titration with a nonacidic quercetin solution, only one equivalent point (pK_2) would be attainable.
Thermodynamic parameters for the dissociation of quercetin were calculated from the slopes of the straight lines $\log K_d^0 = f\left(\frac{1}{T}\right)$: $\Delta H = 72.5$ kJ/mol, $\Delta S = 0.17$ kJ/K mol and $\Delta G = 20.4$ kJ/mol, for the first dissociation constant, and $\Delta H = 86.3$ kJ/mol, $\Delta S = 0.11$ kJ/Kmol and $\Delta G = 54.1$ kJ/mol, for the second dissociation constant of quercetin.

Experimental

1. Apparatus

A pH-meter (pHM-82 Radiometer Copenhagen), accuracy of ± 0.001 pH, equipped with the combined electrode (No. CW. 733 Serial No. 35162, Russel) was used. The temperature was controlled within ± 0.2 K by a circulating water thermostat (Serie U, MLW Freital, Germany).

2. Reagents

Quercetin; absolute ethanol, NaOH, $NaNO_3$, by Merck (Darmstad, Germany); all of *p.a.* grade. The solution of NaOH (carbonate free) was standardized by potentiometric titration against A.R. potassium hydrogen phthalate (dried 1^h at 120 °C). The solution of HCl, added to the quercetin solution before titration, was standardized by potentiometic titration with 0.514 M NaOH.

3. General procedure

Titrations of 0.0025 M quercetin solution with 0.514 M NaOH were carried out in a 51 ml glass vessel closed by a cover with five holes. Through the holes on the lid, the thermometer, the combined electrode, and the nitrogen inlet tubes were inserted. One of the holes was closed with a glass stopper, while the titrant was successively introduced trough the remaining hole. The measurements were performed at three temperatures (28, 34 and 39 °C) and at three values of ionic strength (0.0024, 0.034 and 0.062 M). The ionic strength was adjusted by 2 M $NaNO_3$. Each potentiometric titration, with about 180 experimental points, was done in triplicate.

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Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Comenius University, Bratislava, Slovak Republic

Thermodynamic study of local anesthetics based on heptacainium chloride derivatives

Study of local anesthetics. Part 163*

F. Andriamainty, J. Čižmárik

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Dr. Fils Andriamainty, PhD., Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Comenius University, Odbojárov 10, 832 32 Bratislava, Slovak Republic

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We have previously studied the critical micellar concentration (CMC) of the derivatives of piperidinoethylesters of 2-alkoxyphenylcarbamic acid. We found that in a homologous series of alkyloxy substituents, the CMC decreases with the number of the carbon atoms up to the heptyloxy ($n = 7$) and then increases [1].
The aim of the present paper was to study the thermodynamic parameters of local anesthetics of heptacainium chloride derivatives in the medium of distilled water, using UV spectrophotometry at a temperature range $T = 294–318$ K. Based on our results (Table 1), the thermodynamic magnitudes were calculated ($-\Delta H^\circ$, $-\Delta G^\circ$, $-\Delta S^\circ$) according to the "phase separation (PS_1 and PS_2)" model [2]. The equation $CMC = f(T) = A + BT + CT^2$ represents the dependence of the critical micellar concentration upon temperature at $pH \approx 4.5–5$, where (A, B, C) = constants of the second degree polynomial and T = absolute temperature. Gibbs energy change can be estimated according to the equation;

$$\Delta G^\circ = \gamma\, RT \ln (CMC) \qquad (1)$$

where R = gas constant and γ = degree of counterion binding (if $\gamma = 1$ the anti-ions are completely ionized, if $\gamma = 2$ all the anti-ions are bound to micelles). The enthalpy of micellization is defined by the equation

$$\Delta H^\circ = -\gamma\, RT^2 [\partial \ln (CMC)/\partial T] \qquad (2)$$

and the entropy contribution of micellization can be calculated as follows:

$$\Delta S^\circ = (\Delta H^\circ - \Delta G^\circ)/T \qquad (3)$$

ΔG°, ΔH°, ΔS° values are listed in Table 2.

