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Conductivity Studies of the Molecular Encapsulation of Sodium Perfluoroctanoate by β-Cyclodextrin Derivatives

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Abstract. The molecular encapsulation of sodium perfluoroctanoate (SPFO) by hydroxypropyl-β-cyclodextrin (HP-β-CD) or 2,6-di-*O*-methyl-β-cyclodextrin (DM-β-CD) has been analyzed by measuring the conductivity in solution of the ternary systems formed by CD + SPFO + H_2O. The studies were carried out at 25 °C using a fully computerized electrical conductivity technique. The measurements were made as a function of CD concentration at various non-micellar concentrations of SPFO, and as a function of CD and SPFO concentrations with [CD]/[SPFO] constant at stoichiometric ratio. The inclusion complexes, HP-β-CD·SPFO and DM-β-CD·SPFO, were characterized through the stoichiometry, which has been found to be 1 : 1 in both cases, and the binding constants, which have been evaluated from the conductivity data with a model proposed by us considering the variation of the ionic molar conductivities with the concentration and the association of the surfactant counterion to the inclusion complex. The resulting K values indicate that the interaction between the CD cavity and the monomeric SPFO is strong and similar in both cases.

Key words: Cyclodextrin, sodium perfluoroctanoate, conductivity, encapsulation, surfactant, complex.

1. Introduction

Cyclodextrins (CDs) are cyclic oligoglycosides of six (α-CD), seven (β-CD) or eight (γ-CD) α-D-glucopyranose units linked by α(1 → 4) bonds [1–4]. The circular configuration results in a donut-shaped molecule, whose cavity is capable of binding guest molecules of appropriate size, shape, and polarity, forming noncovalently-bonded inclusion compounds. Due to their cavity size, β-CD and its derivatives are the most commonly used cyclodextrins to include the hydrocarbon tail of surfactants. Since β-CD has a low aqueous solubility [3], hydroxypropyl-β-cyclodextrin (HP-β-CD) and 2,6-di-*O*-methyl-β-cyclodextrin (DM-β-CD), with solubilities 20 or 30 times greater, are becoming increasingly used in recent years [5–9]. The overwhelming majority of studies of the cyclodextrin/surfactant/water systems involves surfactants composed of hydrocarbon backbones. The few reported studies of similar ternary systems containing perfluorinated surfactants have also been found to form inclusion complexes with β-cyclodextrin [10–15]. Since the

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main driving-forces in these associations are thought to be the hydrophobic effect, together with the *key–lock* principle between the interacting partners, these studies suggest that the interaction between the CD cavity and the perfluorinated surfactants is more favorable than that with their hydrocarbon homologues, due to a greater hydrophobicity and the larger cross sectional diameter (6 Å) of the fluorocarbon chain which allows it to fit snugly into the β-CD cavity.

We have recently reported a very precise, fully computerized technique to measure conductivity in liquid mixtures [16]. This technique has been proved to be very powerful in studies of ternary systems consisting of CD/surfactant/water [17] . In this paper, we extend the cyclodextrin/surfactant studies to the characterization of the complexation phenomena between sodium perfluoroctanoate (SPFO) and two β-cyclodextrin derivatives, HP-β-CD and DM-β-CD. In both cases, the conductivity measurements have been carried out with variable CD concentration at constant nonmicellar SPFO concentration, and with variable CD and SPFO concentrations but with the stoichiometric ratio, [CD]/[SPFO] being constant. In both studies, and in accordance with Derenlau [18], the experimental concentrations have been chosen to ensure an optimum degree of complexation (f), ranging from 0.15 and 0.85.

2. Experimental

2.1. Materials

Sodium perfluoroctanoate (SPFO) was purchased from PCR, Inc. It was twice recrystallized from an acetone/methanol mixture (90/10 v/v) and dried under vacuum. Hydroxypropyl-β-cyclodextrin (HP-β-CD) containing an average of 0.4 hydroxypropyl groups per glucopyranose unit (Janssen Biotechnology, Belgium) and 2,6-di-*O*-methyl-β-cyclodextrin (DM-β-CD) (Cyclolab, Hungary) were used without further purification. Thermogravimetric analyses showed that HP-β-CD and DM-β-CD consist of 3.4% and 1.7% water, respectively, which were taken into account in calculating solute concentrations. Doubly distilled water was further purified by using a Super Q Millipore system and was also degassed prior to solution preparation.

