

# AGGREGATION BEHAVIOR OF HYDROPHOBICALLY MODIFIED β-CYCLODEXTRINS IN AQUEOUS SOLUTION

*F. Witte, H. Hoffmann*

*Department of Physical Chemistry I, University Bayreuth  
Universitätsstraße 30, 95440 Bayreuth, Germany*

## ABSTRACT

Three amphiphilic β-cyclodextrins in aqueous solution were investigated upon their aggregation behavior. Surface methods, conductivity and scattering methods were used to determine the cmc and radius of gyration of the aggregates. Depending on the cotenside it was possible to shift the cmc to lower concentrations. Above the cmc small spherelike aggregates existed.

## 1. INTRODUCTION

Modified CDs are widely used in industry e.g. as drug carriers. The substitution leads to increased water solubility and can enhance inclusion complex formation. Substitution of the primary hydroxyl face by alkylamino- or thio-groups leads to amphiphilic cyclodextrins, which are able to form stable langmuir layers and lyotropic liquid crystals in organic solvents. On the other hand by hydrophobic substitution of the secondary hydroxyl face it's possible to get mixed vesicles with phospholipids. Watersoluble surface active cyclodextrins might furthermore aggregate in aqueous solution.

## 2. MATERIALS AND METHODS

### 2.1. Materials

Three partially substituted β-CD derivatives from WACKER Company were investigated:

- W7 CM EHGE (Carboxymethyl-ethylhexylglycidyl-β-CD, **D1015**  
substitution degree : 0.6 / 0.4  
molar weight : ≈ 1900 g/mol

- W7 HP PGE (Hydroxypropyl-phenylglycidyl- $\beta$ -CD, **D1066**  
 substitution degree : 0.5 / 0.4  
 molar weight :  $\approx$  1700 g/mol
- W7 HP HH (Hydroxyhexyl-hydroxypropyl- $\beta$ -CD, **D1069**  
 substitution degree : 0.4 / 0.4  
 molar weight :  $\approx$  1600 g/mol

## 2.2. Methods

To investigate the interface activity of the  $\beta$ -CD derivatives, surface tension and interfacial tension were measured with a ring tensiometer and a drop volume tensionmeter. The aggregate dimensions were determined by light scattering and neutron scattering. Furthermore conductivity of one derivative was investigated. Viscosity was measured with a capillary viscosimeter.

## 3. RESULTS AND DISCUSSION

### 3.1. Surface and interfacial tension

All three CDs show a cmc in surface tension. While the cmc of D1069 is not affected by the decane molecules in interfacial tension, the aggregation concentration of D1015 and D1066 is lowered significantly. At the same time the head group area rises.

TABLE 1. cmc data from surface and interfacial tension

| Sample | cmc [wt-%]<br>(surface tension) | head group area [ $\text{\AA}$ ]<br>(surface tension) | cmc [wt-%]<br>(interfacial tension) | head group area [ $\text{\AA}$ ]<br>(interfacial tension) |
|--------|---------------------------------|---|-------------------------------------|---|
| D1015  | 0.25                            | 224   | 0.07                                | 300   |
| D1066  | 20                              | 149   | 1.3                                 | 180   |
| D1069  | 0.6                             | 125   | 0.6                                 | 124   |

The origin of this behavior must be the interaction between CD-substituents and the decane molecules. To investigate this interaction, several surface and interfacial tension experiments with D1066 were carried out. The interfacial tension depends on the media next to the aqueous phase. An alkane lowers the cmc more than an alcohol. Furthermore it's possible to lower the cmc in surface tension by addition of alcohol to a D1066 solution.

