The Spectral Displacement Technique for Determining the Binding Constants of *β*-Cyclodextrin – Alkyltrimethylammonium Inclusion Complexes

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Abstract

A survey of the literature reveals that the spectroscopic displacement method, in which phenolphthalein is used as a competitive chromophore to determine binding constants of *β*-cyclodextrin with surfactants was successful in the case of homologous hydrocarbon and fluorocarbon anionic surfactants. We show here that this method can be applied also for homologous alkyltrimethylammonium bromides (with alkyl varying from octyl- to hexadecyl) under the condition that the concentration of the cationic surfactant is distinctly lower than the value of its critical micelle concentration.

Introduction

Cyclodextrins (CDs) are macrocyclic oligosaccharides, which have a torus-shaped structure with a hydrophobic cavity exhibiting the ability of formation of inclusates with a variety of inorganic and organic compounds and especially with solutes that contain hydrocarbon or fluorocarbon moieties. Among the most frequently investigated types of CDs is the *β*-CD, which consists of seven D-glucopyranose units linked by *α*(1–4) interglucose bonds. Results of numerous model studies on host–guest interactions of homologous series of compounds with CDs have shown that the binding constants for the formation of such inclusion complexes generally increase strongly with growth in number of carbon atoms in the alkyl or perfluoroalkyl chain [1–16].

The binding constants have been determined by applying various techniques including conductivity [2, 5, 17–21], sound velocity [19, 22–24], surface tension [14, 25–27], emf studies using surfactant selective electrodes [7, 9, 28–32], NMR spectroscopy [8, 33–36], and competitive binding studies using UV, visible, and fluorescence probes [1, 4, 11, 12, 37, 38]. It has been pointed out that the literature data show a large scatter in values of binding constants varying by several orders of magnitude for the same system when different experimental methods are employed [29]. Mwakibete *et al.* [10] suggested that the methods may be divided into two classes, one that relies on direct measurements of the free and bound guest in the solution and the second, which takes the advantage of the existence of any physically observable property (such as conductivity, sound velocity, and surface tension) that is proportional to the extent of binding. These authors indicated that the former class, including emf and competitive binding studies, give binding constant

values that are reasonably close. The spectrophotometric technique involving phenolphthalein as the competing reagent appears to be the most promising one. It is based on the fact that in alkaline solutions a colourless 1:1 complex is formed between phenolphthalein and *β*-CD and that the purple phenolphthalein dianion is partially displaced by a competing reagent to an extent depending upon its affinity to form a complex with the CD host. This substitution method has been applied to obtain 1:1 equilibrium binding constants for inorganic anions [39], adamantane carboxylate anion and adamantanol [37], the dodecylsulphate anion, hexaethyleneglycol monododecyl ether, cyclohexanol, and for homologous aliphatic alcohols (C_4 to C_{10}) [3]. The technique was applied also to obtain binding constants for a homologous series of hydrocarbon ($C_nH_{2n+1}COONa$, $n = 5$–13) and fluorocarbon anionic surfactants ($C_nF_{2n+1}COONa$, $n = 3$–8) with *β*-CD [12]. Gray *et al.* [11] studied the complexation of a variety of anionic surfactants by *β*-CD including alkane-1-sulfonates (C_5–C_{12}) and alkyl sulphates (C_6, C_8, C_{12}). These authors claimed, however, that the technique was not successful for many amines, such as octylamine, and quaternary ammonium cationic surfactants, either because the inclusate caused the phenolphthalein solution to decolorize on its own without CD being present or the CD additions led to cloudiness in solution. The type of cationic surfactants and concentration range examined was, however, not stated. The decolorization may be due to the formation of ion-pairs followed by precipitation of the quaternary ammonium phenolphthaleinate or by binding of the phenolphthalein anion as the counterion at the surface of the micelle formed by long-chain quaternary ammonium salts. Such effects should be concentration dependent. To elucidate the factors affecting the applicability of this substitution method in the determination of binding constants of qua-

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ternary ammonium cations by β-CD we have undertaken detailed studies on systems covering a series of homologous alkyltrimethylammonium bromides with alkyl = C_8, C_{10}, C_{12}, C_{14}, C_{15}, and C_{16}.

