

Solubilization in aqueous solutions of amphiphiles

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Solubilization of organic molecules in aqueous amphiphilic solutions containing surfactant micelles, mixed micelles, vesicles and block copolymer micelles has been actively investigated in recent years. From experimental measurements of the amount solubilized, thermodynamic parameters have been calculated. Theories of solubilization have been developed to predict *a priori* the aggregate shape, the number of surfactant and solubilize molecules in the aggregates, and also the location of solubilizes in the aggregates. The thermodynamic studies in conjunction with the theory provide greater molecular insight and improved quantitative understanding of the solubilization phenomenon.

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Abbreviations

cmc	critical micelle concentration
CTAB	cetyl trimethylammonium bromide
DDAB	dodecyl dimethyl ammonium bromide
MSR	molar solubilization ratio
PEO	poly (ethylene oxide)
PMA	poly (methacrylic acid)
PPO	poly (propylene oxide)
PS	poly (styrene)
PVP	poly (N-vinyl-pyrrolidone)

Introduction

Solubilization refers to the enhancement in the solubility of solvophobic molecules in a solvent medium. This enhancement is caused by the presence of amphiphiles. The amphiphiles self-assemble to form aggregates having microenvironments conducive to the solubilize molecules, and thereby promote the solubility of solvophobic substances. For example, in aqueous solutions containing aggregates such as surfactant micelles, vesicles or block copolymer micelles, the solubility of poorly water-soluble hydrocarbons can be increased by many orders of magnitude. Similarly, in non-polar solvents, the presence of reverse micellar structures promotes the enhanced solubility of polar substances such as water, amino acids and proteins. The phenomenon of solubilization serves as the basis of a wide variety of industrial, pharmaceutical and biological applications of surfactants.

This review concentrates on aqueous solutions of amphiphiles and describes the recent progress in the thermodynamic and theoretical studies of solubilization. Solubilization in aggregates of both low molecular weight

surfactants and higher molecular weight block copolymers are considered. Solubilization in non-polar solvents containing reverse micelles is not reviewed here. The latter is an interesting subject with potential applications in areas such as enzyme technology and nanoparticle synthesis, and deserves to be treated independently. In selecting the time period covered by this review, consideration is given to the fact that the most recent book on solubilization was published in 1995 [1••] and covers the literature only up to 1992 and also that Current Opinion is covering the subject area of solubilization for the first time. Papers published earlier which are relevant to our quantitative understanding of the solubilization phenomenon are also appropriately cited and discussed.

What do we want to know about solubilization?

To exploit the solubilization phenomenon, it is necessary to understand how the extent of solubilization is affected by the molecular properties of the solubilize and the surfactant, the concentration of the surfactant and other solution conditions such as temperature, ionic strength, presence of other additive molecules, and so on. Thermodynamic studies of solubilization are directed towards eliciting such information from experimental solubilization measurements. The studies use assumptions about the structure of the aggregates in order to simplify the estimation of thermodynamic variables. Theoretical studies of solubilization attempt to predict *a priori* the extent of solubilization and the microstructural characteristics of aggregates, given the surfactant and the solubilize.

Many thermodynamic parameters describing solubilization have appeared in the literature [1••]. The most common one is the aggregate-water partition equilibrium constant, K , defined as the ratio between the mole fraction X_m of the solubilize in the aggregate and the mole fraction X_w of solubilize in the aqueous phase. A free energy of solubilization is calculated from K as $\Delta G = -RT \ln K$. From the temperature dependence of K , the enthalpy and the entropy of solubilization are evaluated. In some studies the molar solubilization ratio (MSR), defined as the ratio between the number of solubilize molecules inside an aggregate and the number of surfactant molecules constituting the aggregate, is reported. Evidently, the mole fraction X_m of the solubilizes in the micelle and the molar solubilization ratio MSR are related by $X_m = MSR / (1 + MSR)$. Other variables such as the volume fraction of solubilize in the micelle core have also been used. In addition to these variables, one is also interested in knowing how the critical micelle concentration (cmc) is influenced by the presence of the solubilize. From the dependence of the cmc on the amount of solubilize

present in the solution the partition constant K has been calculated in the literature.

In contrast to the numerous studies in the literature dealing with the above thermodynamic parameters, limited information is available on the structural features of aggregates containing solubilizate. One would like to know how solubilizates modify the number of surfactant molecules in an aggregate, the shape of the aggregate, and the size and composition polydispersity of the aggregates. Furthermore, information about the locus of solubilizates in surfactant aggregates is essential for both the interpretation of experimental solubilization data and the construction of theories of solubilization.

Solubilization in surfactant aggregates

In this section, thermodynamics studies of solubilization in aggregates formed from low molecular weight surfactants are considered. The studies include the solubilization of gases in micelles, the influence of molecular properties of solubilizates on K , the dependence of K on solubilizate loading in the aggregates, the role of poly(ethylene oxide) polar head groups in non-ionic surfactant micelles, the effect of micellar shapes, the influence of surfactant composition in mixed micelles, solubilization in vesicles and the solubilization of hydrocarbon mixtures. Finally, the current state of the thermodynamic theory of solubilization is also discussed.

Solubilization of gases

The maximum extent of solubilization of gas molecules in a micelle is small and rarely exceeds a mole fraction of 0.1. The gas solubility in spherical micelles has been correlated to the molecular size of the solubilizate and surfactant [2*] using the concept of Laplace pressure inside the micelle, proposed many years ago by Mukerjee. The Laplace pressure model assumes that the decreased solubility of gases inside micelles, when compared to that in bulk non-polar solvents (representing the hydrophobic part of the surfactants), is caused by the existence of a Laplace pressure differential across the micelle/water interface. Experimental data obtained for many gases in a number of ionic surfactants are correlated by the relation

$$\ln X_m = \ln X_b - \frac{2\sigma\bar{v}}{\alpha n_c RT} \quad (1)$$

where X_m is the mole fraction of the solubilizate inside the micelle and X_b is that in a bulk solvent equivalent to the hydrophobic tail of the surfactant. σ is the micelle-water interfacial tension, \bar{v} is the partial molar volume of the solubilizate inside the micelle, n_c is the carbon number (or number of segments) of the surfactant tail with α being the segment length, T is the absolute temperature and R is the gas constant. Taking α equal to 0.125 nm and σ equal to 30 mN/m for hydrocarbon micelles and 16 mN/m for fluorocarbon micelles, good correlation to the

gas solubility data has been obtained [2*]. σ is independent of the type of the surfactant for various anionic and cationic surfactants. For non-ionic surfactants, a good correlation of the micellar gas solubilities is obtained by taking $\sigma=0$, implying that the solubilization behavior in micelles is identical to that in a solvent resembling the hydrophobic part of the surfactant. This suggests that the poly(ethylene oxide) polar head group region in non-ionic micelles does not serve as the location of solubilization for gas molecules.