2.2. Conductivity measurements

Conductivity data were obtained at 25.000 ± 0.001 °C using a Hewlett-Packard 4263A LCR Meter, together with a Metrohm electrode with a cell constant of 0.8129 cm^{-1}. The equipment is fully computerized, the conductimeter and the burette being controlled through IEEE-488 and RS-232C interfaces, respectively. The details of the experimental automatic procedure have been previously described [16]. The accuracy on the specific conductivity, obtained as an average of 2400 measurements for each concentration, is ±0.03%.

3. Results and Discussion

Figure 1 shows the plots of the specific conductivity κ vs. [HP-β-CD] at two constant SPFO concentrations. Similar curves (not plotted here) were obtained for the DM-β-CD + SPFO + H_2O system. In all the cases [SPFO] was kept below the critical micellar concentration of the pure surfactant (cmc = 0.032 M) [13,19]. Figures 2 and 3 show the plots of the molar conductance Λ vs. [CD] for the two systems studied. As can be clearly seen in these figures, two straight lines with different slopes can be drawn, intersecting at a CD concentration from which the stoichiometry of the inclusion complex is obtained. The picture that emerges from Figures 1–3 is clear. The addition of cyclodextrin to a surfactant solution results in the formation of the inclusion complex, decreasing the concentration of free surfactant. As the ionic molar conductance of the complexed surfactant is expected to be lower than that of the free surfactant, κ and Λ also decrease, evidently sharper at the first stage of the addition of CD. The stoichiometry of both complexes, HP-β-CD·SPFO and DM-β-CD·SPFO, obtained from Figures 2 and 3, has been found to be 1.05 ± 0.05, similar to that found for the complex β-CD·SPFO [11–15]. It seems that the methylation or hydroxypropylation of β-CD does not significantly affect the stoichiometry of the complex, as was already concluded in our laboratory for other CD/surfactant systems [17,20,21]. Once the stoichiometry of the complex is known, it is possible to study the behaviour of the conductivity in an aqueous solution where both CD and SPFO concentrations vary, keeping their stoichiometric ratio always constant. Figure 4 reports these experimental data, showing how the molar conductance Λ decreases as long as the concentration of CD and SPFO increases, in good agreement with the previous results (Figures 2 and 3).

In addition to the stoichiometry, another parameter of crucial importance when studying and characterizing the inclusion complexes is the association constant K. These constants are not only informative about the noncovalent forces involved in such an interaction, but also provide insight into the driving forces governing the process. Currently, they are the focus of a great deal of studies, which try to relate an experimental magnitude when the complex is formed with the characteristics of this complex. The conductivity data shown in Figures 1–4 can be used to evaluate the K values for the systems studied in this work. With the aim of improving the calculation of the binding constant from conductivity data, we have recently proposed [17] a method which considers the dependency of the ionic molar conductivity λ_i of the species on the concentration and the partial association of the surfactant counterion to the inclusion complex [10]. There are several equilibria to be analyzed. Considering the 1 : 1 stoichiometry found for both complexes, the association constant K governing the inclusion of the monomer by the CD cavity,

