Scientia Pharmaceutica (Sci. Pharm.) **72**, 221–225 (2004)

Study of local anesthetics. Part* 166:Conductometric determination of the critical micelle concentration of local anesthetic heptacainium chloride in aqueous electrolyte solution

F. Andriamainty, J. Čižmárik, M. Holíková

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Comenius University, Odbojárov 10, 832 32 Bratislava, Slovak Republic

Abstract

Specific conductivities of local anesthetic heptacainium chloride XIX (HCC XIX) (N-[2-(2-heptyloxyphenylcarbamoyloxy)-ethyl]-piperidinium chloride), in aqueous electrolyte solution (0.05 $mol.l^{-1}$ NaCl) were measured as a function of the concentration and temperature. The critical micelle concentrations (c.m.c) and the counterion (β) binding of the micelles were estimated from the dependence of the specific conductivity of the substrate concentration. The temperature dependence of ln c.m.c was fitted to the function of the second degree polynomial. From the fitting parameters, Gibss free energies (ΔG^0), enthalpies (ΔH^0), and entropies (ΔS^0) of micellization as a function of temperature were estimated. The „mass action model" was applied to micelle formation to calculate the micellization parameters.

Keywords:

Heptacainium chloride, conductivity, micellization

Introduction

The formation of micelles is a cooperative process which occurs at a critical micelle concentration (c.m.c), characteristic of the surfactant species and various factors such as temperature and pH of solution. The c.m.c can serve as a measure of micelle stability in a given state, and the thermodynamics of micellization can be determined from a study of the temperature dependence of the c.m.c.

In this paper we report our results of the measured conductivity of heptacainium chloride XIX (HCC XIX) in aqueous electrolyte solution (0.05 mol.l^{-1} NaCl) at various temperatures.

We have determined conductometrically the temperature dependence of c.m.c and the counterion binding, β, of the spherical micelles of HCC XIX in the 25-40 °C temperature range at 5 °C intervals.

Results and discussion

Conductometric determination of the c.m.c was carried out by investigating the change in the slope when the specific conductivity versus HCC XIX concentration solutions is plotted (Fig. 1). The c.m.c values were determined by the intersection of these lines. The equation c.m.c = f (t) (t: temperature measured in °C) represents the dependence of c.m.c upon temperature, for exemple: at t= 25 °C c.m.c=0.00098 mol.l^{-1}, at t= 30 °C c.m.c=0.00102 mol.l^{-1}, at t= 35 °C c.m.c=0.00107 mol.l^{-1} and t= 40 °C c.m.c=0.00131 mol.l^{-1}, respectively.

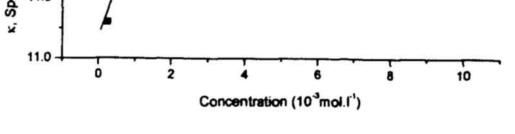

Fig. 1. Electrical conductivity *vs.* HCC XIX concentration

Ionic spherical micelles bind a considerable amount of counterions. The counterion binding (β) of micelles is determined from the ratio of the premicellar slope to the postmicellar slope, shown in Fig. 1 (for illustration at t=25 °C).The ratio of these two slopes yields the degree of surfactant ionization (α) and then β value is calculated using the formula $\beta = 1 - \alpha$ [1]. The results are presented in the Tab.1. The extent of counterion binding (β) oscillated with temperature and exhibeted no definite trend. Similar behaviour was also observed for parameter α.