Influence of solubilizate molecular structure on K

The solubilization of hydrophobic substances existing as liquids and solids has been investigated in many surfactant systems. The dependence of K (in the limit of $X_m=0$) on the molecular structure of the solubilizate has been studied for polycyclic aromatic molecules in 1-dodecane sulfonic acid micelles [3*], dodecyl ammonium trifluoro acetate micelles [4*] *n*-alkyl benzenes in 1-dodecane sulfonic acid micelles [5]. In 1-dodecane sulfonic acid micelles, the increase in K parallels the increase in the hydrophobicity of the solubilizate indicating that solubilization is controlled mainly by hydrophobic interactions. For naphthalene, anthracene and pyrene, a negative entropy change on solubilization is found implying that solubilization is enthalpy driven. For benzene, the enthalpy change is of a smaller magnitude and the entropy change is positive suggesting that benzene sits in the outer interfacial region of the micelles.

The polarity of the microenvironment of the solubilizate inferred from the thermodynamic measurements has been compared to the micropolarity estimates obtained from spectroscopic measurements [3*,4*]. The spectroscopic approach utilizes the fact that there are solvent-induced bands in the absorption spectra of aromatic molecules which are absent in the vapor phase. The absorbance of these bands has a linear correlation with the dielectric constant of the solvent. Using this correlation and the measured absorbance of the spectral band in the micellar environment, the dielectric constant of the microenvironment has been estimated. These spectroscopic estimates suggest a more polar microenvironment in the micelles for all the solubilizates than that indicated by the thermodynamic measurements.

In dodecyl ammonium trifluoro acetate micelles containing the fluorinated counterion, the solubilization of the aromatic molecules is found to be enthalpy driven. Whereas the benzene molecules are considered to sit at the micelle/water interface, the other three polycyclic aromatic molecules of larger hydrophobicity are considered to be in the region between the hydrophobic micellar interior and the outer layer of fluorocarbon counterions. For the solubilization of *n*-alkyl benzenes, both the enthalpic (ΔH) and entropic ($-T\Delta S$) contributions to the free energy of solubilization are negative implying that both factors play a role favoring the solubilization. As the alkyl chain length is increased, the spectroscopic

measurements suggest that the solubilize molecule is located more in the core region of the micelle whereas for benzene and toluene, the spectra suggest that the molecules sit near the micelle/water interface.

The free energies defined by $\Delta G = -RT \ln X_m$ have been correlated to the molecular refractions of the solubilize. The correlation is based on experimental data for benzene, naphthalene, anthracene and six halogen derivatives of benzene solubilized in sodium dodecyl sulfate and dodecyl trimethyl ammonium bromide micelles [6]. The molecular refraction can be taken as a measure of the electronic polarizability of the solubilize molecules and hence of the dispersion type interactions between the solubilize molecules and the micelles. The free energy of solubilization of these molecules in micelles is found to be close to their free energy of transfer from water to a bulk alkane solvent. This implies that these solubilize molecules are predominantly localized in the micellar nucleus rather than in the surface layer. The free energies ($-RT \ln X_m$) of alkanes, aromatic hydrocarbons, halogenated hydrocarbons, aliphatic alcohols, ketones, nitriles, and esters solubilized in non-ionic Triton X-100 micelles have also been correlated to the molar refraction of the solubilize molecules [7]. It has been found that the correlation is not universal, but each family of solubilizes follows the same type of correlating equation.

The partition coefficient K has been measured for benzene, toluene and chlorobenzene in a number of anionic, cationic and non-ionic surfactants by using the head space gas chromatography technique [8]. Increased solubilization of benzene with increasing chain length of the surfactant is found for sodium alkyl sulfates. Also, the solubilization is found to decrease the Krafft temperature as revealed by the absence of solubilization of benzene in sodium tetradecyl sulfate at 25°C at low benzene concentrations, and the large solubilization occurring at higher benzene concentrations. At low benzene concentrations, the surfactant exists as a precipitate but goes into solution forming micelles as the amount of benzene is increased. The solubilization in cationic surfactants is found to be larger than that in anionic surfactants and the difference is attributed to possible interactions between the aromatic electrons of the solubilize and the positively charged surfactant head groups. This interpretation also implies that aromatic molecules are initially solubilized at the micelle/water interface. For sodium dodecyl sulfate, an increase in the ionic strength of the solution increases K , whereas K is unaffected by changes in the surfactant concentration. A comparison of the three solubilizes leads to the conclusion that the amount solubilized decreases with increasing molecular size of the solubilize.

These experimental observations are consistent with the semitheoretical relation presented previously for the molar

solubilization ratio, MSR, of a number of aromatic and aliphatic hydrocarbons at saturation conditions [9]:

$$\text{MSR} = a \left[\frac{\sigma_{ow} v_o^{2/3}}{kT} \right]^{-b} \quad (2)$$

Here, a and b are positive constants that are dependent on the surfactant molecule, σ_{ow} is the solubilize-water interfacial tension reflecting the polarity of the solubilize, v_o is the molecular volume of the solubilize, k is the Boltzmann constant and T is the absolute temperature. The preferential location of polar solubilizes near the micelle/water interface is implied in the correlation. This preferential location lowers the micelle-water interfacial tension because σ_{ow} is smaller than the surfactant tail-water interfacial tension. According to this correlation, the MSR increases with the increasing polarity of solubilize and the decreasing molecular size of the solubilize.

The partition coefficient K has also been estimated by other means that do not directly measure the mole fraction X_m of the solubilize in micelles. The approach is based on measurements of the cmc as a function of the solubilize concentration in the solution. Thermodynamic relations used to estimate K from the cmc data are summarized in [10].

Dependence of K on solubilize loading

Experimental measurements of K show that it is not a constant but depends on the amount of solubilize in the micelles [8, 11, 12]. An empirical correlation

$$K = K_0(1 - BX_m)^2 \quad (3)$$

has been found valid for many systems [11, 12] where K_0 is the partition coefficient in the limit of zero solubilize concentration. The parameter B depends upon both the surfactant and the solubilize.

Solubilization site on non-ionic micelles

The hypothesis that solubilize molecules are present not only in the hydrophobic core of non-ionic micelles but also in the poly(ethylene oxide) corona region, proposed many years ago by Mukerjee, has been tested in a study [13] involving 17 non-ionic surfactants with six drug and insecticide molecules as solubilizes. Three of these solubilizes including furathiocarb are highly soluble in isooctane, 4-methylanisole and tridecane (non-polar solvents resembling the tail groups of surfactants examined) and also in polyethylene glycol, PEG (resembling the head group of surfactants). The other three solubilizes including carbofuran are much more soluble in PEG than in the non-polar solvents mentioned above.

