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# Influence of auxiliary substances on the critical micellar concentration of Tweens®

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The aim of the present study was to investigate the influence of auxiliary substances used in suspension technology (benzyl alcohol, lignocaine, carboxymethylcellulose sodium) on the critical micellar concentrations (CMC) of Tweens®. Tween 20 proved to be the least sensitive to auxiliary substances. Benzyl alcohol decreases CMC of the employed surface active substances and lignocaine hydrochloride and carboxylmethyl cellulose sodium salt increase its value.

## 1. Introduction

Under the critical micellar concentration (CMC) we understand a known mean value of narrow concentration range wherein the properties of most amphiphilic solutions change. During micelle creation a reversible polymultimerization takes place, above CMC monomers and polymultimers exist [1–4]. The narrower this concentration range is the lower this association degree remains.

The border between the associated and non-associated state agrees with the equilibrium rule but leads to incorrect conclusions and conceptions [5–8]. CMC is determined by the very structure of amphiphilic materials and environmental conditions. Apart from temperature and pressure, the type of solvent and the presence of foreign substances influence CMC. They also greatly influence solubility. If we increase solubility, monomers reach their saturation concentration quicker and the precipitation of micelli occurs at lower concentrations. It is possible to move CMC in a solvent like water thanks to a change of polarity of the added component. If the arrangement of liquid takes place we encounter hydrophobization or hydrophilization of the solvent.

This study seeks to determine the influence of auxiliary substances used in microcrystalline injection suspensions on CMC of some Tweens.

## 2. Investigations, results and discussion

The determined CMC values for Tween 80, 60, 40 and 20 are summarized in Table 1. They were taken from the literature [9–10]. Critical micellar concentrations based on stalagmetric and conductometric measurements prove the fact that determining the quantity of surface active compound (ZPC) which induces micelle creation is difficult. In order to be able to compare research results, we accepted as standard a border midpoint of the transition between the beginning of micelle creation and complete saturation of the border surface. Tween 20 is characterized by the highest value (0.6649 $g/dm^3$) of CMC and Tween 80 by the lowest (0.285 $g/dm^3$).

**Table 2: Influence of auxiliary substances on the concentration dependency of surface tension of Tweens**

| Auxiliary substances | % Concentration | Tween 80 σ ($dyn/cm^2$) | Tween 60 σ ($dyn/cm^2$) | Tween 40 σ ($dyn/cm^2$) | Tween 20 σ ($dyn/cm^2$) |
|---|---|---|---|---|---|
| Benzyl alcohol (9 $g/dm^3$) | 0.05 | 51.0 | 49.7 | 48.3 | 46.5 |
| | 0.1 | 49.6 | 47.7 | 47.3 | 45.7 |
| | 0.2 | 48.3 | 45.9 | 45.7 | 44.8 |
| | 0.3 | 48.0 | 45.8 | 44.4 | 44.0 |
| | 0.4 | 48.1 | 46.2 | 43.5 | 43.1 |
| | 0.5 | 48.1 | 46.3 | 43.6 | 42.3 |
| | 1 | 48.6 | 46.5 | 44.1 | 42.3 |
| | 1.5 | 49.1 | 47.0 | 44.6 | 42.8 |
| | 2 | 49.6 | 47.4 | 45.1 | 43.2 |
| CMC-Na (4 $g/dm^3$) | 0.05 | 54.9 | 53.0 | 50.4 | 48.2 |
| | 0.1 | 50.2 | 51.9 | 49.6 | 47.3 |
| | 0.2 | 46.2 | 50.8 | 48.9 | 46.4 |
| | 0.3 | 42.3 | 49.7 | 48.1 | 45.6 |
| | 0.4 | 41.3 | 48.7 | 47.4 | 44.8 |
| | 0.5 | 42.4 | 47.6 | 46.7 | 43.9 |
| | 1 | 47.0 | 46.1 | 43.8 | 42.0 |
| | 1.5 | 53.2 | 47.3 | 44.5 | 42.6 |
| | 2 | 59.6 | 48.6 | 45.3 | 43.1 |
| Lignocaine HCl (5 $g/dm^3$) | 0.05 | 57.9 | 60.4 | 58.3 | 54.2 |
| | 0.1 | 54.6 | 59.4 | 57.5 | 53.5 |
| | 0.2 | 48.3 | 57.5 | 56.1 | 52.1 |
| | 0.3 | 42.7 | 55.6 | 54.6 | 50.6 |
| | 0.4 | 38.6 | 53.9 | 53.2 | 49.3 |
| | 0.5 | 40.1 | 52.7 | 52.0 | 48.0 |
| | 1 | 48.4 | 53.4 | 49.7 | 42.4 |
| | 1.5 | 58.5 | 54.0 | 50.0 | 42.6 |
| | 2 | 70.8 | 54.8 | 50.2 | 42.7 |
| Benzyl alcohol CMC-Na, Lignocaine HCl | 0.05 | 48.5 | 48.2 | 47.3 | 45.5 |
| | 0.1 | 46.9 | 47.5 | 46.7 | 44.9 |
| | 0.2 | 43.7 | 46.2 | 45.4 | 44.0 |
| | 0.3 | 42.3 | 46.0 | 4.3 | 43.0 |
| | 0.4 | 42.5 | 46.3 | 43.7 | 41.9 |
| | 0.5 | 42.7 | 46.7 | 44.2 | 41.1 |
| | 1 | 43.5 | 48.3 | 46.7 | 41.2 |
| | 1.5 | 44.2 | 50.2 | 49.4 | 42.3 |
| | 2 | 45.1 | 52.2 | 52.2 | 43.4 |

