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Short communication

Determination of CMC of sodium glucocorticides hemisuccinates by CE

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Abstract

The capillary zone electrophoresis (CZE) method was applied to the determination of the critical micelle concentration (CMC) and the anionic mobilities (μ_e) for sodium glycocorticides hemisuccinates (Urbason® solubile forte 1000, Hydrocortison 100 Rotexmedica®, Prednisolut 100®) in phosphate solution at pH 7.2. The CZE enables an efficient and very fast determination of parameters for characterizing physicochemical properties of micelles.

Keywords: Critical micelle concentration; Capillary zone electrophoresis; Sodium glycocorticides hemisuccinates

1. Introduction

Capillary electrophoresis is a powerful tool for determining physicochemical properties, such as the dissociation constants [1,2], protein-ligand binding constants [3], aggregation constants [4,5], critical micellar concentrations (CMCs) [6] and thermodynamic parameters such as enthalpy and entropy changes.[7]. In this article, the ionic mobilities and the CMCs of drugs (Urbason® solubile forte 1000, Hydrocortison 100 Rotexmedica®, Prednisolut 100®) were determined in phosphate solutions at pH 7.2 using the CE system by measuring the electric current at 25 °C. These drugs are used as lyophiliates and can be redispersed without any additional exicipient. Therefore, formation of micelles seems to be very important for the processes of lyophilisation and of redispersion before the parental administration, respectively. The CMC for these drugs is not known in the literature so far.

2. Experimental

2.1. Apparatus

CE experiments were performed on a Hewlett–Packard Model G1600A (Waldbronn, Ger-

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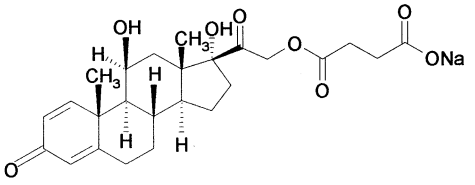
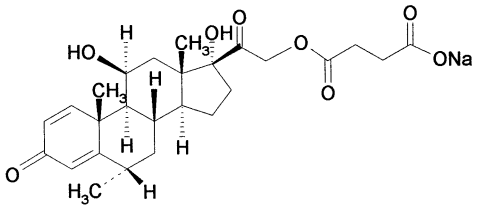
many)[3D] CE system. The detection wavelength was 200 nm. Fused-silica capillaries from Hewlett–Packard (Waldbronn, Germany) with a total length of 48.5 cm, a length to the detector of 40 cm and an internal diameter of 50 μm were used.

Table 1
Determination of CMC and μ_e using CZE (current) in phosphate buffer at pH 7.2

	CMC (%) (m V^{-1})	$\mu_e = 10^{-5}$ s^{-1} cm^2 V^{-1}
Prednisolut 100	3.84	−17.56
Urbason solubile forte 1000	4.44	−18.69
Hydrocortison 100 Rotexmedica	4.38	−21.63





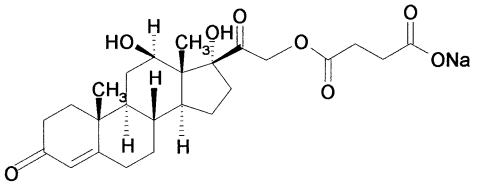


Fig. 1. Structural formulas of prednisolone hemisuccinate (Prednisolut® 100), methylprednisolone hemisuccinate (Urbason® solubile forte 1000) and hydrocortisone hemisuccinate (Hydrocortison 100 Rotexmedica).

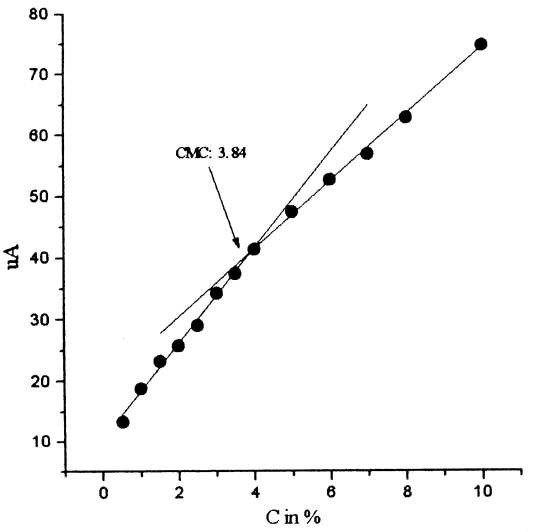


Fig. 2. Electric current, *I*, vs. the concentration of Prednisolut® 100.

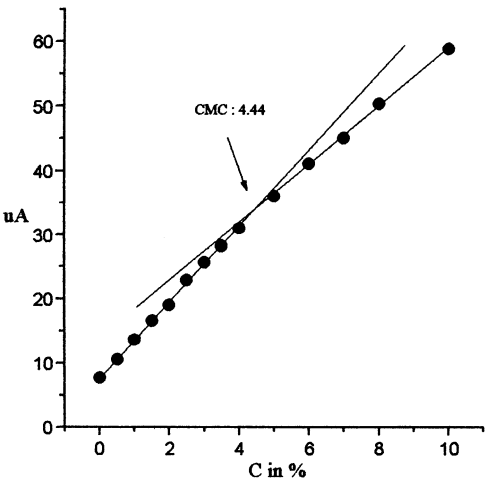


Fig. 3. Electric current, *I*, vs. the concentration of Urbason solubile® 1000.