Given the appreciable solubility of all six solubilizates in PEG, they are ideal candidates to test whether solubilization occurs in the micellar corona where ethylene oxide chains are present. The simple linear relation

$$[\text{MSR}] = N_{\text{R}}[\text{MSR}]_{\text{R}} + N_{\text{EO}}[\text{MSR}]_{\text{EO}} \quad (4)$$

assumes that the solubilizate molecules are distributed between the two regions of non-ionic micelles in proportion to the size of the hydrophobic and the hydrophilic portions of the surfactant molecule. Here, $[\text{MSR}]_{\text{R}}$ denotes the mole ratio of solubilizate to the hydrophobic alkyl segments of the surfactant tail whereas $[\text{MSR}]_{\text{EO}}$ is the mole ratio of solubilizate to the ethylene oxide (EO) units in the hydrophilic head group. N_{R} and N_{EO} are the numbers of alkyl segments in the tail and the numbers of EO groups in the head group, respectively. The plot of $[\text{MSR}]/N_{\text{EO}}$ against $1/N_{\text{EO}}$ should be linear with the intercept being $[\text{MSR}]_{\text{EO}}$. The ratio $N_{\text{EO}}[\text{MSR}]_{\text{EO}}/[\text{MSR}]$ provides the fraction Y of the total solubilizate that is present in the hydrophilic corona region of the micelle. The experimental solubilization data for all six solubilizates in the 17 surfactants (having EO head groups and alkyl or alkyl phenyl hydrophobic tails) fitted to Equation 4 do not lead to any unambiguous conclusions. In a number of cases, the linear relation is not obeyed by the experimental data implying either the absence of solubilization in the corona region or a more complex dependence of solubilization on the EO chain length. In some systems, the linear relation is found valid, but the fraction Y of the total solubilizate in the micellar corona region is estimated to be close to zero, implying absence of solubilization in the corona region. Only in a few cases, the linear relation is found valid along with the fraction Y solubilized in the corona region being significant, as well. In such cases, the partitioning of the solubilizate between both the core and corona regions visualized by Equation 4 is valid.

These conclusions regarding the location of solubilizates obtained from measurements of the amount solubilized were contradictory to the conclusions derived from solubility behavior of solubilizates in solvents of different polarities and those from UV spectroscopic measurements of micropolarity. For example, the solubilizates which obeyed the linear Equation 4, but with $Y=0$, were those that displayed large solubility in the PEG solvent and low solubilities in the hydrophobic solvents. Thus the solubility behavior in solvents of different polarities predicts that the corona region should be an important location for these solubilizates whereas the solubilization data plotted according to Equation 4, rules out any role for the corona region entirely. It is concluded that the distribution of the solubilizate between the core and the corona regions is influenced by several microstructural features of micelles such as their size, shape, and so on, and not simply related to the length of the ethylene oxide head group as implied by Equation 4. Although these

results do not rule out the presence of solubilizates in the corona region, they do not confirm it.

Similar conclusions follow from head space gas chromatography measurements [8**] of the solubilization of benzene in non-ionic surfactants. The amount solubilized increases with the hydrophobic tail length of the surfactant but decreases with the length of the polar EO chain. The influence of the polar group is small at low benzene concentrations but becomes significant at higher benzene concentrations close to saturation. If benzene molecules are solubilized in both the hydrophobic core and the hydrophilic head group region, one may expect the amount solubilized to increase with both an increase in the EO content and an increase in the micellar core volume. As the EO chain length increases, however, the aggregation number of the micelle will decrease resulting in decreasing volume of the hydrophobic core. Therefore, the net effect could be an increase or a decrease in the amount of solubilization with an increase in the EO chain length.

Influence of micelle structure

The solubilization of substituted and non-substituted aromatic molecules in the rodlike micelles of cetyl trimethyl ammonium bromide (CTAB) has been investigated by spectroscopic and viscometric techniques [14]. The solubilizate molecules are found to distribute themselves between the non-polar micelle interior and the more polar interfacial region depending upon their polarities which increase in the order *t*-butyl benzene < isopropyl benzene < ethyl benzene < toluene < benzene ~ naphthalene ~ anthracene. In this same order, the solubilization of the molecules promotes the axial growth of the rodlike micelles. Therefore, the location of solubilizates at the micelle/water interface rather than in the micellar interior, favors the linear growth of aggregates.

Solubilization in mixed micelles

The solubilization behavior of a number of molecules in various types of binary surfactant mixtures has been investigated [15**,16,17,18*]. The surfactants forming the mixtures differ from one another both in their polar head groups and their hydrophobic tails. From thermodynamic arguments, it has been suggested [15**,18*] that the partition coefficient in the mixed micelle K_{mix} , can be expressed as a function of the micelle composition in the form

$$\ln K_{\text{mix}} = X_{\text{A}}^{\text{m}} \ln K_{\text{A}} + (1 - X_{\text{A}}^{\text{m}}) \ln K_{\text{B}} + \beta_0 X_{\text{A}}^{\text{m}} (1 - X_{\text{A}}^{\text{m}}) \quad (5)$$

Here X_{A}^{m} is the mole fraction of surfactant A in the mixed micelle defined on a solubilizate-free basis by considering only the two surfactants A and B. K_{A} and

K_B are the partition coefficients of the solubilize in the pure (A or B) surfactant micelles, and β_0 is a parameter representing the non-ideality of interactions between the surfactants [15••,18•]. With pentanol, barbituric acid and butobarbital as solubilizates and a number of surfactant systems displaying a variety of non-ideal behavior, β_0 is given by [15••]

$$\beta_0 = 0.194 + 0.343\beta \quad (6)$$

where β is the parameter appearing in the regular solution model for the cmc of surfactant mixtures in the absence of any solubilize. The surfactant systems examined include ionic–non-ionic mixtures with small negative values of β , anion–cation mixtures with very large negative values, and hydrocarbon–fluorocarbon mixtures with positive values. It is concluded that if the solubilize has some polarity and is of medium size (thus ensuring that it is located at the micelle/water interface) then the empirical correlation (Equation 6) is valid.

In most cases, the solubilization decreases upon surfactant mixing (β_0 is negative). The solubilization of hydrophobic and hydrophilic perfume molecules in anionic–non-ionic mixed micelles (β is negative) shows [17] that K_{mix} is smaller than K for the pure component micelles (β_0 is negative). Synergistic solubilization (β_0 is positive) is seen with non-polar solubilizates if the surfactants strongly interact and so give rise to micellar structural changes. Such is the case for anionic–cationic mixtures for which the β values are large and negative but β_0 values are positive. For benzene in anionic–cationic mixed micelles, K_{mix} is larger than K in the pure surfactants as long as the surfactant mixture does not precipitate [8••]. When the aggregate structural changes are small, the solubilization behavior is found to follow ideal behavior (β_0 close to zero). The solubilization of pentanol in an anionic–non-ionic mixed micelle system is found [16] to follow ideal behavior ($\beta_0 = 0$).