Table 1: CMC (mol/l) values in relation to temperature T (K)

T (K)	CMC (mol/l)			
	n = 5	n = 7	n = 8	n = 9
294	3.990×10^{-4}	3.151×10^{-4}	3.914×10^{-4}	4.763×10^{-4}
298	4.016×10^{-4}	3.199×10^{-4}	4.122×10^{-4}	4.841×10^{-4}
303	4.145×10^{-4}	3.212×10^{-4}	4.198×10^{-4}	4.906×10^{-4}
308	4.311×10^{-4}	3.258×10^{-4}	4.288×10^{-4}	5.029×10^{-4}
313	4.399×10^{-4}	3.332×10^{-4}	4.419×10^{-4}	5.084×10^{-4}
318	4.424×10^{-4}	3.545×10^{-4}	4.539×10^{-4}	5.243×10^{-4}

Table 2: Thermodynamic parameters of local anesthetics of heptacainium chloride derivates in distilled water medium and temperature range T = 294–318 K

Substance	T (K)	ΔG° (kJ/mol)		ΔH° (kJ/mol)		ΔS° (kJ/mol)	
		PS_1	PS_2	PS_1	PS_2	PS_1	PS_2
13 (n = 5)	294	−19.14	−38.28	−3.10	−6.20	16.04	32.08
	298	−19.36	−38.71	−3.58	−7.16	15.78	31.56
	303	−19.62	−39.23	−4.20	−8.41	15.41	30.82
	308	−19.87	−39.73	−4.87	−9.74	15.00	30.00
	313	−20.10	−40.21	−5.57	−11.13	14.54	29.07
	318	−20.33	−40.66	−6.30	−12.61	14.03	28.05
19 (n = 7)	294	−19.69	−39.38	0.91	1.82	20.60	41.20
	298	−19.96	−39.92	−0.44	−0.88	19.52	39.04
	303	−20.27	−40.55	−2.23	−4.46	18.04	36.09
	308	−20.56	−41.11	−4.14	−8.28	16.42	32.83
	313	−20.81	−41.61	−6.17	−12.34	14.63	29.27
	318	−21.02	−42.05	−8.33	−16.66	12.70	25.39
22 (n = 8)	294	−19.08	−38.17	−2.02	−4.04	17.06	34.12
	298	−19.31	−38.62	−2,51	−5.03	16.80	33.60
	303	−19.59	−39.18	−3.16	−6.33	16.42	32.85
	308	−19.85	−39.71	−3.85	−7.70	16.00	32.00
	313	−20.11	−40.21	−4.58	−9.16	15.53	31.05
	318	−20.35	−40.70	−5.35	−10.70	15.00	29.99
25 (n = 9)	294	−18.69	−37.39	−2.14	−4.29	16.55	33.10
	298	−18.92	−37.84	−2.42	−4.83	16.50	33.01
	303	−19.19	−38.38	−2.77	−5.54	16.42	32.84
	308	−19.46	−38.92	−3.15	−6.29	16.31	32.63
	313	−19.72	−39.44	−3.54	−7.08	16.18	32.36
	318	−19.98	−39.95	−3.96	−7.92	16.02	32.04

Based on the results presented it can be generalized that

- ΔG° values are negative and decline slightly with temperature.
- Depression of standard molar enthalpy ΔH° is more significant at more negative values. This means that the micellization process becomes more exothermic with increasing temperature.
- ΔS° values are positive and decline with increasing temperature.
- It was noticed that the dependence of ΔG° on n is paraboloid and for all temperature intervals has a minimum at (n = 7).

These conclusions correspond with the results, which had bean reached for the basic substance heptacainium chloride [3].

Experimental

The derivatives of piperidinoethyl esters of 2-alkoxyphenylcarbamic acid (substances 13 where R = C_5H_{11}, 19 where R = C_7H_{15}, 22 where R = C_8H_{17}, and 25 where R = C_9H_{19}) were synthesised as described earlier [4].
Distilled water was used to prepare stock solutions (10^{-3} mol/l). From the appropriate stock solutions various concentrations of diluted solutions were prepared with pH ≈ 4.5–5.0 at temperature range T = 294–318 K. pH was measured with a pH meter (Portamess 943 pH, Elekronische Messgeräte GmbH Co., Berlin) and the temperature was controlled by a Thermostat (Veb ML W Prüfgerate-Werk Medingen/Sity/Freital (BRD). The critical micellar concentration was determined using an HP 8452 A Diode Array spectrophotometer (Hewlett Packard, BRD) [5].

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