

COMMUNICATIONS

Effect of structural variations of non-ionic surfactants on surface properties: surfactants with semi-polar hydrophobes

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Abstract—The surface properties of a series of non-ionic surfactants in which a polar group (either an ether or a keto group) has been introduced into a hydrocarbon chain of octadecylpolyoxyethylene glycol monoether ($C_{18}E_{17-19}$) have been investigated. Surface tension measurements indicated that the critical micelle concentrations for these semi-polar surfactants in aqueous solution were all significantly higher than those of $C_{18}E_{22}$, the corresponding unsubstituted octadecylpolyoxyethylene glycol monoether. The minimum areas per molecule of the semi-polar surfactants in the surface monolayer were all larger than the area obtained for $C_{18}E_{22}$, from which it was concluded that the hydrophobe, and not the polyoxyethylene chain was the main determinant of surface area.

Recent attempts to improve the solubilizing capacity of non-ionic polyoxyethylene n-alkyl ether surfactants (general formula C_mE_n) by lengthening the hydrocarbon chain have been limited by the necessity of retaining a 'fluid like' micellar core (Arnarson & Elworthy 1980). For surfactants from the series $C_mE_{1.25m}$ at 298K, maximal solubilization was achieved at an alkyl chain length of $m=16$ (Elworthy & Patel 1982). For surfactants containing an alkyl chain longer than $m=16$, experimental evidence (Elworthy & Patel 1984a, b) suggests that for micellization to occur oxyethylene groups must intrude into the core in order to cause a depression of its melting point. This intrusion of oxyethylene chains into the core effectively causes a dilution of the oxyethylene rich region close to the micellar core, thus destroying the main locus of solubilization for most drugs (Patel et al 1981).

Attwood et al (1989) investigated an alternative approach to increasing solubilization whereby a semi-polar group (either an ether or keto group) was introduced into the hydrocarbon core of a $C_{18}E_{22}$ micelle in an attempt to promote solubilization in this region. Although some drugs exhibited an increase in solubilization due to an increased solubility in the core, drugs which were solubilized largely at the polyoxyethylene/core interface experienced a decrease in solubilization, due to a reduction in micellar size. The reduced micelle size was a consequence both of the increased polarity of the hydrophobe and the geometric constraints on packing resulting from the introduction of the polar group into the core of the micelle.

This paper reports a further study of the non-ionic surfactants of the type investigated previously (Attwood et al 1989). The aim of this work was to determine the effects of the incorporated semi-polar groups on the surface properties at the air/water interface.

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Materials and methods

Synthetic surfactants. The semi-polar surfactants examined in this study included those of Attwood et al (1989) namely $CH_3(CH_2)_{11}O(CH_2)_5(OCH_2CH_2)_{18}OH$ [$C_{18(e,6)}E_{18}$], $CH_3(CH_2)_6O(CH_2)_{10}(OCH_2CH_2)_{17}OH$ [$C_{18(e,11)}E_{17}$] and $CH_3(CH_2)_5CO(CH_2)_{11}(OCH_2CH_2)_{18}OH$ [$C_{18(k,12)}E_{18}$]. The letters e and k represent ether and keto groups, respectively, and the number following this letter specifies the position of the group in the chain. The hydrophobe is denoted as C_m where m represents the number of atoms in the back bone. The hydrophile is denoted in the usual way as E_n , where n is the average number of oxyethylene units, E.

The semi-polar surfactant $CH_3(CH_2)_{11}O(CH_2)_2CH(CH_3)(CH_2)_2(OCH_2CH_2)_{19}OH$ [$C_{18(e,6,b,3)}E_{19}$, where b denotes the methyl branch] was synthesised as follows. The hydrophobe 3-methyl-6-oxaocetadecanol was prepared from 1-bromodecane and a four molar excess of the mono-sodium salt of 3-methyl-1,5-pentanediol, by the Williamson ether synthesis. Distillation yielded the desired product, which was then ethoxylated to give the crude surfactant. Purification by the method of Longman (1978) gave the final surfactant which was shown to contain no glycols or starting alcohols by TLC on silica. Elemental analysis, MS, IR and NMR spectra for the hydrophobe and surfactant were consistent with the expected structure. The sample of $C_{18}E_{22}$ was that of Patel (1982).