**Tabelle 1: Critical micellar of concentration Tween solutions and surface tension index decrease Δσ in the critical area**

| Type of auxiliary substances | Tween 20 | | Tween 40 | | Tween 60 | | Tween 80 | |
|---|---|---|---|---|---|---|---|---|
| | CMC ($g/dm^3$) | Δσ ($dyn./cm^2$) | CMC ($g/dm^3$) | Δσ ($dyn/cm^2$) | CMC ($g/dm^3$) | Δσ ($dyn/cm^2$) | CMC $g/dm^3$) | Δσ ($dyn/cm^2$ |
| Solutions ZPC | 0.66 | 28.20 | 0.42 | 19.89 | 0.29 | 14.27 | 0.28 | 12.7 |
| Benzyl alcohol | 0.59 | 30.45 | 0.35 | 28.90 | 0.13 | 26.34 | 0.16 | 24.7 |
| Lignocaine HCl | 0.89 | 30.00 | 0.64 | 22.90 | 0.43 | 19.72 | 0.39 | 33.9 |
| CMC-Na | 0.77 | 30.59 | 0.91 | 28.76 | 0.71 | 27.03 | 0.33 | 31.4 |
| 1 + 2 + 3 + 4 | 0.57 | 32.07 | 0.36 | 28.85 | 0.27 | 26.42 | 0.24 | 30.10 |

The influence of the auxiliary substances used in suspensions on surface tension of ZPC solutions is shown in Table 2.

Tween 20 was the least sensitive to the auxiliary substances (with the smallest changes of activity resulting from slopes of the surface tension logarithm/Tween concentration curves) and the most sensitive was Tween 80.

Benzyl alcohol (9 $g/dm^3$) used as preservative and light local anaesthetic causes a decrease in surface tension of those agents with the greatest numerical index of the decrease of this value for Tween 80.

The sodium salt of carboxymethyl cellulose (4 $g/dm^3$) significantly influences the course of the curves and above the CMC, a change of surface activity occurs.

In the presence of 5 $g/dm^3$ lignocaine hydrochloride in case of Tween 20, 40 and 60 there is an increase in surface tension and in the case of Tween 80, a decrease.

