Thermochimica Acta, 199 (1992) 125–132
Elsevier Science Publishers B.V., Amsterdam

Calorimetric investigation of the complex formation between surfactants and α-, β- and γ-cyclodextrins [1]

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(Received in final form 16 September 1991)

Abstract

A calorimetric technique has been used to study complex formation between α-, β- and γ-cyclodextrins (αCD, βCD and γCD) and some surfactants (sodium dodecylsulphate (SDS), hexadecyl trimethylammonium bromide (CTAB) and *p*-(1,1,3,3-tetramethylbutyl) phenoxypoly(oxyethyleneglycol) (Triton X-100)). The experimental data indicate that some complexes (SDS–αCD, SDS–βCD and CTAB–αCD) are very stable and allow direct determination of their stoichiometry and molar enthalpy of complex formation. Those for other complexes closely fit a model based on an equilibrium reaction between surfactant, cyclodextrin and a single complex. According to the model, data analysis allows determination of the stoichiometry, stability constant and molar enthalpy of their complex formation. The thermodynamic parameters indicate that stoichiometry and complex stability are strongly influenced by entropic contributions.

INTRODUCTION

Cyclodextrins are water soluble, non-reducing, cyclic oligosaccharides shaped like a rigid, truncated cone with a hydrophilic external surface and a relatively non-polar cavity [1,2]. This peculiar structure allows them to form inclusion complexes with a wide variety of compounds such as dyes, drugs or surfactants [3–6].

The encapsulated molecules often display advantageous modifications of their physical and chemical properties. Thus, liquid or gaseous, non-polar or amphiphilic substances can be transformed into solids with high solubility in water.

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[1] Presented at the 12th National Conference on Calorimetry and Thermal Analysis, Bari, Italy, 11–13 December 1990.

When the complexed species are surfactants, a linear increase of the critical micellar concentration (CMC) with increasing cyclodextrin concentration has been rationalized in terms of displacement of the micellization equilibrium due to formation of the surfactant–cyclodextrin complex [7].

It was also noted that surfactant–cyclodextrin complexes display unexpectedly high stability constants that increase with the chain length, i.e. with surfactant hydrophobicity [4]. However, the hydrophobic interactions are not solely responsible for the stability of these complexes, because other interactions, such as hydrogen bonding or van der Waals forces, can contribute [8].

Conductometry [9], potentiometry [10] and spectrophotometry [4] employed to determine the stoichiometry and thermodynamic functions of surfactant–cyclodextrin complex formation have led to divergent results [11]. In addition, the molar enthalpy of complex formation has been generally estimated from the temperature dependence of the complex stability constant [4,12,13], but it is well known that this procedure can lead to wrong results and that enthalpy changes are best determined from direct calorimetric measurements [3,5].

Given the utility of the enthalpy of surfactant–cyclodextrin complex formation as evidence of the various interactions involved in the process and their lack in the literature, this paper describes calorimetric determination of the enthalpy of formation of the complexes formed between α-, β-, or γ-cyclodextrins (αCD, βCD, γCD) and sodium dodecylsulphate (SDS); hexadecyl trimethylammonium bromide (CTAB) and *p*-(1,1,3,3-tetramethylbutyl)phenoxypoly(oxyethyleneglycol) (Triton X-100) at 25°C. It will be shown that determination of the molar enthalpy involves contemporaneous evaluation of the stoichiometry and stability constant of the complex. The major objective of the research described in this paper was to obtain some information concerning the competition between the binding of surfactant molecules to cyclodextrins and that to their own micellar aggregates. This was achieved using surfactants of different size, hydrophilic head group and hydrophobicity at concentrations above the CMC.

EXPERIMENTAL

Materials

The α- and γ-CD (Fluka products with 97% of stated purity) and β-CD (Sigma product with 97% of stated purity) were recrystallized from water and dried under high vacuum for several days.

SDS (Fluka puriss.), CTAB (Sigma product with 99% of stated purity) and Triton X-100 (Fluka) were used without further purification.

Water was deionized and doubly distilled.

Methods

Calorimetric measurements were carried out at 25°C with an LKB Thermal Activity Monitor (TAM) equipped with a flow-mix cylinder (LKB 2277-204). The solutions were driven by a peristaltic pump (Gilson, Minipuls 2) and the flow rates (about 0.003 g s^{-1}) were determined by mass.