2.2. Chemicals

Prednisolone-21-hydrogensuccinate sodium (Prednisolut® 100, B.N., 01034) was obtained from Jenapharm, Germany. Methylprednisolone-21-hydrogensuccinate sodium (Urbason® solubile forte 1000, B.N., H097) was obtained from Hoechst, Germany. Hydrocortisone-21-hydrogensuccinate sodium (Hydrocortisone 100-Ro-

texmedica®, B.N., 80103) was obtained from Rotexmedica, Germany.

2.3. Sample preparation

Standard solutions of the drugs were prepared from 0 to 10% (m V^{-1}). These samples were filtered through a 0.45 μm syringe filter.

2.4. Run solution preparation

For capillary electrophoresis the buffer solutions were filtered through a 0.45 μm syringe filter and degassed by ultrasound for at least 10 min before use.

2.5. Analysis conditions

Before each injection, the capillary was flushed with 0.1 M NaOH for 3 min and with the actual buffer solution for 5 min. The temperature was kept at 25 °C.

2.6. Determination of the CMC

The CMC of glucocorticoids in phosphate buffer at pH 7.2 was determined using CE by measuring the electric current at different concentrations of glucocorticoids (0–10% (m V^{-1})).

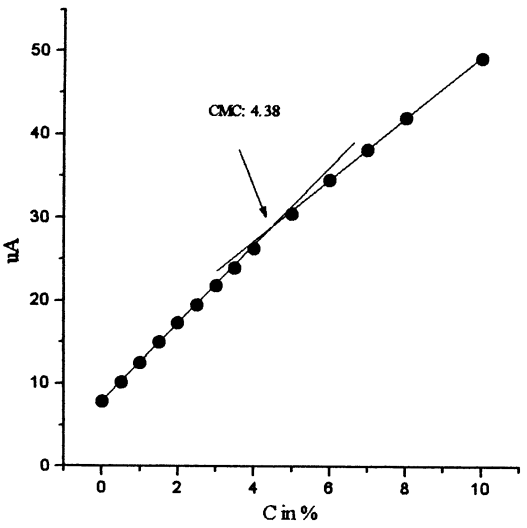


Fig. 4. Electric current, *I*, vs. the concentration of Hydrocortison® 100 Rotexmedica.

3. Results and discussion

The substance class used in the present study belongs to the group used as sodium hemisuccinates glucocorticoides. They are used for parentally administration in the treatment of many diseases such as bronchial asthma, allergic reaction to insectbites, blood diseases, skin diseases, rheumatism and serious infectious diseases. At pH 7.2 all of the substances have negative electrophoretic mobility (Table 1) and migrate in the direction of the cathode. DMSO was used as a marker substance for the determination of the electroosmotic mobility. The samples (100 μg ml^{-1}) were injected at a pressure of 50 mbar for 5 s (hydrodynamic injection). In this paper, the CMC and the anionic mobilities of three sodium hemisuccinates were determined using capillary zone electrophoresis (CZE). Table 1 summarizes the CMC values and the ionic mobilities of glucocorticoides obtained by CZE.

In the literature a method for the determination of the CMC for these drugs is not known. By use of CZE we tried to determine the CMC by measuring the electric current at different concentrations of glucocorticoides (0–10% (m V^{-1})) at a temperature of 25 °C. In Tables 2–4 the standard deviations (S.D.) of the electric current at different concentrations of glucocorticoides are presented. The temperature of the capillary was controlled by means of a high velocity air stream. These substances have similar chemical structures (Fig. 1). Therefore, similar CMC for these drugs were expected. Figs. 2–4 show the electric current versus the concentration and the CMC values of the drugs.

Therefore, the CZE gives better and more exact information on the CMC compared with other parameters which can be obtained by different methods such as specific electric conductivity, turbidity coefficient, solubilization, osmotic pressure, surface tension and viscosity [8,9]. The low sample volume required, the low costs and the short analysis time are the main advantages of the method described here.

Table 2
Electric current of prednisolone hemisuccinate at different concentrations

Concentration % (m V^{-1})	0.0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	5.0	6.0	7.0	8.0	10.0
Mean values (μA)	7.811	13.345	18.750	23.215	25.706	29.373	34.241	37.412	41.422	47.488	52.723	56.912	62.820	74.656
S.D. ± μA	0.016	0.164	0.147	0.091	0.060	0.325	0.031	0.021	0.044	0.055	0.030	0.023	0.056	0.218

S.D., standard deviation of the electric current.

Table 3
Electric current of methylprednisolone hemisuccinate at different concentrations

Concentration % (m V^{-1})	0.0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	5.0	6.0	7.0	8.0	10.0
Mean values (μA)	7.811	10.173	12.484	15.035	17.303	19.523	21.791	23.956	26.275	30.495	34.608	38.252	42.042	49.214
S.D. ± μA	0.016	0.047	0.090	0.028	0.003	0.022	0.010	0.036	0.029	0.063	0.030	0.016	0.013	0.021

Table 4
Electric current of hydrocortisone hemisuccinate at different concentrations

Concentration % (m V^{-1})	0.0	0.5	1.0	1.5	2.0	2.5	3.0	3.5	4.0	5.0	6.0	7.0	8.0	10.0
Mean values (μA)	7.811	10.655	13.680	16.629	19.054	22.842	25.623	28.229	31.023	36.097	41.184	45.106	50.383	58.893
S.D. ± μA	0.016	0.129	0.050	0.037	0.032	0.014	0.015	0.017	0.048	0.068	0.027	0.020	0.049	0.065

4. Conclusion

CZE was introduced to evaluate the CMC of drugs in phosphate buffer at pH 7.2. The CMC determined by this method provides fundamental information about the physicochemical and the surfactant properties. The method described is easy, rapid and reproducible and opens a new way for the determination of the CMC of all charged glucocorticoides hemisuccinates.

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