Phase behavior of nonionic surfactant solutions in the presence of polyvinylpyrrolidone

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Abstract

The phase separation behavior of four nonionic polyoxyethylene alkyl ether surfactants was examined in aqueous solutions containing polyvinylpyrrolidone (PVP) of various molecular weights. It was found that PVP decreases the cloud point (CP) and increases the Krafft point (KP) of the surfactants. The decrease in CP is dependent on the concentration of PVP, the molecular weight of PVP, and the structure of the surfactant hydrophobic group. The increase in KP is only dependent on PVP concentration. The effect of PVP on the CP and KP of these surfactants is smaller than that of PEG of the same nominal molecular weight.

Keywords: Nonionic surfactant; Cloud point; Krafft point; Polymer; Polymer-surfactant; Polyvinylpyrrolidone

1. Introduction

There is much interest today in the interactions between polymers and surfactants in solution, and several books and reviews have been published on this topic (Saito, 1987; Dubin and Tong, 1993; Goddard and Ananthapadmanabhan, 1993). Polymer-surfactant interactions are of particular relevance to pharmaceutical scientists because of the extensive use of these materials together in drug delivery and processing. Most of the litera-

ture demonstrates that strong interactions exist when at least one of the components (either polymer or surfactant) is charged. Nonionic surfactant-uncharged polymer systems have received comparatively little attention because early results showed little or no interaction. However, such systems are of pharmaceutical interest because nonionic surfactants (such as alkyl polyoxyethylene ethers, polyoxyethylene sorbitan ethers and esters, etc.) and uncharged water-soluble polymers (such as polyethylene glycols, polyvinylpyrrolidone, cellulose derivatives, etc.) are used extensively in formulation and processing. A few recent reports have shown that mea-

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surable interactions do exist when both components are uncharged. These include the interaction of ethoxylated alcohols with PEO (Wormuth, 1991), a weak interaction between ethylhydroxyethylcellulose and nonionic surfactants (Karlstrom et al., 1990), an interaction between hydroxyethylcellulose and an oxyethylene nonylphenyl ether (Boscher et al., 1983), and an interaction between agarose, and hexaethylene glycol mono-n-dodecyl ether (Penders et al., 1993).

We recently reported on the interactions between polyethylene glycol (PEG) polymers and two alkyl POE ether surfactants—polyoxyethylene (10) oleyl ether, (I), and polyoxyethylene (10) cetyl ether (II)—in aqueous solution (Pandit et al., 1995). Our results showed a strong segregative interaction that reduces the aqueous solubility of the surfactants and dramatically reduces the temperature range where they are soluble. The presence of PEG results in a reduction of the cloud point (CP) of the surfactant by depletion flocculation, and an increase in the Krafft Point (KP) of the surfactant.

We report here the interaction of four nonionic surfactants I and II used in the previous study, polyoxyethylene (10) stearyl ether (III), and polyoxyethylene (20) stearyl ether (IV), with another pharmaceutically important polymer, polyvinylpyrrolidone (PVP). In particular, we were interested in the temperature-solubility behavior (cloud points and Krafft points) of the surfactants in the presence of PVP. Surfactants I–IV were chosen as models because, in the temperature range of 0–100°C, I exhibits a cloud point (CP), II and III exhibit both a CP and a Krafft point (KP), and IV shows only a KP. As with PEGs, there is much published evidence that PVP interacts with *ionic* surfactants (Goddard and Ananthapadmanabhan, 1993). A few studies of PVP-nonionic surfactant systems failed to demonstrate any measurable binding or interaction (Brackman et al., 1988; Saito, 1987; Shinoda, 1978). On the basis of our earlier results with nonionic surfactant-PEG systems, we believed that a similar interaction should exist in the nonionic surfactant-PVP system, and would be demonstrable using CP and KP measurements.

An explanation of these phase separation temperatures, and their utility in studying polymer-surfactant interactions was discussed in our previous paper (Pandit et al., 1995).

2. Materials and methods

2.1. Materials

Surfactants I–IV were kindly donated by ICI Surfactants, Wilmington, DE, and were used as received. PVP 10 000, 40 000 and 360 000 were from Aldrich and were also used as received. Water was deionized and passed through a Millipore filtration system.

2.2. Cloud point and Krafft point measurements

All solutions were made on a w/w basis in water. The surfactant solutions were made by weighing out the appropriate amount of surfactant and mixing it with approximately 90% of the water required. This mixture was then heated slowly with stirring to rapidly hydrate the surfactant. When the surfactant was uniformly dispersed the solution was cooled, and enough water added to achieve the final total weight. Mixtures containing surfactant and PVP, or surfactant, PVP and a salt were made similarly, with PVP and the salt being added to the cooled mixture just before adjusting final weight. All mixtures were equilibrated at room temperature before KP or CP measurement. The exceptions to this were mixtures whose CPs were below room temperature. These were cooled in an ice bath until they were clear before CP measurement.