Surface tension measurements. Surface tensions (γ) of aqueous solutions at $298 \pm 0.1K$ were measured by the Wilhelmy plate method. The usual precautions were taken to ensure clean glassware; the water was doubly distilled from alkaline potassium permanganate. Measurements were made 15 min after dilution and checked several times at 5 min intervals until no significant change occurred. Surface tension was generally found to be invariant after 30 min even for the most dilute solutions used in the study. The external accuracy of the measurement was checked by frequent replicate measurements of γ for pure water.

Results and discussion

Surface tension and critical micelle concentration. Fig. 1 shows the variation of surface tension, γ , of aqueous solutions of the semi-polar surfactants and $C_{18}E_{22}$, with log of bulk phase concentration, C, (mol dm^{-3}). Critical micelle concentrations (CMC) taken from inflection points of γ -log C plots are listed in Table 1 together with the value of γ at the CMC. No minima were observed at the CMCs for any surfactant indicating the absence of significant amounts of surface active impurities. Since

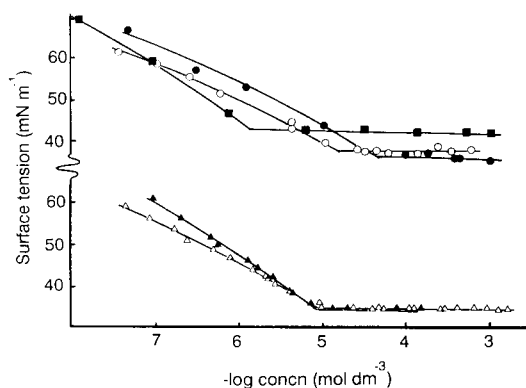


FIG. 1. Surface tension, γ , as a function of log concentration for ●, $C_{18(e,11)}E_{17}$; ▲, $C_{18(e,6)}E_{18}$; ○, $C_{18(k,12)}E_{18}$; △, $C_{18(e,6,b,3)}E_{19}$; ■, $C_{18}E_{22}$ in water at 298K.

the semi-polar surfactants all have very similar ethylene oxide chain lengths, the influence of the hydrophile may be reasonably assumed to be constant in all instances. Similarly, the slightly longer polyoxyethylene chain of $C_{18}E_{22}$ is not thought to affect significantly the CMC and it is not unreasonable to draw conclusions from comparisons with this compound. The reduction of micellizing tendency as indicated by the increase in CMC of the semi-polar surfactants compared to $C_{18}E_{22}$ is a consequence both of the increased polarity of the hydrophobe (log P of the semi-polar surfactants lies between 7.49 and 7.65 compared with a value of 9.71 for the octadecyl chain) and of its configuration in the micelle core. Calculations of the core radius of the micelles of the semi-polar surfactants based on experimental determinations of their micellar size (Attwood et al 1989) have shown that the hydrophobes are present in the core in a bent (*cis*) rather than the fully extended (*trans*) form. Consequently, due to the 'V' shape of the hydrophobe there will be loss of some hydrocarbon/water interaction thus reducing the interfacial energy change on micellization. It is this, together with the increased polar nature of the hydrophobe, that is responsible for the increase in the CMC of the semi-polar surfactants. Furthermore, in the case of $C_{18(e,6,b,3)}E_{19}$ the presence of the branched methyl group would be expected to increase the CMC slightly compared with the straight chain surfactant containing the equivalent number of carbon atoms in the hydrophobe (i.e. $m=19$) (Elworthy & Florence 1964). This effect is due to the more compact nature of the branched hydrophobe which presents a smaller surface area to the water, resulting in a smaller interfacial energy change on micellization.