Solubilization in vesicles

Only a few studies of solubilization of hydrophobic substances in vesicles are to be found in the literature [19•]. Experiments on the solubilization of octane, octanol and octanoic acid in vesicles formed by dodecyl dimethyl ammonium bromide (DDAB) show that the octane molecules are solubilized in the interior of the vesicles whereas the other two polar solubilizates are located at the vesicle surface. The encapsulation efficiency of the vesicle decreases with increasing solubilization of octane indicating that the vesicle size diminishes on solubilization. Also, the increasing solubilization of the polar molecules causes the vesicle structure itself to disappear giving rise instead to closed micellar structures.

Solubilization of hydrocarbon mixtures

In the case of binary mixtures of hydrocarbons, it has been shown that molecules are selectively solubilized

depending upon their molecular volumes and polarities [9]. When the selectivity is not very large, the ratio between the molar solubilization ratios of the two components should be the same as the ratio of their bulk phase mole fractions. A simple theoretical model to predict the MSR values in the case of solubilize mixtures (MSR_{Am} of A, MSR_{Bm} of B) from the MSR values of pure solubilizates (MSR_A , MSR_B) has been developed [20•,21]. For bulk phase mole fractions X_A and X_B of solubilizates A and B, respectively, in the binary solubilize mixture, it has been shown [21] that

$$MSR_{Am} = X_A[X_A MSR_A + X_B MSR_B - X_A X_B MSR_{AP}] \quad (7)$$

$$MSR_{Bm} = X_B[X_A MSR_A + X_B MSR_B - X_A X_B MSR_{AP}]$$

where P can take values in the range from zero to $(1 + MSR_B/MSR_A)$. P accounts for the size differences between the solubilizates and the consequent packing entropy changes inside the micelle. The relation has been shown to be reasonable for the solubilization of hexane–cyclohexane and dodecane–hexadecane mixtures which show no preferential solubilization behavior as specified in the above model. Even binary mixtures of hexane and benzene and of cyclohexane and benzene which display selective solubilization behavior are found to obey Equation 7.

Theory of solubilization

A molecular thermodynamic theory of solubilization has been developed to predict *a priori* the microstructural features of aggregates containing solubilizates from knowledge of the surfactant and the solubilize [22,23]. The concentration of aggregates containing g surfactant and j solubilize molecules, X_{gj} , is calculated using the equilibrium relation

$$X_{gj} = X_1^g f^j / g \exp - \left[\frac{g \Delta \mu_{gj}^0}{kT} \right] \quad (8)$$

where X_1 is the concentration of the singly dispersed surfactant, f is the fractional saturation of the solubilize in water and $\Delta \mu_{gj}^0$ is the change in the standard state free energy when g surfactant molecules transfer from their singly dispersed state in water to a micelle and j solubilize molecules transfer from a pure solubilize phase into an isolated micelle in the aqueous solution. When the solution is saturated with the solubilize, $f = 1$. From the size and composition distribution Equation 8, one can calculate the partition coefficient K as a function of the solubilize concentration, the average MSR, the average aggregation number, and the size and composition polydispersity of the aggregates.

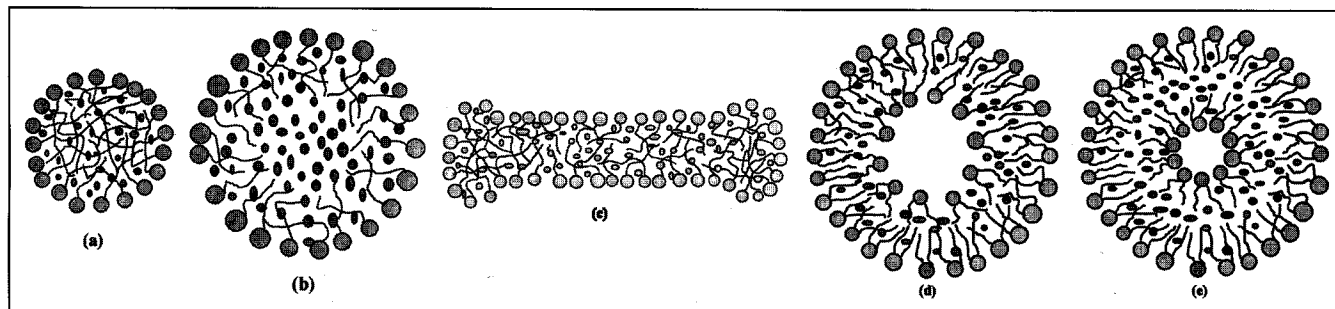
In developing an explicit expression for the standard state free energy difference that is needed for the predictive calculations, various structural descriptions of aggregates shown in Figure 1 are considered. In Figure 1a,c,d, the aggregates hold all the solubilize molecules in the surfactant tail region such that one dimension of the aggregate is limited to the extended length of the surfactant tail. That is, the radius of the spherical micelle (Fig.1a), the radius of the rodlike micelle (Fig.1c), and the half-thickness of the spherical vesicle (Fig. 1d) are all limited to the extended length of the surfactant tail. In contrast, in Figure 1b,e, the solubilize molecules are considered to be present not only in the tail region but also as a pure solubilize phase and the aggregate dimensions are not restricted to the length of the surfactant tail. In spherical micelles (Fig. 1b), the pure solubilize phase is present in the inner core whereas in the vesicles (Fig. 1e), the pure solubilize phase is present in the region between the inner and the outer monolayers.

For each of the aggregate structures in Figure 1, expressions for $\Delta\mu_{gj}^0$ have been developed by considering all the physicochemical changes accompanying solubilization ([23]; R Nagarajan, unpublished data). The various contributions to $\Delta\mu_{gj}^0$ include the free energy of transfer of the surfactant tail from water into the aggregate ($\Delta\mu_{gj}^0$)_{tr}, the free energy of chain packing or deformation inside the aggregate ($\Delta\mu_{gj}^0$)_{def}, the free energy of formation of the aggregate/water interface ($\Delta\mu_{gj}^0$)_{int}, the free energy of interaction between surfactant head groups located at the aggregate/water interface due to steric repulsions ($\Delta\mu_{gj}^0$)_{steric}, dipolar interactions in the case of zwitterionic surfactants ($\Delta\mu_{gj}^0$)_{dipole}, ionic repulsions in the case of ionic surfactants ($\Delta\mu_{gj}^0$)_{ionic} and the entropy and the enthalpy of mixing of the surfactant and the solubilize molecules in the surfactant tail region of the aggregates ($\Delta\mu_{gj}^0$)_{mix}. The polarity of the solubilize was taken into account in the calculation of the aggregate-water

interfacial free energy with the implication that polar solubilizes will be preferentially located near the interface. In the case of surfactants with poly(ethylene oxide) head groups, these interfacial energies were estimated by taking into account the interactions of the EO groups with the solubilize at the interface. The possible presence of the solubilizes in the head group corona region, however, was not considered.