As a standard procedure the aqueous solutions of the surfactant were mixed in the calorimetric cell with pure water and the signal was taken as baseline. After replacing water with an aqueous solution of the cyclodextrins at fixed concentration (about 0.01 mol g^{-1}), the measured heat flux q was attributed to the cyclodextrin–surfactant complex formation process. Preliminary experiments showed that the enthalpy of dilution of the cyclodextrins is negligible. The experimental molar enthalpy (ΔH_{exp}) of complex formation was calculated using the equation

$$\Delta H_{exp} = q \times 10^3/([CD]\theta) \quad (1)$$

where [CD] is the stoichiometric CD concentration in the mixed solution and θ is the total flow rate. It must be pointed out that ΔH_{exp} can be identified with the molar enthalpy (ΔH) of complex formation when the cyclodextrin is totally complexed.

The estimated error of the experimental molar enthalpies is ± 0.5 kJ mol^{-1}.

RESULTS AND DISCUSSION

The ΔH_{exp} of complex formation as a function of the surfactant/cyclodextrin molar ratio (R) are plotted in Fig. 1. The data are confined to the more dilute surfactant solutions ($0 < R < 15$) to permit better appreciation of some features of the experimental trends of the SDS–CD systems. As can be seen, the SDS–αCD, SDS–βCD and CTAB–αCD plots show an initial linear increase of ΔH_{exp} with R followed by a well defined break point at $R = 0.5$ for SDS–αCD and CTAB–αCD, and $R = 1$ for SDS–βCD. After the break point, ΔH_{exp} shows a constant trend.

This behaviour strongly suggests that a single complex with a very high stability constant is formed [4]. Accordingly, the break point indicates the stoichiometry of the complex, so that it can be stated that αCD forms 2:1 complexes with SDS and CTAB, whereas βCD forms a 1:1 complex with SDS. Moreover, the ΔH_{exp} value after the break point can be identified with the molar enthalpy of complex formation. These data are collected in Table 1.

The plots of the other systems show a continuous variation of ΔH_{exp} with R. In particular, ΔH_{exp} becomes more negative as R increases and levels off at higher R.

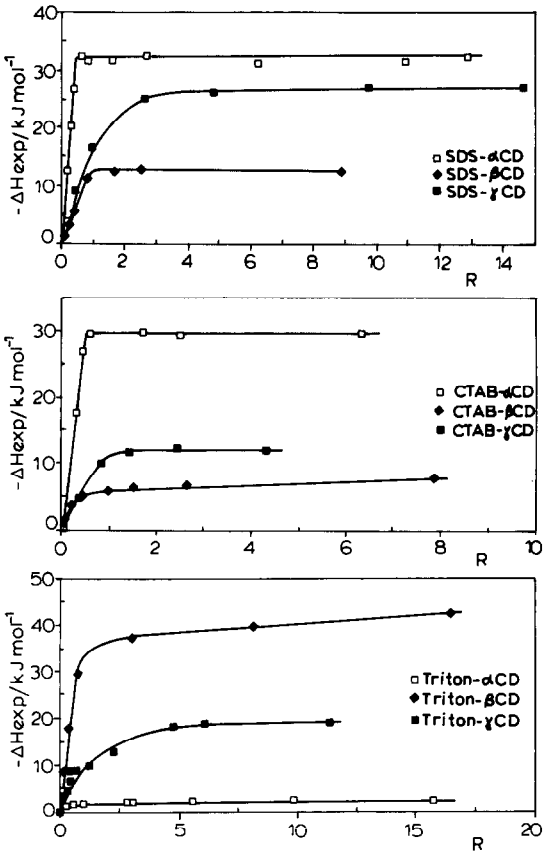

Fig. 1. Experimental molar enthalpies (ΔH_{exp}) of the complex formation as a function of the surfactant/cyclodextrin molar ratio (R).