The introduction of a polar group into the hydrophobe generally causes a significant increase in the CMC, the carbon atoms between the polar group and the hydrophilic head having about one-half the effect on the CMC as they would in the absence of the polar group (Rosen 1978). On this basis, $C_{18(e,11)}E_{17}$ would be expected to have a CMC similar to that of a compound with an alkyl chain length of 12, while the alkyl chain length corresponding to the $C_{18(e,6)}E_{18}$ compound would be about 14–15. Examination of the literature (Mukerjee & Mysels 1971) shows that, for compounds of general formula C_mE_{1-25m} , the CMC is related to m by

$$\log_{10} \text{CMC} = 1.58 - 0.44m \text{ for } 4 \leq m \leq 16 \text{ (} r = 0.996 \text{)} \quad (1)$$

The experimentally determined CMCs for $C_{18(e,11)}E_{17}$ and $C_{18(e,6)}E_{18}$ thus correspond to values for alkyl chain lengths of 14 and 15, respectively, in general agreement with predictions. The situation is more complex with the keto containing surfactants due to the intrusion of the oxyethylene chains into the micellar core (Elworthy & Patel 1984a, b).

Surface area. The excess surface concentration, Γ , was calculated from the slope of γ vs $\log_{10}C$ just below the CMC using the Gibbs equation

$$\Gamma = -(1/2.303RT) (d\gamma/d \log_{10}C) \quad (2)$$

Since the CMC is low, the excess surface concentration can be equated with the surface concentration and the area per molecule, A_{obs} , can be calculated from $A_{\text{obs}} = 1/(N\Gamma)$ where N is the Avogadro constant. Values of A_{obs} are listed in Table 1.

It is generally observed that, within a homologous series of non-ionic surfactants, the area per molecule varies systematically with the oxyethylene and alkyl chain lengths (Attwood & Florence 1983). The surfactants of this study have similar oxyethylene chain lengths and the differences in A_{obs} of Table 1 can be attributed mainly to the influence of the semi-polar groups of the alkyl chain. The experimental values of A_{obs} are supported by measurements of projected area, A_{calc} , of the hydrophobe using Catalin models. The assumption was made that the hydrophobes were anchored in the air/water interface by the polar group and the first oxyethylene oxygen atom, while the distal portion of the hydrophobe was removed from the aqueous environment.

Thermodynamic parameters. For a sufficiently high aggregation number, the standard free energy of micellization of a non-ionic species, ΔG_m^{\ominus} , may be approximated to

$$\Delta G_m^{\ominus} = RT \ln(\text{CMC}) \quad (3)$$

With the CMC in mol dm^{-3} , these quantities refer to the transfer of 1 mol of chains from their ideally dilute solution standard state to their micellar standard state. Values of ΔG_m^{\ominus} calculated from this equation are listed in Table 1.

The free energy change associated with the transfer of an oxyethylene group ΔG_E^{\ominus} in the micelle (ca +0.63 kJ mol^{-1} for $C_{16}E_{17}$) is less than that for a methylene group (ca -3.1 kJ mol^{-1} for $C_{16}E_{17}$) and furthermore decreases with increasing oxyethylene chain length (ΔG_E^{\ominus} for $C_{16}E_{63}$ is +0.08 kJ mol^{-1} , Barry & El Eini 1976). It is therefore not unreasonable as a first approximation to consider the changes in ΔG_m^{\ominus} within the C_mH_{1-25m} series solely in terms of the transfer of the methylene groups. From equations 1 and 3 it can be shown that the molar -CH₂- contribution is approximately -2.55 kJ mol^{-1} for $m=4$ to 16 which is in reasonable agreement with values for other surfactant series (Corkill & Goodman 1969). The ΔG_m^{\ominus} value for $C_{18}E_{22}$ is lower than the predicted value (-36.2 kJ mol^{-1}). This discrepancy is even more pronounced with the longer alkyl chain length compounds. The ΔG_m^{\ominus} values for $C_{22}E_{21}$ and $C_{32}E_{41}$ for example, calculated from the reported CMCs (Arnarson & Elworthy 1980, 1981) are -35.1 and -29.1 kJ mol^{-1} compared with predicted values of -46.2 and -71.3 kJ mol^{-1} , respectively. Other workers (Teo et al 1984) have noted similar