$$CD + S^- \rightleftharpoons CDS^-$$

is given by

$$K_{CDS^-} = [CDS^-]/([CD][S]) \tag{1}$$

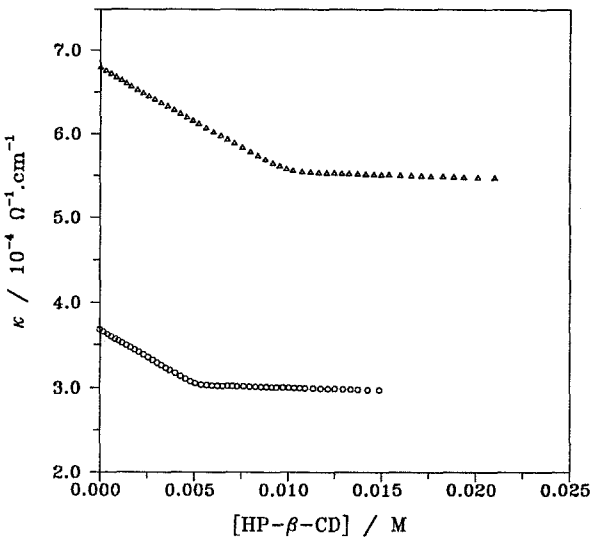

Figure 1. Values of specific conductivity (κ) as a function of HP-β-CD concentration at two constant SPFO concentrations: ○, 4.9 mM; Δ, 9.5 mM.

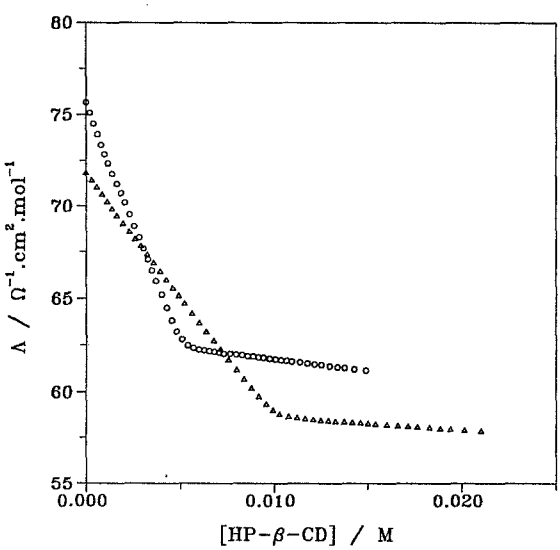

Figure 2. Values of molar conductivity (Λ) as a function of HP-β-CD concentration at two constant SPFO concentrations: ○, 4.9 mM; Δ, 9.5 mM.

while the partial association of the sodium counterion to the inclusion complex follows the equilibrium

$$CDS^- + Na^+ \rightleftharpoons CDSNa$$

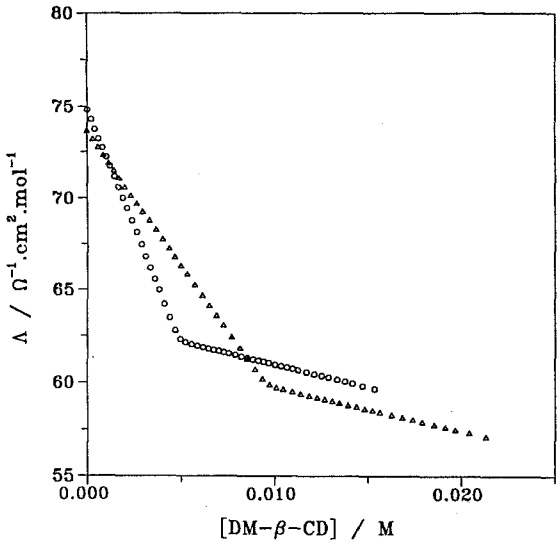

Figure 3. Values of molar conductivity (Λ) as a function of DM-β-CD concentration at two constant SPFO concentrations: ○, 5.0 mM; Δ, 9.4 mM.

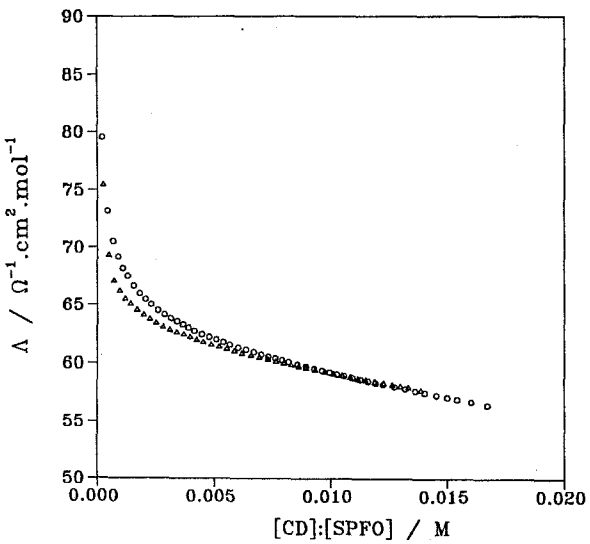

Figure 4. Values of molar conductivity (Λ) as a function of CD and SPFO concentrations at stoichiometric ratio: ○, HP-β-CD; Δ, DM-β-CD.