The theory predicted the formation of aggregate structures shown in Figure 1b,e in preference to the structures shown in Figure 1a,d as the amount of solubilization is increased. The lowering of the cmc and the increase in the aggregation number on solubilization were also predicted. The standard deviation of the molar solubilization ratio MSR from the average MSR was found to be very small when spherical aggregates formed. This implies that all the micelles present in solution have approximately the same compositions. The theory was also used to predict the fraction of the total solubilizes present in the surfactant tail region of the micelles and the fraction that is present in the interior core region of the aggregates. The calculations showed that both aromatic and aliphatic molecules are present in these two regions of micelles with aromatics displaying a greater preference for the tail region. For example, in sodium dodecyl sulfate, the fraction of the solubilize present in the surfactant tail region is larger for aromatics (0.56 and 0.61 for benzene and toluene) than for aliphatics (0.17 and 0.3 for decane and hexane). The theory predicted the retention of the rodlike shape of the micelle and the growth of cylindrical micelles for aromatic solubilizes and a transition from cylindrical micelle to spherical micelle for saturated hydrocarbon solubilizes. In the case of non-ionic surfactants with poly(ethylene oxide) head groups, the theory underpredicted the molar solubilization ratio for aromatic hydrocarbons. Although the discrepancy may be due to yet unresolved problems in the modeling of

Figure 1



Schematic representation of solubilization of hydrophobic substances in surfactant aggregates. (a) Spherical micelles in which the radius of the micelle cannot exceed the extended length of the surfactant molecule. (b) Spherical micelles in which a core of pure solubilize phase is present. (c) Cylindrical micelle whose radius is limited to the extended length of the surfactant molecule. (d) Spherical bilayer vesicle in which the solubilize is present only in the surfactant tail region. (e) Spherical bilayer vesicle in which the solubilize is present in the surfactant tail region and also between the two monolayers.

such non-ionic micelles as a function of the ethylene oxide chain length ([23], R Nagarajan, Abstract 190, 68th Annual Colloid and Surface Science Symposium, Stanford, June 1994), another possible reason is the presence of aromatic molecules in the corona region of the micelles which is not considered in the model calculations. The theory has also been shown to predict the solubilization of binary mixtures of hydrocarbons in micelles [23].

The solubilization of hydrocarbons in mixed micelles has also been modeled (R Nagarajan, unpublished data) by extending the theory for single component micelles. For anionic-cationic surfactant mixtures, dramatic growth in the aggregate size and in the molar solubilization ratio are predicted. For ionic-non-ionic surfactant mixtures, the solubilization in mixed micelles is predicted to be smaller than that anticipated by simple composition averaging of the pure surfactant values (i.e. β_0 is negative in Equation 6). The above predictions in anionic-cationic and in ionic-non-ionic surfactant mixtures are in agreement with known experimental measurements [15••]. In the case of hydrocarbon-fluorocarbon surfactant mixtures, it is known that demixing of micelles leading to two coexisting micelle populations can occur over a domain of overall surfactant composition. Theoretical calculations of solubilization behavior in such surfactant mixtures show that the domain of existence of demixed micelles is enlarged by the presence of the solubilizates. This prediction remains to be tested experimentally.

Theory of phase equilibria

The theory outlined above neglects interaggregate interactions and hence is valid only for dilute surfactant solutions. A theory of solubilization applicable to more concentrated systems in which other aggregate phases are present has also been developed [24••,25,26]. In this approach, besides the various free energy contributions identified for dilute micellar solutions, contributions accounting for hydration interactions and van der Waals interactions between the aggregates are also considered. In the limit of dilute solutions, the free energy expressions developed in this work [24••] are qualitatively similar to those in [23], but differ in almost all of the details. Explicit phase equilibria calculations are presented [24••,26] showing the domains of existence of the dilute micellar phase, the lamellar phase and the reverse micellar phase. These illustrative results suggest that the main features of a complex phase diagram for a ternary surfactant-solubilize-water system are satisfactorily captured by this model.

Solubilization in block copolymer aggregates

Block copolymers are the analogs of conventional low molecular weight surfactants. In block copolymer micelles, the hydrophobic blocks constitute the interior of the aggregate and the hydrophilic blocks, along with the

solvent water, form the corona region of the aggregate. The solubilization of many aliphatic and aromatic hydrocarbons in aqueous solutions of two block copolymers was reported a number of years ago [27]. Recent studies on solubilization and theoretical modeling of solubilization in block copolymer micelles are discussed here.

Influence of solubilize molecular structure

Studies of the solubilization of aromatic and aliphatic hydrocarbons in block copolymer micelles show that the interactions between the solubilize and the hydrophobic block significantly influence the magnitude of solubilization [27]. This is in contrast to the behavior of low molecular weight surfactants where interfacial energy effects significantly control the nature of solubilization, as represented by Equation 2. Experimental solubilization data obtained with poly(ethylene oxide)-poly(propylene oxide) (PEO-PPO) block copolymers and poly(N-vinylpyrrolidone)-poly(styrene) (PVP-PS) block copolymers are empirically correlated [27] in the form

$$\text{MSR} = a\chi_{AJ}^{-b} = a\left[\frac{(\delta_A - \delta_J)^2 v_J}{kT}\right]^{-b} \quad (9)$$

Here, χ_{AJ} is the solubilize J-hydrophobic block A interaction parameter, δ_A and δ_J are the Hildebrand-Scatchard solubility parameters of the hydrophobic block A and the solubilize J, and v_J is the molecular volume of the solubilize. The positive constants a and b are dependent on the block copolymer molecule. Such a correlation has been shown to describe well the experimental solubilization data in PS-poly(methacrylic acid) (PS-PMA) block copolymer micelles obtained for 18 different solubilizates including aliphatic, cyclic and aromatic hydrocarbons, chlorinated hydrocarbons, and esters [28•]. In this work, the PS-solubilize interaction parameters have not been calculated from the solubility parameters for the molecules involved, as suggested in Equation 9, but have been obtained experimentally using the inverse gas chromatography technique.

The partition equilibrium constants for toluene, naphthalene and phenanthrene in PVP-PS block copolymer solutions reported recently [29], confirm the first published report [27] of the large solubilization capacity of PVP-PS block copolymer micelles for aromatics.

The partition coefficient of naphthalene solubilized in various PEO-PPO-PEO triblock copolymer micelles has been measured [30•]. The results show that K is independent of the block copolymer concentration. Its variation with the molecular weight and the composition of the block copolymer suggest that it is influenced by changes in the aggregate size.

Solubilization isotherms of toluene, benzene, chlorobenzene, and p-xylene have been obtained in a number of PEO-PPO-PEO triblock copolymer micelles [31•]. The partition coefficient K is found to be strongly dependent on the amount of solubilize already present in the micelles. At very low solubilize concentrations, an increase in K with increasing amount of solubilize is seen for low molecular weight block copolymers suggesting that the presence of the solubilize promotes the aggregate formation. At higher solubilize concentrations, K decreases with increasing amount of solubilizes, similar to the behavior shown by small surfactant molecules (Eq 3). Furthermore, the partition coefficients are found to depend on the block copolymer concentration for the lower molecular weight block copolymers and are concentration-independent for higher molecular weight block copolymers. This is again consistent with the concentration dependence of the aggregation properties for the low molecular weight block copolymers forming small aggregates in contrast to the concentration invariance of the aggregation behavior in higher molecular weight block copolymers.