Experimental

β-CD (Sigma) was used as received and the water content, amounting to 14% by weight as determined thermogravimetrically, was accounted for in the preparation of stock solutions. Octyltrimethylammonium bromide (C8TAB) was prepared by quaternization of trimethylamine with octyl bromide and purified as described earlier [40]. Decyl-(C10TAB), pentadecyl-(C15TAB), and hexadecyl-(C16TAB) homologues were prepared similarly. The dodecyl-(C12TAB) and tetradecyl-(C14TAB) homologues were from Aldrich and were used as received. Phenolphthalein was a reagent grade sample. A stock solution of the indicator (1.5×10^{-3} M) was prepared in 96% ethyl alcohol. It was used to prepare a series of solutions of phenolphthalein in aqueous Na_2CO_3 (4×10^{-3} M, pH $\approx$ 10.5). The concentration of phenolphthalein, C_p, ranged from 3×10^{-6} to 3×10^{-5} M. Absorptions of the solutions were measured at a fixed wavelength (550 nm) using a Spekol 221 spectrophotometer at the temperature of 298 ± 1 K. The results served to prepare a calibration curve, which enabled the estimation of concentration of free uncomplexed phenolphthalein, [P], in systems with β-CD. The binding constant, K, for the β-CD-phenolphthalein complex was calculated from the relation:

$$(C_P - [P])/(C_\beta - C_P + [P]) = K[P], \qquad (1)$$

where C_β denotes the total molar concentration of β-CD. For this purpose a series of solutions was prepared with a constant concentration of phenolphthalein, $C_p = 3 \times 10^{-5}$ M and of Na_2CO_3 (4×10^{-3} M) and the concentration of β-CD varying in the range of 5×10^{-5} to 5×10^{-4} M. The concentration of free phenolphthalein, [P], in these solutions was determined spectroscopically. The relevant data served to calculate the value of K from Equation (1) by least squares analysis.

In order to determine the binding constant, K', for the complexation of alkyltrimethylammonium bromides by β-CD, the concentration of free phenolphthalein was determined spectrophotometrically in a series of solutions, in which the total concentrations of the indicator, β-CD, and Na_2CO_3 were constant and amounted to 3×10^{-5} M, 2×10^{-4} M, and 4×10^{-3} M, respectively, whereas the total concentration of the surfactant, C_s, varied in the range from 1×10^{-5} M to 5×10^{-3} M for C8TAB, C10TAB, and C12TAB, and to 1×10^{-3} M, 4×10^{-4} M, and 5×10^{-4} M for C14TAB, C15TAB, and C16TAB, respectively.

Results and discussion

The binding constant, K, for the complexation of phenolphthalein by β-CD calculated by fitting the spectroscopic
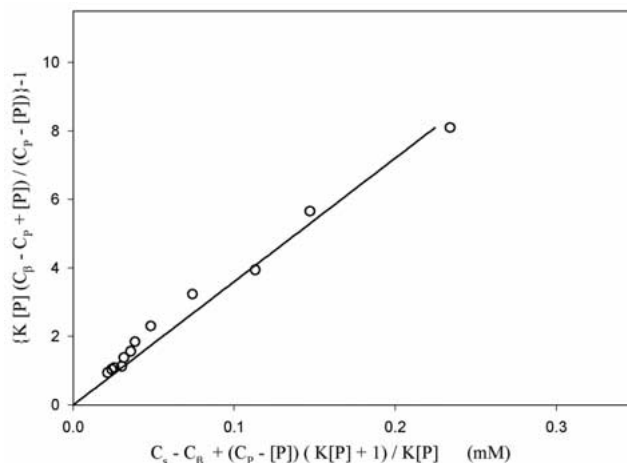

Figure 1. Fit of experimental data for C14TAB to Equation (5).

data to Equation (1) amounts to $(2.48 \pm 0.02) \times 10^4$ M^{-1} and is close to the more recent literature values of $(2.40 \pm 0.16) \times 10^4$ M^{-1} [41], of $(2.04 \pm 0.42) \times 10^4$ M^{-1} [11], and $(2.5 \pm 0.3) \times 10^4$ M^{-1} [12].

Assuming that β-CD forms only 1:1 complexes with alkyltrimethylammonium bromides, and taking into account that phenolphthalein forms also such complexes, the total concentration of β-CD, C_β, phenolphthalein, C_p, and the ammonium salt, C_s, in their aqueous mixtures can be expressed by the following relations:

$$C_\beta = [\beta] + K[\beta][P] + K'[\beta][S], \qquad (2)$$

$$C_P = [P] + K[\beta][P], \qquad (3)$$

$$C_S = [S] + K'[\beta][S], \qquad (4)$$

where K' is the binding constant of the ammonium salt with β-CD and $[\beta]$, [P], and [S] are the concentrations of the uncomplexed forms of the reagents.