Table 1. Surface properties and thermodynamic parameters for micellization of $C_{18(e,11)}E_{17}$, $C_{18(e,6)}E_{18}$, $C_{18(e,6,b,3)}E_{19}$, $C_{18(k,12)}E_{18}$ and $C_{18}E_{22}$ in water at 298K.

Surfactant	CMC mol dm^{-3}	γ CMC mN m^{-1}	A_{obs} nm^2	A_{calc} nm^2	ΔG_m^{\ominus} kJ mol^{-1}
$C_{18(e,11)}E_{17}$	4.6×10^{-5}	37.0	0.91	0.91	-24.7
$C_{18(e,6)}E_{18}$	1.1×10^{-5}	34.0	0.71	0.76	-28.3
$C_{18(e,6,b,3)}E_{19}$	8.7×10^{-6}	35.0	0.85	0.84	-28.9
$C_{18(k,12)}E_{18}$	1.3×10^{-5}	38.5	0.97	1.01	-27.9
$C_{18}E_{22}$	1.3×10^{-6}	43.0	0.68	—	-33.6

^a For solution standard state of 1 mol dm^{-3} .

discrepancies for other homologous series of polyoxyethylene alkyl ether surfactants. The reduction in the free energy of micellization for these long alkyl chain compounds is a consequence of intrusion of the oxyethylene chains into the micellar core. ¹H NMR studies on such compounds have indicated both line broadening and loss of intensity of the alkyl protons suggesting a considerable reduction in chain mobility (Elworthy & Patel 1984a; Lawrence 1985). The entropy decrease associated with the loss of chain mobility is partly responsible for the observed reduction in free energy change.

The ΔG_m^\ominus values calculated for the semi-polar surfactants are all lower than that of the C₁₈E₂₂ compound reflecting the influence of the semi-polar group in reducing the free energy of transfer to the micellar phase.

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Differential scanning calorimetry characterization of process-induced variations in an ointment base

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Abstract—Preparation of an experimental emollient wax-gelled ointment base by two processes differing only in cooling rate produced material with markedly different physical properties. Differential scanning calorimetry showed that a major endotherm, possibly related to a phase change in a major triglyceride wax component, Synchronax HGLC, was different in the two products. Mean enthalpies for this major endotherm for the two products were 7.36 J g⁻¹ (s.d. = 0.49, n = 5) in slow cooled samples and 4.35 J g⁻¹ (s.d. = 0.21, n = 5) in fast cooled samples. The degree of order of the Synchronax HGLC in the ointment is suggested as being different in the two preparations and it is this that controls the physical properties of the ointment.

Ointment vehicles are greasy, usually anhydrous, semi-solid formulations used for topical application to provide for drug delivery or can be used unmedicated, for example, for their skin protecting properties. One simple approach to the formulation of an ointment base is to thicken or gel an oil such as mineral oil with a suitable agent. Like all semi-solid formulations, gelled oil vehicles might be susceptible to process-induced variation in finished product properties. In the case of a complex, emollient, wax-gelled oil ointment base developed for a novel topical corticosteroid (O'Laughlin et al 1989), the degree of agitation and also rate of cooling were found to produce marked differences in consistency in the finished product. Although it has been found possible to control the processing of this particular ointment to realize a reproducible product with desired physical properties, further investigation of the nature of the process-induced variation has been undertaken by application of differential scanning calorimetry (DSC) to discern the

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