The results shown in Table 2 at a stable content of carbomethyl cellulose sodium salt proved that the addition of lignocaine hydrochloride and benzyl alcohol causes a change of the configuration surface activity.

The surface tension index for all Tweens decreased proportionally with the employed tenside from Tween 20, through Tweens 40 and 60 to Tween 80. The auxiliary substances used increased the surface tension index value in the critical area in all cases. Benzyl alcohol decreases micellar concentration of each surface active compound but lignocaine hydrochloride and carboxymethyl cellulose sodium salt increase it. The use of all auxiliary substances at the same time cause a decrease of CMC and the used ZPC solubility which must be taken into consideration when determining the quantity of surface active substances.

## 3. Experimental

### *3.1. Reagents*

Tween 20 (polyoxyethylenosorbitane monolaurate) Sigma 91H; Tween 40 (polyoxyethylenosorbitane palmitate) Sigma 40H; Tween 60 (polyoxyethylenosorbitane stearate) Sigma 90H; Tween 80 (polyoxyethylenosorbitane oleate) Sigma 90H; carboxymethyl cellulose sodium salt (CMC-Na, Blanose cellulose gum type 7 MF, lot 03-432); Aqualon BV; lignocaine hydrochloride (s. 2807 PZF Cefarm) imported from Italy; benzyl alcohol (KI 1515/84 POCH Gliwice; sodium chloride (KI 906/87) Gliwice FP V; sterile water according to FP V.

### *3.2. Methods*

#### *3.1.1. Stalagmometry*

A degreased and dried thermostated stalagmometer was filled with sterile water. Relative surface tension of the examined liquid was calculated as usual based on a water surface tension of 72.44 $dyne/cm^2$.

In order to calculate surface tension of surface active substances their density was determined with a vacuum pycnometer of 20 $cm^3$ volume at 22 °C. Density of the solutions was examined at 22 °C considering, therefore, a correction for water density $d_{H_2O}$ (22 °C) = 0.9978 and correction for weighing in an air environment = 0.0012 [11].

Course analysis of the relationship $\sigma^{25}_{sol} = f(c \cdot g/dm^3)$ confirmed that slopes of the curves in the appropriate concentration ranges make it possible to describe them with simple regression relationship equations $\sigma^{25}_{sol} = f(c)$. Critical micellar concentration [12] was determined by describing both straight lines ($y_1 = a_1 + b_1 \cdot c$, $y_2 = a_2 + b_2 \cdot c$) where their point of intersection correspond to CMC. This was calculated from the equation:

$$\text{CMC } 1 = \frac{a_2 - a_1}{b_1 - b_2}$$

where indexes (displacement on the axis constants y)

$$a_1;\ a_2 = \bar{x} - \frac{1}{b}\ \bar{y}$$

$b_1$; $b_2$: – regression factors (slope of the curve)

$$b_1;\ b_2 = \frac{\sum xy - n\bar{x}\bar{y}}{\sum x^2 - n(\bar{x})^2}$$

were: x, y = variables' values; n = number of measurements; x, y = mean variables' values.

#### *3.1.2. Conductivity*

Conductivity measurements were effected with an electrode with platinum plates (L = 0.82 cm) at 22 °C. Critical micellar concentration was determined similarly to the stalagmometric method. In order to better display the influence of auxiliary substances a numerical value of surface tension index decrease ($\sigma^{22}_{CMC}$) in the critical area of CMC was also determined:

$$\Delta\sigma^{22}\text{CMC} = \sigma^{22}_{H_2O} - \sigma^{22}\text{CMC}$$

where: $\sigma^{22}_{H_2O}$ = surface tension of water at 22 °C

$\sigma^{22}$CMC = solution surface tension in acritical area

Studies of changes in surface tension of Tween solutions depending on moistening agent proved that the course of the relationship $\delta^{25}_{sol} = f(c)$ did not show a minimum which is evidence of great purity of the used tensides and the uniform distribution of mean molar mass of the used surface active substances.

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