (075-15-2021-671).

The authors declare the absence a conflict of interest warranting disclosure in this article.

Работа выполнена в НИИ термодинамики и кинетики химических процессов Ивановского государственного химико-технологического университета в рамках проекта государственного задания (базовая часть) FZZW -2020-0009. Исследование проведено с использованием ресурсов Центра совместного использования научной аппаратуры ИГХТУ (при поддержке Минобрнауки России, грант № (075-15-2021-671).

Авторы заявляют об отсутствии конфликта интересов, требующего раскрытия в данной статье.

ЛИТЕРАТУРА

1. **Gadade D.D., Kulkarni D.A., Rathi P.B., Pekamwar S.S., Joshi S.S.** Increasing the solubility of Lornoxicam using Crystal Engineering. *Indian J. Pharm. Sci.* 2017. V. 9(2). P.277-286. DOI: 10.4172/pharmaceutical-sciences.1000226.
2. **Savjani K.T., Gajjar A.K., Savjani J.K.** Drug solubility: importance and enhancement techniques. *ISRN Pharm.* 2012. P. 1-10. DOI: 10.5402/2012/195727.
3. **Rasenack N., Müller B.W.** Dissolution rate enhancement by in situ micronization of poorly water-soluble drugs. *Pharm Res.* 2002. V. 19. P. 1894-1900. DOI: 10.1023/a:1021410028371.
4. **Rawat S., Jain S.K.** Solubility enhancement of celecoxib using β-cyclodextrin inclusion complexes. *Eur. J. Pharm. Biopharm.* 2004. V. 57. P. 263-267. DOI: 10.1016/j.ejpb.2003.10.020.
5. **Modi A., Tayade P.** A comparative solubility enhancement profile of valdecoxib with different solubilization approaches. *Indian J. Pharm. Sci.* 2007. V. 69. P. 274-278. DOI: 10.4103/0250-474X.33156.
6. **Chaudhari P., Sharma P., Barhate N., Kulkarni P., Mistry C.** Solubility enhancement of hydrophobic drugs using synergistically interacting cyclodextrins and cosolvent. *Curr. Sci.* 2007. V. 92. P. 1586-91.
7. **Meshkov A.N., Gamov G.A.** KEV: A free software for calculating the equilibrium composition and determining the equilibrium constants using UV-Vis and potentiometric data. *Talanta*. 2019. V. 198. P. 200-205. DOI: 10.1016/j.talanta.2019.01.107.
8. **Lytkin A.I., Barannikov V.P., Badelin V.G., Krutova O.N.** Enthalpies of acid dissociation of L-carnosine in aqueous solution. *J. Therm. Anal. Calorim.* 2020. V. 139. P. 3683–3689. DOI: 10.1007/s10973-019-08604-y.
9. **Krutova O.N., Chernikov V.V., Volkov A.V., Skvortsov I.A., Krutov P.D**. Enthalpies of dissolution of 2,3-dicyano-5,7,7-trimethyl-6,7-dihydro-1h-1,4-diazepine in KOH aqueous solutions at 298.15K. *J. Molec. Liq.* 2020. V. 313. P. 113634. DOI: 10.1016/j.molliq.2020.113634.

REFERENCES

1. **Gadade D.D., Kulkarni D.A., Rathi P.B., Pekamwar S.S., Joshi S.S.** Increasing the solubility of Lornoxicam using Crystal Engineering. *Indian J. Pharm. Sci.* 2017. V. 9(2). P.277-286. DOI: 10.4172/pharmaceutical-sciences.1000226.
2. **Savjani K.T., Gajjar A.K., Savjani J.K.** Drug solubility: importance and enhancement techniques. *ISRN Pharm.* 2012. P. 1-10. DOI: 10.5402/2012/195727.
3. **Rasenack N., Müller B.W.** Dissolution rate enhancement by in situ micronization of poorly water-soluble drugs. *Pharm Res.* 2002. V. 19. P. 1894-1900. DOI: 10.1023/a:1021410028371.
4. **Rawat S., Jain S.K.** Solubility enhancement of celecoxib using β-cyclodextrin inclusion complexes. *Eur. J. Pharm. Biopharm.* 2004. V. 57. P. 263-267. DOI: 10.1016/j.ejpb.2003.10.020.
5. **Modi A., Tayade P.** A comparative solubility enhancement profile of valdecoxib with different solubilization approaches. *Indian J. Pharm. Sci.* 2007. V. 69. P. 274-278. DOI: 10.4103/0250-474X.33156.
6. **Chaudhari P., Sharma P., Barhate N., Kulkarni P., Mistry C.** Solubility enhancement of hydrophobic drugs using synergistically interacting cyclodextrins and cosolvent. *Curr. Sci.* 2007. V. 92. P. 1586-91.
7. **Meshkov A.N., Gamov G.A.** KEV: A free software for calculating the equilibrium composition and determining the equilibrium constants using UV-Vis and potentiometric data. *Talanta*. 2019. V. 198. P. 200-205. DOI: 10.1016/j.talanta.2019.01.107.
8. **Lytkin A.I., Barannikov V.P., Badelin V.G., Krutova O.N.** Enthalpies of acid dissociation of L-carnosine in aqueous solution. *J. Therm. Anal. Calorim.* 2020. V. 139. P. 3683–3689. DOI: 10.1007/s10973-019-08604-y.
9. **Krutova O.N., Chernikov V.V., Volkov A.V., Skvortsov I.A., Krutov P.D**. Enthalpies of dissolution of 2,3-dicyano-5,7,7-trimethyl-6,7-dihydro-1h-1,4-diazepine in KOH aqueous solutions at 298.15K. *J. Molec. Liq.* 2020. V. 313. P. 113634. DOI: 10.1016/j.molliq.2020.113634.