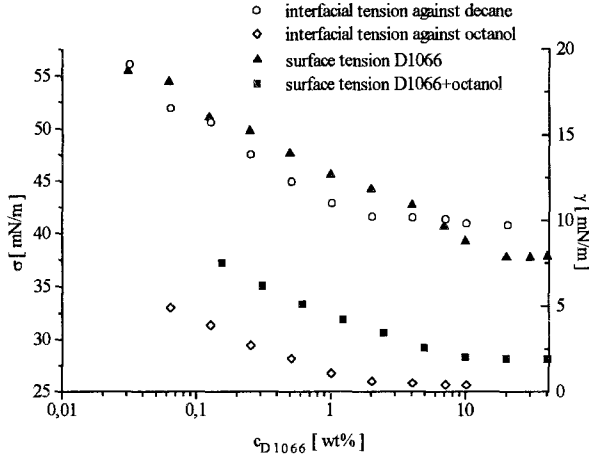


Fig. 1: Surface and interfacial tensions of D1066

### 3.2. Light scattering, neutron scattering and conductivity

The aggregate molar weight, determined by static light scattering, indicates very small aggregates consisting of only few monomers. This is confirmed by neutron scattering, which shows aggregates with radii of about 15 Å. The cmc of D1015 in light scattering (0.8 wt-%) corresponds to that measured by conductivity, but it differs significantly from that given by surface tension measurement (0.25 wt-%).

### 3.3. Viscosity

The viscosities of all three derivatives show a similar course with a divergence at high concentrations. To determine the aggregate shape from viscosity data the theoretical viscosity for hard spheres is calculated. The case of hard spheres with a viscosity divergence at the maximum packing volume is described by the Dougherty-Krieger formular:

$$\frac{\eta}{\eta_0} = \left(1 + x - \frac{\Phi}{\Phi_m}\right)^{-2.5 \cdot \Phi_m} \quad (1)$$

with  $\Phi_m$  = maximum packing volume fraction and  $x$  = thickness of hydrate shell in % of total aggregate radius.

The displayed fit, calculated for  $\Phi_m=0.5$  and  $x=0.35$  corresponds well to the experimental data.

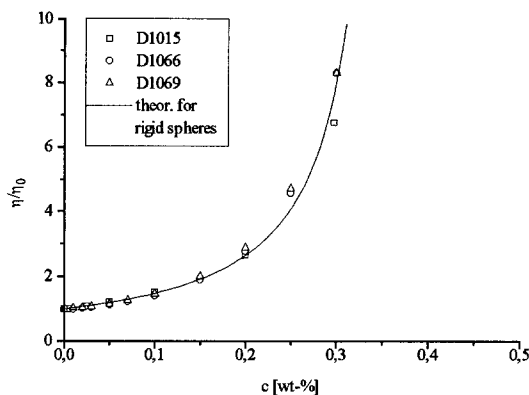


Fig. 2 Experimental viscosity data and calculated viscosity (Dougherty-Krieger)

#### 4. CONCLUSIONS

All investigated  $\beta$ -CD derivatives have a critical aggregation concentration. While the cmc of derivative D1069 isn't affected by the nature of the molecules at the interface, in case of D1015 and D1066 they have a rather strong influence on the aggregation. Because the lowering of the cmc is accompanied by a significant increase of head group area, the following model is proposed: The hydrophobic molecules at the interface insert into the space between the hydrophobic chains of the  $\beta$ -CD derivative and enhance the amphiphilic character of the CD. Hydrophobisation by inclusion complex forming wouldn't explain the strong increase in head group area. The aggregates above the cmc are small and spherelike. The driving force for aggregation should be hydrophobic interaction of the substituents like in classical micelles, not inclusion of hydrophobic chains from neighbour CDs. Not already explainable are the different cmc values from interface methods (e.g. surface tension) and volume methods (e.g. conductivity).

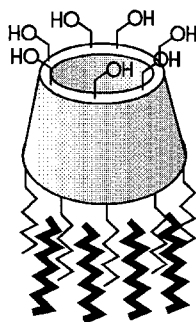


Fig. 3 Interaction between  $\beta$ -CD derivative and hydrophobic molecules