To interpret this behaviour we assume that a single complex is in equilibrium with the surfactant and the cyclodextrin molecules. The corresponding equilibrium constant (K) can be written as

$$K = [S \cdot CD_a] / \{([S] - [S \cdot CD_a])([CD] - a[S \cdot CD_a])^a\} \quad (2)$$

where [S] and [CD] are the stoichiometric concentration of the surfactant and of the cyclodextrin, $[S \cdot CD_a]$ is the equilibrium concentration of the complex and a is the number of cyclodextrin molecules in the complex (i.e. $a = 1$ for 1:1 complexes or $a = 2$ for 2:1 complexes).

In contrast, the molar enthalpy (ΔH) of complex formation is related to the equilibrium concentration of the complex by the equation

$$\Delta H = q \times 10^3 / ([S \cdot CD_a] \theta a) \quad (3)$$

It must be noted that ΔH in eqn. (3) is defined as the enthalpy change occurring when one mole of cyclodextrin is complexed.

TABLE 1

Stoichiometry, association constants and molar enthalpies of cyclodextrin–surfactant complexes at 25°C

Complex	Stoichiometry	K (molality scale)	ΔH (kJ mol^{-1})	ΔH^* (kJ mol^{-1})	SD_1	SD_2
SDS–αCD	2:1 [a,d,f,h]	Very high [a]	−31.9 [a]	−32.0		
	1:1 [b,c,g,i]	2480 [b]	−7.1 [c]			
		130 [c]	−38 [f]			
		(4.9×10^8) [f]				
		754 [h]				
		111 [i]				
SDS–βCD	1:1 [a,b,c,d,e,g,h,i]	Very high [a]	−12.6 [a]	−12.8		
		6600 [b]				
		180 [c]				
		3630 [e]				
		356 [i]				
SDS–γCD	1:1 [a,c,d,h]	940 [a]	−28.1 [a]	−28.3	0.002	0.008
		210 [c]				
		830 [d,h]				
CTAB–αCD	2:1 [a]	Very high [a]	−29.6 [a]	−34.1		
	1:1 [g,i]	1110 [i]				
CTAB–βCD	2:1 [a]	(5.0×10^5) [a]	−7.9 [a]	−12.4	0.005	0.002
	1:1 [g,i]	2240 [i]				
CTAB–γCD	1:1 [a]	(9400) [a]	−12.3 [a]	−21.4	0.001	0.003
Triton–αCD	2:1 [a]	(9.7×10^5) [a]	−2.6 [a]	1.9	0.001	0.0006
Triton–βCD	2:1 [a]	(1.8×10^5) [a]	−45.5 [a]	−41.0	0.009	0.005
Triton–γCD	2:1 [a]	(3×10^4) [a]	−25.1 [a]	−20.6	0.007	0.004

[a] This work. [b] Ref. 10. [c] Ref. 18. [d] Ref. 8. [e] Ref. 11. [f] Ref. 4. [g] Ref. 6. [h] Ref. 9. [i] Ref. 7.

According to eqn. (3), the experimental quantity q/θ plotted against $[S \cdot CD_a]$ gives points lying along a straight line constrained to pass through the origin (Fig. 2). Besides, the $[S \cdot CD_a]$ values can be obtained by means of eqn. (2) if the stoichiometry and the K value are known.

For each system, the a and the K values giving the best linear plot of q/θ versus $[S \cdot CD_a]$ (i.e. the lowest standard deviation of the plotted points from the best straight line fitted using the least squares method) were taken as the best estimation of these quantities. The corresponding ΔH was obtained from the slope of the best straight line. It was generally found that the standard deviations obtained assuming $a = 1$ or $a = 2$, SD_1 or SD_2 respectively, differ so greatly that the complex stoichiometry can be unequivocally determined.

The results of this analysis (stoichiometry, K, ΔH, SD_1 and SD_2) are reported in Table 1, together with the comparable literature data. Since calorimetric measurements do not allow accurate determination of very high stability constants, our K values may be considered only as a rough