10. **Лыткин А.И., Крутова О.Н., Тюнина Е.Ю., Крутов П.Д., Дударь В.В.** Термохимическое исследование кислотно-основных реакций в водном растворе пиридоксина. *Изв. вузов. Химия и хим. технология.* 2020. Т. 63. Вып. 6. С. 25-29. DOI: 10.6060/ivkkt.20206306.6183.
11. **Archer D.G.** Thermodynamic properties of the $KCl+H_2O$ system. *J. Phys. Chem. Ref. Data.* 1999. V. 28. N 1. P. 1-16. DOI: 10.1063/1.556034.
12. **Васильев В.П., Бородин В.А., Копнышев С.Б.** Стандартная энтальпия горения и образования иминодиуксусной и этилендиаминтетрауксусной кислот. *Журн. физ. химия.* 1988. Т. 62. № 8. С. 2243.
13. **Лыткин А.И., Черников В.В., Крутова О.Н., Нягоя Г.** Термохимическое исследование реакций кислотно–основного взаимодействия в водном растворе β-аминомасляной кислоты. *Журн. физ. химия.* 2020. Т. 94. № 2. С. 323-326. DOI: 10.1134/S0036024420020259.
14. **Тахистов А.В., Пономарев Д.А.** Органическая масс-спектрометрия. СПб.: ВВМ. 2002. С. 346.
15. **Васильев В.П.** Термодинамические свойства растворов электролитов. М: Высш. шк. 1982. 200 с.
16. **Васильев В.П., Бородин В.А., Козловский Е.В.** Использование компьютеров в химико-аналитических расчетах. М.: Высш. шк. 1993. 112 с.
17. **Бородин В.А., Васильев В.П., Козловский Е.В.** Обработка результатов калориметрических измерений с использованием ЭВМ при исследовании сложных равновесий в растворах. *Журн. общ. химия.* 1982. Т. 27. С. 2169 − 2171.
18. **Tyunina E.Yu., Krutova O.N., Lytkin A.I.** Determination of the complexation parameters of L-asparagine with some biologically active pyridine derivatives in aqueous solutions from calorimetric results. *Thermochim. Acta.* 2020. V. 690. P. 178704. DOI: 10.1016/j.tca.2020.178704.
19. **Лыткин А.И., Крутова О.Н., Тюнина Е.Ю., Крутова Е.Д., Мохова Ю.В.** Термодинамические характеристики взаимодействий кислотно-основных реакций в водном растворе пиридоксаль-5'-фосфата. *Изв. вузов. Химия и хим. технология.* 2020. Т. 63. Вып. 7. С. 10-14. DOI: 10.6060/ivkkt.20206307.6184.
20. **Usacheva T.R., Pham L., Kuzmina K.I., Shamin V.A.** Thermodynamics of complex formation between Cu(II) and glycyl-glycyl-glycine in water-ethanol and water-dimethylsulfoxide solvents. *J. Therm. Anal. Calorim.* 2017. V. 130. N 1. P. 471-478. DOI: 10.1007/s10973-017-6207-6.
21. **Usacheva T.R., Sharnin V.A.** Thermodynamics of molecular complexation "guest-host" in non-aqueous media on the example of the interaction of amino acids and crown esters. *Proc. Acad. Sci. Chem. Ser.* 2015. N 11. P. 2536-2544. DOI: 10.1007/s11172-015-1189-7.
22. **Kustov A.V., Korolev V.P.** Temperature dependence of the interaction between hydrophobic and hydrophilic solutes – a calorimetric study. *Thermochim. Acta.* 2005. V. 437. N 1-2. P. 190-195. DOI: 10.1016/j.tca.2005.05.012.
23. **Kustov A.V., Smirnova N.L., Berezin D.B., Berezin M.B.** Thermodynamics of solution of hemato- and deuteroporphyrins in N,N- dimethylformamide. *J. Chem. Eng. Data.* 2013. V. 58. N 9. P. 2502-2505. DOI: 10.1021/je400388j.
24. **Kustov A.V., Bekeneva A.V., Saveliev V.I., Korolev V.P.** Solvation of tetraethyl- and tetrabutylammonium bromides in aqueous acetone and aqueous hexamethyl phosphoric triamide mixtures in the water-rich region. *J. Solution Chem.* 2002. V. 31. N 1. P. 71-80. DOI: 10.1023/A:1014809219103.
25. **Kustov A.V., Smirnova N.L.** Standard enthalpies and heat capacities of solution of urea and tetramethylurea in water. *J. Chem. Eng. Data.* 2010. V. 55. P. 3055-3058. DOI: 10.1021/je9010689.