The temperature dependence of ln c.m.c was fitted to the function of the second degree polynomial: $\ln c.m.c = A + B.T + C.T^2$, which was used to determine the values of A, B and C. The obtained results were: A= 136.97±58.48, B= -0.96±0.38, C= 0.0016±0.00063. The fit was quite good with the correlation coefficient 0.9803. From the fitting parameters, Gibss free energies (ΔG^0), enthalpies (ΔH^0), and entropies (ΔS^0) of micellization as a function of temperature were estimated. The „mass action model" was applied to micelle formation to calculate the thermodynamic micellization parameters [2]. The free energy of micellization, ΔG^0, can be given by the equation;

$$\Delta G^0 = (2-\beta)\, RT \ln c.m.c$$

Hence, ΔG^0 was calculated using the c.m.c and β previously determined. Since the enthalpy of micellization, ΔH^0, is related to ΔG^0 through the Gibbs-Helmholtz equation:

$$\Delta H^0 = \partial(\Delta G^0/T)/\partial(1/T)$$

It was calculated from the relation:

$$\Delta H^0 = -(2-\beta)\, RT^2\, [\partial \ln c.m.c/\partial T]$$

Finally the entropy contribution of micellization (ΔS^0) was determined from the equation;

$$\Delta S^0 = (\Delta H^0 - \Delta G^0)/T$$

The results of ΔG^0, ΔH^0 and ΔS^0 calculated by these equations are summarized in Tab. 1:

Based on the presented results it can be generalized that:

The free energy, ΔG^0, appeared to be independent of temperature, which is consistent with previously made observations [3,4].

ΔH^0 and ΔS^0 were quite sensitive to temperature. ΔH^0 decreased with temperature, whereby at t=25 °C, it was endothermic, but at t>25 °C, it was exothermic and became larger in magnitude as the temperature increased. It means ΔH^0 becames exothermic and its effect more significant. ΔS^0 also decreased with temperature.

Temperature (°C)	α	β	ΔG^o (kJ.mol^{-1})	ΔH^o(kJ.mol^{-1})	ΔS^o(kJ.mol^{-1}.K^{-1})
25	0.28	0.72	-21.96	5.29	0.0912
30	0.25	0.75	-21.76	-9.93	0.0390
35	0.09	0.91	-19.03	-22.71	-0.0118
40	0.33	0.67	-23.01	-45.95	-0.0733

Tab. 1. Determined thermodynamic parameters for micellization

Experimental

Heptacainium chloride (HCC XIX) was prepared by a method as previously described [5,6]. NaCl (Lachema, s.p., Brno) was used to prepare the stock solution with a concentration of 0.05 mol.l^{-1} NaCl. NaCl solution was used to prepare the local anesthetic solutions with pH≈4.5-5.0 at 25-40 °C. 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 micelle concentrations (c.m.c) were determined by electrical conductometry. For the conductivity measurements of the HCC XIX solutions, a Model HI 8733 conductivity meter was used.

*Part 165: Farm. Obz. 73, 100 (2004)

Acknowledgement: This study was supported by the VEGA grant: 1/1186/04

References

[1] Dominguez A, Fernandez A, Gonzalez N, Iglesias L, Montenegro J.
Determination of critical micelle concentration of some surfactants by three Techniques.
J. Chem. Edu. 1997;74:1227-1231.

[2] Lee D J.
Enthalpy-Entropy compensation in ionic micelle information.
Colloid Polym. Sci. 1995;273:539-543.

[3] Andriamainty F, Čižmárik J.
Thermodynamic study of the local anaesthetic heptacaine
Pharmazie 1999;54:629-630.

[4] Andriamainty F, Čižmárik J.
Thermodynamic study of local anesthetics based on heptacainium chloride derivatives. Pharmazie
Pharmazie 2003;58:440-441.

[5] Čižmárik J, Borovanský A, Švec P.
Study of local anaesthetics. LII. Piperidinoethyl ester of Alkoxyphenylcarbamic acids.
Acta Fac. Pharm. Univ. Comen. 1976;29:53-80.

[6] Čižmárik J, Borovanský A., Švec P.
N-[2-(heptyloxyphenylcarbamoyloxy)-ethyl]-piperidinium chloride, heptacaine a new local anaesthetic.
Pharmazie 1978;33:297-298.

Received March 5th, 2004
Accepted August 11th, 2004