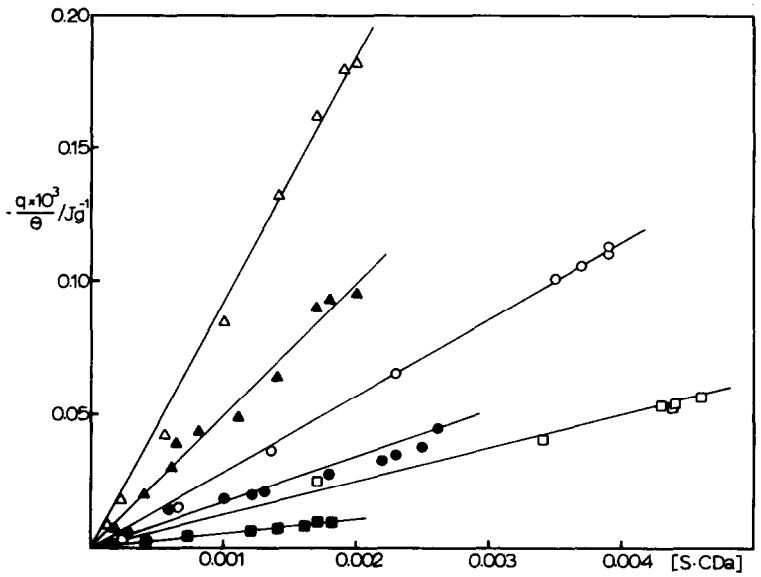

Fig. 2. Fits of eqn. (3) for the formation of SDS–γCD (○), CTAB–βCD (●), CTAB–γCD (□), Triton–αCD (■), Triton–βCD (△) and Triton–γCD (▲) complexes.

estimation of the complex stability constants. The estimated error of the ΔH values is ± 0.5 kJ mol^{-1}.

Since our calorimetric measurements were generally performed at surfactant concentrations greater than their CMCs ($CMC_{SDS} = 8.3 \times 10^{-3}$ M, $CMC_{CTAB} = 9.2 \times 10^{-4}$ M and $CMC_{Triton\ X\text{-}100} = 2.4 \times 10^{-4}$ M) [14], the ΔH values in Table 1 include the contribution due to demicellization of the surfactant. In this table are also reported the molar enthalpy of complex formation less the demicellization contribution (ΔH^*) obtained using the literature values for the molar enthalpy of micellization of SDS, CTAB and Triton X-100, i.e. -0.2 kJ mol^{-1} [15], -9.1 kJ mol^{-1} [16] and 9.0 kJ mol^{-1} [17].

Our results for the stoichiometry of the αCD–SDS, βCD–SDS and γCD–SDS complexes are in agreement with those of Robinson and coworkers [4] and Palepu and Reinsborough [9], and differ from those of Aman and Serve [11] and Okubo et al. [7,18] who assumed a 1:1 stoichiometry and did not compare the fitting of a 2:1 stoichiometry.

Our estimations of the stability constants of SDS–αCD, SDS–βCD and SDS–γCD and of the molar enthalpy of SDS–αCD complex formation are in qualitative accord with those of Hersey et al. [4] and Palepu and Reinsborough [9], whereas all the other comparisons fail poorly.

A perusal of Table 1 shows that αCD forms very stable 2:1 complexes with all the surfactants examined. This also holds for Triton X-100, even if its ΔH is rather low. By increasing the radius of the hydrophobic cavity

(αCD → βCD → γCD) there is a constant trend toward less stable complexes. As expected, the tighter the fit of the surfactant molecule in the inner cavity of the cyclodextrin, the more stable the complex.

The stability of the complex always decreases in the order anionic > cationic > nonionic surfactant, showing it is partly determined by interactions between the hydrophilic head group of the surfactant and the external part of the CD molecules. These interactions also provide a reason why surfactant molecules much prefer complexation to micellization.

A less regular trend is shown by the ΔH values. Evidently, complex stoichiometry and complex formation not only depend on enthalpic contributions, but are also strongly influenced by entropic contributions. The main entropic contributions could be attributed to the hydrophobic interaction between the alkyl chain and the inner wall of the CD molecule, to the release of "high energy" and "low entropy" water molecules from the cavity of the CD during the penetration process into the cavity and to the conformational changes of the surfactant alkyl chain [18].

The very low molar enthalpy of the Triton–αCD, the very high molar enthalpy of the Triton–βCD, and the 2:1 stoichiometry of the Triton–γCD are very surprising. No explanation of these findings can be advanced in the absence of further investigations.

ACKNOWLEDGEMENT

We thank the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (M.U.R.S.T.) for financial support.

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