10. **Lytkin A.I., Krutova O.N., Tyunina E.Yu., Krutov P.D., Dudar V.V.** Thermochemical study of acid-base reactions in aqueous solution of pyridoxine. *ChemChemTech [Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.].* 2020. V. 63. N 6. P. 25-29. DOI: 10.6060/ivkkt.20206306.6183.
11. **Archer D.G.** Thermodynamic properties of the $KCl+H_2O$ system. *J. Phys. Chem. Ref. Data.* 1999. V. 28. N 1. P. 1-16. DOI: 10.1063/1.556034.
12. **Vasiliev V.P., Borodin V.A., Kopnyshev S.B.** Standard enthalpy of combustion and formation of iminodiacetic and ethylenediaminetetraacetic acids. *J. Phys. Chem.* 1988. V. 62 (8). P. 2243 (in Russian).
13. **Lytkin A.I., Chernikov V.V., Krutova O.N., N'yagoya G.** Thermochemical Study of the Reactions of Acid–Base Interaction in an Aqueous Solution of β-Aminobutyric Acid. *Russ. J. Phys. Chem. A.* 2020. V. 94. N 2. P. 323–326. DOI: 10.1134/S0036024420020259.
14. **Takhistov A.V., Ponomarev D.A.** Organic Mass Spectrometry. SPb.: VVM. 2002. P. 346 (in Russian).
15. **Vasilyev V.P.** Thermodynamic Properties of Electrolyte Solutions. M.: Vyssh. Shk. 1982. 200 p. (in Russian).
16. **Vasiliev V.P., Borodin V.A., Kozlovsky E.V.** The Use of Computers in Chemical Analytical Calculations. M: Vyssh. Shk. 1993. 112 p. (in Russian).
17. **Borodin V.A., Vasil'ev V.P., Kozlovsky E.V.** Processing the results of calorimetric measurements by using an computer in the study of complex equilibria in solutions. *Russ. J. Gen. Chem.* 1982. V. 27. P. 2169 − 2171 (in Russian).
18. **Tyunina E.Yu., Krutova O.N., Lytkin A.I.** Determination of the complexation parameters of L-asparagine with some biologically active pyridine derivatives in aqueous solutions from calorimetric results. *Thermochim. Acta.* 2020. V. 690. P. 178704. DOI: 10.1016/j.tca.2020.178704.
19. **Lytkin A.I., Krutova O.N., Tyunina E.Y., Krutova E.D., Mokhova Y.V.** Thermodynamic characteristics of acid-core reactions interactions in the water solution piridoxal-5'-phosphate. *ChemChemTech [Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.].* 2020. V. 63. N 7. P. 10-14. DOI: 10.6060/ivkkt.20206307.6184.
20. **Usacheva T.R., Pham L., Kuzmina K.I., Shamin V.A.** Thermodynamics of complex formation between Cu(II) and glycyl-glycyl-glycine in water-ethanol and water-dimethylsulfoxide solvents. *J. Therm. Anal. Calorim.* 2017. V. 130. N 1. P. 471-478. DOI: 10.1007/s10973-017-6207-6.
21. **Usacheva T.R., Sharnin V.A.** Thermodynamics of molecular complexation "guest-host" in non-aqueous media on the example of the interaction of amino acids and crown esters. *Proc. Acad. Sci. Chem. Ser.* 2015. N 11. P. 2536-2544. DOI: 10.1007/s11172-015-1189-7.
22. **Kustov A.V., Korolev V.P.** Temperature dependence of the interaction between hydrophobic and hydrophilic solutes – a calorimetric study. *Thermochim. Acta.* 2005. V. 437. N 1-2. P. 190-195. DOI: 10.1016/j.tca.2005.05.012.
23. **Kustov A.V., Smirnova N.L., Berezin D.B., Berezin M.B.** Thermodynamics of solution of hemato- and deuteroporphyrins in N,N- dimethylformamide. *J. Chem. Eng. Data.* 2013. V. 58. N 9. P. 2502-2505. DOI: 10.1021/je400388j.
24. **Kustov A.V., Bekeneva A.V., Saveliev V.I., Korolev V.P.** Solvation of tetraethyl- and tetrabutylammonium bromides in aqueous acetone and aqueous hexamethyl phosphoric triamide mixtures in the water-rich region. *J. Solution Chem.* 2002. V. 31. N 1. P. 71-80. DOI: 10.1023/A:1014809219103.
25. **Kustov A.V., Smirnova N.L.** Standard enthalpies and heat capacities of solution of urea and tetramethylurea in water. *J. Chem. Eng. Data.* 2010. V. 55. P. 3055-3058. DOI: 10.1021/je9010689.

Поступила в редакцию (Received) 05.05.2022
Принята к опубликованию (Accepted) 10.10.2022