Studies on the solubilization of a drug molecule known as estriol in a PEO-PPO-PEO triblock copolymer showed [32] that the solubilization is driven by favorable entropy changes, as may be expected for a very hydrophobic solubilize. The estimated partition coefficient shows an increase in value beyond a transition concentration of the block copolymer; the transition has been attributed to a possible growth in the aggregate. The increase in K with increasing temperature can be attributed to a possible decrease in χ_{AJ} and also to an increase in the aggregate size. Similar increases in the partition coefficient have been reported for hydrophobic fluorescent probe molecules in PEO-PPO-PEO triblock copolymer micelles [33].

Theory of solubilization in block copolymer micelles

A thermodynamic theory of solubilization in block copolymer micelles has been formulated [34,35••] in a manner analogous to that for low molecular weight surfactants. The concentration X_{gj} of the aggregates containing g block copolymer and j solubilize molecules is calculated from the equilibrium relation given previously (Eq 8). It is necessary to develop an expression for $\Delta\mu_{gj}^0$ which is the difference in the standard state free energy when g block copolymer molecules and j solubilize molecules are transferred into an isolated micelle in the aqueous solution from their singly dispersed state and from a pure solubilize phase, respectively. In developing an expression for $\Delta\mu_{gj}^0$, two structural descriptions of micelles, shown in Figure 2, are considered. In Figure 2a, all the solubilize molecules interact with the hydrophobic blocks of the micelle. In case Figure 2b, the solubilize molecules are considered to be present not only in the region of the hydrophobic blocks but also in a core region as a pure solubilize phase.

For both aggregate structures, expressions for $\Delta\mu_{gj}^0$ have been developed in terms of a number of contributions [34,35••]. These include the mixing or dilution free energy when the hydrophobic block A of a singly dispersed molecule is transferred into the aggregate core where it interacts with the solubilize ($\Delta\mu_{gj}^0$)_{A,dil}, the free energy of chain deformation (or packing) of the hydrophobic block inside the aggregate ($\Delta\mu_{gj}^0$)_{A,def}, the free energy of formation of the aggregate/water interface ($\Delta\mu_{gj}^0$)_{int}, the dilution or mixing free energy of the hydrophilic block B when transferred from its singly dispersed state in water into the aggregate corona region ($\Delta\mu_{gj}^0$)_{B,dil}, the free energy of chain deformation (or packing) of the hydrophilic block inside the corona region ($\Delta\mu_{gj}^0$)_{B,def}, and the free energy of localization of the segment connecting the hydrophobic and hydrophilic blocks at the aggregate/water interface ($\Delta\mu_{gj}^0$)_{loc}. For triblock copolymers, an additional free energy contribution is considered to account for the backfolding or loop formation by the block copolymer in the aggregate. The polarity of the solubilize is taken into account in the calculation of the aggregate/water interfacial free energy implying that the polar solubilizes will be located preferentially near the interface. The possible presence of the solubilizes in the solvent-rich corona region is, however, not considered.

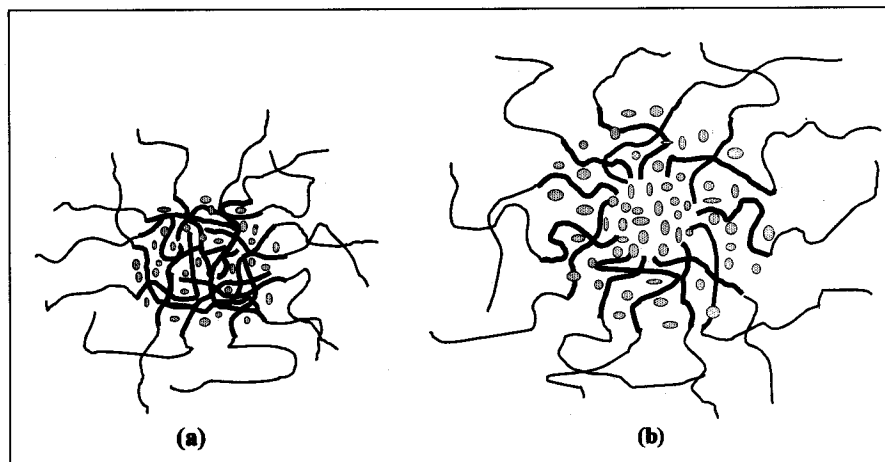
The theory predicts that aggregates of the type shown in Figure 2a are generally formed rather than those shown in Figure 2b, which have a separate inner core of pure solubilize phase. The standard deviation of the aggregation numbers of the micelle from the average aggregation number and the standard deviation of the molar solubilization ratios from the average MSR are very small indicating narrow size and composition distributions of the micelles. The micellar aggregation number dramatically changes with the amount of solubilize present and is considerably different from that of micelles in the absence of solubilizes. For a given block copolymer chemical structure (say, PEO-PPO-PEO triblock copolymers), the amount solubilized (MSR or partition coefficient) will change with the molecular weight and the composition of the block copolymer because these variations induce changes in the size of the aggregates.

The theory has been extended to aggregates having cylindrical and lamellar shapes [35••] and predicts that by increasing the amount solubilized, one can induce a transition from spherical aggregates to cylindrical and lamellar aggregates. Depending upon the block copolymer, it is also possible to generate coexisting populations of aggregates of differing shapes. These theoretical predictions pertaining to non-spherical aggregate shapes have not yet been observed experimentally.

An alternative theoretical approach has been developed that is based on a lattice model and employs self-consistent mean-field calculations [30•,36,37,38••]. In this approach, it is possible to predict rather than assume how the

Figure 2

Schematic representation of a spherical block copolymer micelle containing a solubilizate. The darker lines denote the hydrophobic block (e.g. polypropylene oxide, PPO) and the lighter lines, the hydrophilic block (e.g. polyethylene oxide, PEO). In structure (a) all the solubilizate molecules are interacting with the hydrophobic block. In structure (b), some of the solubilizate molecules are present in a separate domain and the remaining number interact with the hydrophobic block.



solubilizate, the hydrophobic and hydrophilic blocks of the copolymer, and the solvent water are distributed within the aggregate structure. Detailed computations based on the model have been presented for the solubilization of naphthalene in PEO-PPO-PEO triblock copolymer micelles. The calculations suggest that there is a considerable amount of water inside the micellar core and that the solubilization of naphthalene decreases this water content somewhat. Also, the hydrophilic ethylene oxide block is present in significant amounts in the core region. The model calculations show that naphthalene is entirely confined to the core region and is not present in the corona region with the PEO blocks. The model also predicts the increase in partition coefficient with increasing PPO content and traces this effect to the increasing size of the aggregate.