From Equations (2) to (4) one may derive Equation (5), which relates the total concentrations of the three reagents with the spectroscopically determined concentration of uncomplexed phenolphthalein [P]:

$$K[P](C_\beta - C_P + [P])/(C_P - [P])$$
$$= K'\{C_s - C_\beta + (C_P - [P])(K[P] + 1)/K[P]\} + 1. \quad (5)$$

A fit of the experimental data to this equation is exemplified in Figure 1 for C14TAB, where the low concentration range was taken into account. At higher concentrations of the surfactants a distinct leveling off of such plots was observed in all cases studied.

Least-squares analysis of the data corresponding to the linear fragments of the plots yielded values of K' collected in Table 1 together with the concentration range of C_s taken into account in the calculations. In the last two columns are given, for comparison, relevant literature values reported for K' and values calculated from the empirical Equation (6) derived from the present K' data for alkyltrimethylammonium

Table 1. Present and literature values of binding constants (K') for the inclusion complexes of alkyltrimethylammonium bromides with β-CD

Ammonium salt	Highest concentration of Cs (mM)	CMC (mM)	Binding constant (M^{-1})		
			Present values	Calculated values from Equation (6)	Literature values
C8TAB	5.0	298	356 ± 16	419	–
C10TAB	2.5	69	4143 ± 27	3961	3981 [7]
C12TAB	0.5	16	13810 ± 446	14107	17800 [7], 18100 [28], 22100 [9]
C14TAB	0.3	3.7	36050 ± 1749	34340	39811 [7], 11700 [19], 39750 [10], 44000 [9]
C15TAB	0.25	1.8	54891 ± 3906	49327	–
C16TAB	0.12	0.87	60733 ± 11484	68141	70790 [7], 22000 [32], 67700 [10], 59800 [9], 65500 [25]

bromides as a function of number, n, of carbon atoms in the alkyl chain:

$$\sqrt[3]{K'} = -25.88 + 4.171n \quad (r^2 = 0.994). \qquad (6)$$

Comparison of the present K' values with literature data shows, unexpectedly, a satisfactory agreement especially with values derived from potentiometric measurements of Jezequel *et al.* [7]. The success of the visible spectral displacement technique involving phenolphthalein as the competing reagent applied here for the determination of binding constants of quaternary ammonium ions with β-CD, appears to be limited to the low concentration range, which is lower compared to cmc of the surfactant (see Table 1) by a factor of about 60, 28, 32, 12, 7, and 7 for the C8, C10, C12, C14, C15, and C16TAB homologues, respectively. The cmc values were estimated from the relation: log cmc $= 0.317n + 2.01$ reported by Zana [42]. This relation is valid for surfactants in pure water. In aqueous systems here studied two opposite effects may influence the value of cmc. It is generally known that β-CD shifts the cmc to higher values. On the other hand the presence of sodium carbonate and of phenolphthalein distinctly lower the cmc of the surfactant. The bulky phenolphthalein dianion may induce premicellar aggregation via formation of hydrophobic ion-pairs with the cationic surfactants. It seems thus plausible to assume that the limits of application of the technique, given in Table 1, may correspond to the critical concentration at which such processes become important. Aggregation of the surfactant impedes the process of competition for the site in CD because growth of activity of the surfactant above cmc with growth of its analytical concentration is completely hindered. Some emf results suggested even that activity of the surfactant in micellar systems slightly decreases with growth of concentration of the surfactant [43, 44]. This effect is augmented by adsorption of the phenolphthalein dianion as a counter-ion in the Stern layer of the micelle. Furthermore, the alkalinity of the micelle – bulk solution interface is probably higher than that corresponding to the nominal pH of 10.5 due to adsorption of hydroxide anions. In such microenvironment, the purple phenolphthalein dianion may undergo transformation to a colourless trianion [45] rendering the discussed method still less valid.

Reassuming it may be stated that the spectral displacement technique with phenolphthalein as the chromophore may be applied to determine 1:1 binding constants of homologous alkyltrimethylammonium salts with β-CD under the condition that the concentration range of the cationic taken into account in the calculations is distinctly lower than the cmc.

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