with

$$K_{\mathrm{CDSNa}} = [\mathrm{CDSNa}]/([\mathrm{CDS}^-][\mathrm{Na}^+]). \qquad (2)$$

The specific conductivity κ of the solution is related to the ionic molar conductivities λ_i and the concentration of the ionic species by,

$$\kappa = \lambda_{Na^+}[Na^+] + \lambda_{S^-}[S^-] + \lambda_{CDS^-}[CDS^-] \tag{3}$$

where, according to the mass balance for both species, the total surfactant concentration (C_s) and the total cyclodextrin concentration (C_h) are given by,

$$C_s = [S^-] + [CDS^-] + [CDSNa] = [Na^+] + [CDSNa] \tag{4}$$

$$C_h = [CD] + [CDS^-] + [CDSNa]. \tag{5}$$

At low concentration, the ionic molar conductances can be estimated by the Onsager equation [17]. The constants α, β, B, and a_n in this equation, and the ionic molar conductivity at infinite dilution for the sodium ion ($\lambda^0_{Na^+}$) are taken from the literature [22–24]. The ionic molar conductivity of the perfluoroctanoate ion at infinite dilution ($\lambda^0_{PFO^-}$) has been obtained from the conductivity data (below the cmc) measured in our laboratory in the absence of cyclodextrin [16].

In the presence of cyclodextrin, the unknown parameters K, K_{CDSNa} and $\lambda^0_{CDS^-}$ have been determined from the conductivity data by using Equations (1)–(5) with a non-linear regression method based on a Marquardt algorithm. The K_{CDSNa} values indicate, within their large uncertainty, that around 1% of sodium counterion concentration is associated with the cyclodextrin, qualitatively in agreement with what was found for the β-CD + SPFO system by Reinsborough *et al.* [10] from emf experiments. Table I reports the average values (over all the different studies) of the binding constant K, and the ionic molar conductivity at infinite dilution λ^0_i for both inclusion complexes. Values of $\lambda^0_{PFO^-}$ and $\lambda^0_{CDS^-}$ in Table I indicate that when the surfactant ion associates with CD, the mobility of the surfactant ion decreases about 50%, independently of the host molecule, HP-β-CD or DM-β-CD. This decrease in $\lambda^0_{CDS^-}$ with respect to $\lambda^0_{PFO^-}$, which cannot be considered negligible in any case, implies a significant reduction in the contribution of the associated species to the solution conductivity, as is experimentally corroborated in Figures 1–3. A similar behaviour has been also observed by us [17] in the complexes formed by β-CD and dodecyltrimethylammonium bromide ($D_{12}TAB$). From the K values in Table I, it can be also concluded that the perfluoroctanoate surfactant ion associates strongly with HP-β-CD or DM-β-CD, with a similar binding constant, within the experimental uncertainty. This feature can be qualitatively deduced from the behaviour of Λ vs. [CD] and [SPFO] at 1 : 1 stoichiometric ratio (Figure 4). Moreover, the K values obtained in this work for a perfluorinated surfactant of eight carbon atoms are slightly less than those found for a dodecyltrimethylammonium bromide with 12 carbon atoms, in keeping with the higher hydrophobicity of the fluorinated chains as compared with their hydrocarbon homologues.

Table I. Values of the ionic molar conductivities at infinite dilution (λ_i^0) and the binding constant (K) of the inclusion complex.

Ion	λ_i^0, Ω^{-1} cm^2 mol^{-1}	K, M^{-1}
Na^+	50.1	–
PFO^-	35.1	–
HP-β-CD·PFO^-	18 ± 2	2400 ± 600
DM-β-CD·PFO^-	18 ± 2	2500 ± 600

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