A theory of solubilization in micelles allowing for possible radial variations in the composition of solubilizates has also been developed using the analogy with star polymers and employing the scaling analysis [39]. To test the theory, it is necessary to measure the solubilization behavior in block copolymers having a wide range of molecular weights for both the core block and the corona block. Such experimental results are presently not available. Measurements in such block copolymer systems will be of interest also from the point of view of generating non-spherical aggregate structures.

Conclusions

In the past few years, many studies of solubilization in aqueous media containing surfactant or block copolymer aggregates have appeared in the literature. Aggregate-water partition coefficients have been estimated from the measured amounts of solubilizate in the aggregates or based on the dependence of the cmc on the amount of solubilizate in solution. A variety of aggregates, including spherical and cylindrical mi-

celles, mixed micelles, vesicles formed from conventional low molecular weight surfactants and spherical micelles formed from higher molecular weight block copolymers have been studied. The partition coefficients have been related to the molecular properties of surfactants and solubilizates based either on thermodynamic arguments or by following an empirical approach. Thermodynamic arguments have also been used to relate the partition coefficient in mixed micelles to that in pure component micelles, and the partition coefficient in the case of solubilizate mixtures to that of pure solubilizates. Often, simplifying assumptions are invoked in the course of these thermodynamic analyses, the most critical assumption being the absence of any change in the micelle aggregation number or shape. There have been important theoretical developments which parallel experimental studies. The theory is capable of predicting all the microstructural features of solubilization in addition to the partition coefficient. Theoretical calculations require molecular constants related to both the surfactant and the solubilizate. The theory predicts significant variations in the aggregation numbers and also dramatic variations in aggregate shapes on solubilization, under certain circumstances.

A closer link should be established between the thermodynamic studies, based on experiments, and the theoretical studies so that the experimental data can be interpreted without invoking questionable assumptions. As experimentally determined thermodynamic parameters have become available for a large variety of surfactant and solubilizate systems they provide a good basis for testing the theories of solubilization, because they can be used to evaluate, as well as improve, the predictive ability of the theories and their quantitative accuracy. A key area requiring extended experimental investigations is the determination of aggregate structural properties in the presence of solubilizates; such information is essential to test available theoretical predictions.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Christian SD, Scamehorn JF (Eds): *Solubilization in Surfactant Aggregates*. New York: Marcel Dekker; 1995.

This is the most recent review of the subject area of solubilization. With few exceptions, the references cited in all the articles cover the literature published before 1992. The book includes a large collection of experimental data.

2. King AD: **Solubilization of gases**. In *Solubilization in Surfactant Aggregates*. Edited by Christian SD, Scamehorn JF. New York: Marcel Dekker; 1995:35–58.

The Laplace pressure model is shown to provide a good description of gas solubility data in a number of ionic surfactants. For non-ionic surfactants, the lipophilic region is suggested as the site for solubilization of gases, with complete exclusion of gases from the ethylene oxide head group region of the micelles. Provides a large collection of experimental data. This review paper includes references to all important original articles.

3. Moroi Y, Mitsunobu K, Morisue T, Kadobayashi Y, Sakai M: **Solubilization of benzene, naphthalene, anthracene, and pyrene in 1-dodecanesulfonic acid micelle**. *J Phys Chem* 1995, **99**:2372–2376.

The aggregation number of solubilize-free micelles measured by static light scattering has been used in the determination of the partition coefficient, K . Any uncertainty in the aggregation number measurements will be transferred to the estimated values of K .

4. Morisue T, Moroi Y, Shibata O: **Solubilization of benzene, naphthalene, anthracene, and pyrene in dodecyl ammonium trifluoro acetate micelles**. *J Phys Chem* 1994, **98**:12995–13000.

The aggregation numbers determined from static light scattering used in the estimation of K are very large and are not consistent with spherical micellar structures. If they correspond to rodlike micelles, then the micelles are necessarily polydispersed and this may affect the estimated K values.

5. Moroi Y, Mitsunobu K, Morisue T, Kadobayashi Y, Sakai M: **Solubilization of n-alkylbenzenes into 1-dodecanesulfonic acid micelles**. *Langmuir* 1995, **11**:4719–4723.

6. Suslov DA, Solomonov BN: **The influence of molecular polarizability of aromatic hydrocarbons and their halogen derivatives on the free energy of solubilization in micellar solutions of ionogen surfactants**. *Russ J Phys Chem* 1993, **67**:757–760.

7. Suslov DA, Solomonov BN: **Effect of solute structure on solubilization of organic non-electrolytes in Triton X-100 micelles**. *Russ J Phys Chem* 1995, **69**:1140–1143.

Correlation equations are given relating the molar refraction of the solubilizes to the free energy of solubilization.

8. Gadelle F, Koros WJ, Schechter RS: **Solubilization isotherms of aromatic solutes in surfactant aggregates**. *J Colloid Interface Sci* 1995, **170**:57–64.

This systematic study, including various types of micelles and mixed micelles, contains extensive experimental data that can be used to test and/or develop theories of solubilization.

9. Chaiko MA, Nagarajan R, Ruckenstein E: **Solubilization of single component and binary mixtures of hydrocarbons in aqueous micellar solutions**. *J Colloid Interface Sci* 1984, **99**:168–182.

10. Treiner C: **The partitioning of neutral solutes between micelles and water as deduced from critical micelle concentration determinations**. In *Solubilization in Surfactant Aggregates*. Edited by Christian SD, Scamehorn JF. New York: Marcel Dekker; 1995:384–428.

A comprehensive discussion is presented of all the thermodynamic equations available in the literature to calculate the partition coefficient K based on experimental critical micelle concentration (cmc) data obtained as a function of the solubilize concentration.

11. Christian SD, Tucker EE, Scamehorn JF, Uchiyama H: **On the interpretation of solubilization results obtained from semi-equilibrium dialysis experiments**. *Colloid Polym Sci* 1994, **271**:745–754.

12. Rouse JD, Sabatini DA, Deeds NE, Brown RE, Harwell JH: **Micellar solubilization of unsaturated hydrocarbon concentrations as evaluated by semi-equilibrium dialysis**. *Environ Sci Technol* 1995, **29**:2484–2489.

13. Goldenberg MS, Bruno LA, Rennwanz EL: **Determination of solubilization sites and efficiency of water-insoluble agents in ethylene oxide-containing non-ionic micelles**. *J Colloid Interface Sci* 1993, **158**:351–363.

14. Heindl A, Strnad J, Kohler HH: **Effect of aromatic solubilizes on the shape of the CTAB micelles**. *J Phys Chem* 1993, **97**:742–746.

15. Treiner C: **The thermodynamics of micellar solubilization of neutral solutes in aqueous binary surfactant systems**. *Chem Soc Rev* 1994, **23**:349–355.

A comprehensive review of solubilization in various types of binary surfactant mixtures is presented here. The emphasis is on representing experimental data using classical thermodynamic relations.

16. Milioto S, Crisantino R, De Lisi R: **Thermodynamics of solubilization of pentanol in sodium dodecyl sulfate–dodecyl dimethyl amine oxide mixed micelles**. *J Colloid Interface Sci* 1994, **166**:356–362.

17. Tokuoka Y, Uchiyama H, Abe M: **Solubilization of some synthetic perfumes by anionic–nonionic mixed surfactant systems. 2**. *J Phys Chem* 1994, **98**:6167–6171.

18. Nishikido N: **Solubilization in mixed micelles**. In *Solubilization in Surfactant Aggregates*. Edited by Christian SD, Scamehorn JF. New York: Marcel Dekker; 1995:143–189.

Provides a compilation of solubilization studies in mixed surfactant systems. The thermodynamic equations discussed are different forms of Equation 5 in the text.

19. Abe M, Ogino K, Yamauchi H: **Solubilization of organic compounds by vesicles**. In *Solubilization in Surfactant Aggregates*. Edited by Christian SD, Scamehorn JF. New York: Marcel Dekker; 1995:333–363.

One of the first reviews of the solubilization of hydrocarbons in vesicles. Indicates the paucity of studies on non-polar solubilizes.

20. Ward AJ: **Kinetics of solubilization in surfactant based systems**. In *Solubilization in Surfactant Aggregates*. Edited by Christian SD, Scamehorn JF. New York: Marcel Dekker; 1995:237–273.

The kinetic studies suggest that equilibrium solubilization affects the rate of solubilization.

21. Carroll BJ: **Solubilization of two-component oil mixtures by micellar surfactant solutions**. *J Chem Soc Faraday Trans 1* 1986, **82**:3205–3214.

22. Chaiko MA, Nagarajan R, Ruckenstein E: **Locus of solubilization of benzene in surfactant micelles**. *J Phys Chem* 1984, **88**:2916–2922.

23. Nagarajan R, Ruckenstein E: **Theory of surfactant self-assembly: a predictive molecular thermodynamic approach**. *Langmuir* 1991, **7**:2934–2969.

24. Jönsson B, Landgren M, Olofsson G: **Solubilization of unchanged molecules in ionic micellar solutions: toward an understanding at the molecular level**. In *Solubilization in Surfactant Aggregates*. Edited by Christian SD, Scamehorn JF. New York: Marcel Dekker; 1995:115–141.

The basic elements of the theory of solubilization developed by this group are discussed. To find explicit equations with which to perform calculations, one has to look at other papers of the authors cited in this reference.

25. Aamodt M, Landgren M, Jönsson B: **Solubilization of uncharged molecules in ionic surfactant aggregates. 1. The micellar phase**. *J Phys Chem* 1992, **96**:945–950.

26. Landgren M, Aamodt M, Jönsson B: **Solubilization of uncharged molecules in ionic surfactant aggregates. 2. Phase equilibria**. *J Phys Chem* 1992, **96**:950–961.

27. Nagarajan R, Barry M, Ruckenstein E: **Unusual selectivity in solubilization by block copolymer micelles**. *Langmuir* 1986, **2**:210–215.

28. Tian M, Arca E, Tuzar Z, Webber SE, Munk P: **Light scattering study of solubilization of organic molecules by block copolymer micelles in aqueous media**. *J Polym Sci B: Polym Phys* 1995, **33**:1713–1722.

A simplified thermodynamic expression for the amount of solubilize contained in a block copolymer micelle is developed here to represent the experimental data.

29. Haulbrook WR, Feerer JL, Hatton TA, Tester JW: **Enhanced solubilization of aromatic solutes in aqueous solutions of N-vinyl pyrrolidone/styrene**. *Environ Sci Technol* 1993, **27**:2783–2788.

30. Alexandridis P, Hatton TA: **Poly(ethylene oxide)–poly(propylene oxide) block copolymer surfactants in aqueous solutions**

and at interfaces: thermodynamics, structure, dynamics, and modeling. *Colloid Surface A* 1995, **96**:1-46.

A comprehensive review of PEO-PPO-PEO block copolymers [where PEO is poly(ethylene oxide) and PPO is poly(propylene oxide)] from many points of view. A very useful starting point for anyone interested in working with these block copolymers.

31. Gadelle F, Koros WJ, Schechter RS: **Solubilization of aromatic solutes in block copolymers.** *Macromolecules* 1995, **28**:4883-4892.
- Careful measurements of the partition coefficient K are given as a function of the solubilize concentration for many block copolymers. Provides data of a quality needed to test theories of solubilization.
32. Saito Y, Kondo Y, Abe M, Sato T: **Solubilization behavior of estriol in an aqueous solution of Pluronic L-64 as a function of concentration and temperature.** *Chem Pharm Bull* 1994, **42**:1348-1350.
33. Kabanov AV, Nazarova IR, Astafieva IV, Batrakova EV, Alakhov VY, Yaroslavov AA, Kabanov VA: **Micelle formation and solubilization of fluorescent probes in poly(oxyethylene-b-oxypropylene-b-oxyethylene) solutions.** *Macromolecules* 1995, **28**:2303-2314.
34. Nagarajan R, Ganesh K: **Block copolymer self-assembly in selective solvents: theory of solubilization in spherical micelles.** *Macromolecules* 1989, **22**:4312-4325.

35. Nagarajan R: **Solubilization of hydrophobic substances by block copolymer micelles in aqueous solutions.** In *Solvents and Self-Organization of Polymers*. Edited by Webber SE, Munk P, Tuzar Z. Amsterdam: Kluwer Publishers.
- A theory of solubilization in diblock and triblock copolymer micelles is completely described. Explicit equations needed for the calculation of solubilization characteristics are given. The theory is applicable to spherical, cylindrical and lamellar aggregates.
36. Hurter PN, Scheutjens JM, Hatton TA: **Molecular modelling of micelle formation and solubilization in block copolymer micelles. 1. A self-consistent mean-field lattice theory.** *Macromolecules* 1993, **26**:5592-5601.
37. Hurter PN, Scheutjens JM, Hatton TA: **Molecular modelling of micelle formation and solubilization in block copolymer micelles. 2. Lattice theory for monomers with internal degrees of freedom.** *Macromolecules* 1993, **26**:5030-5040.
38. Hurter PN, Alexandridis P, Hatton TA: **Solubilization in amphiphilic block copolymer solutions.** In *Solubilization in Surfactant Aggregates*. Edited by Christian SD, Scamehorn JF. New York: Marcel Dekker; 1995:191-235.
- Provides a compilation of studies of solubilization in block copolymer micelles. Presents a review of the authors published work.
39. Nagarajan R, Ganesh K: **Solubilization in spherical block copolymer micelles: scaling analysis based on star model.** *J Chem Phys* 1993, **98**:7440-7450.