The CP was determined by heating approximately 20 ml of the sample mixture in closed containers with stirring at a rate of approximately 2°C/min. Slower heating rates gave the same readings. The phase separation temperatures were determined by visual observation against a black background. The KP was taken as the temperature at which the mixture became completely clear, and the CP as the temperature where the solution became distinctly cloudy. Slight haziness persisted in many solutions, presumably due to
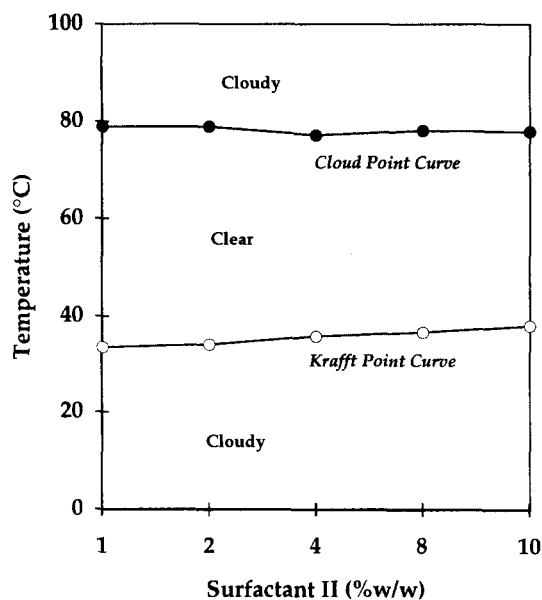
Fig. 1. Cloud point and Krafft point curves of aqueous solutions of surfactant II.
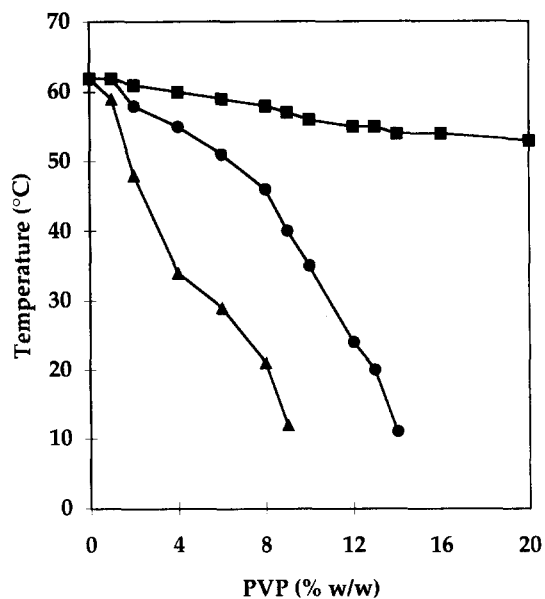

Fig. 2. Effect of PVP concentration and molecular weight on the CP of a 2% w/w solution of surfactant I. Key: (■) PVP 10 000; (●) PVP 40 000; (▲) PVP 360 000.

small amounts of impurities, and was not considered phase separation. The reproducibility of CP and KP measurements was ± 1°C.

3. Results and discussion

3.1. Phase separation temperatures of surfactants I–IV

The phase separation curve for surfactant II is shown in Fig. 1, and is typical for polyoxyethylene alkylether type of surfactants. The CP and KP temperatures are typically quite insensitive to surfactant concentration. Table 1 lists the

Table 1
Cloud Point (CP) and Krafft Point (KP) temperatures for 2% w/w aqueous solutions of Surfactants I–IV

Surfactant	KP (°C)	CP (°C)
I	<0	62
II	34	77
III	48	60
IV	45	>100

CP and KP temperatures for 2% w/w solutions of surfactants I–IV. All our experiments used 2% w/w aqueous solutions of the surfactants. Previous studies on the relationship of surfactant structure and CP temperatures (Schott, 1969) found that, at constant ethylene oxide content, the CP is lowered by an increase in surfactant molecular weight and branching of the alkyl chain. An increase in the ethylene oxide content increases the CP. This is consistent with our results. The effect of structure on the KP of nonionic surfactants has also been discussed previously (Schott and Han, 1976). For a given ethylene oxide content, the KP parallels the melting points of the homologous series of fatty acids. An increase in the ethylene oxide content makes the surfactant less hydrophobic and increases the critical micelle concentration (cmc), resulting in a decrease of the KP. Our results are consistent with these explanations.

3.2. Effect of PVP on phase separation temperatures

Figs. 2–5 show the effect of PVP concentration

and molecular weight on the phase separation temperatures on surfactants I–IV. Only CPs are reported for surfactant I because the KPs are less than 0°C, and were not investigated. Similarly, only KPs are reported for surfactant IV because the CPs are greater than 100°C, even in the presence of PVP, and were not measured. PVP lowers CP and raises KP, which effectively decreases the temperature range in which the surfactants form clear solutions in water. The lowering of the CP increases with PVP concentration and molecular weight. The increase in the KP depends only upon the concentration of PVP, but not on its molecular weight. For certain systems, the CP and KP curves meet at a particular PVP concentration, above which the mixtures are cloudy at all temperatures.

These systems show the same pattern of behavior as nonionic surfactant-PEG mixtures (Pandit et al., 1995), and we believe that a depletion flocculation mechanism may be responsible for the enhanced phase separation (lower CP) in these
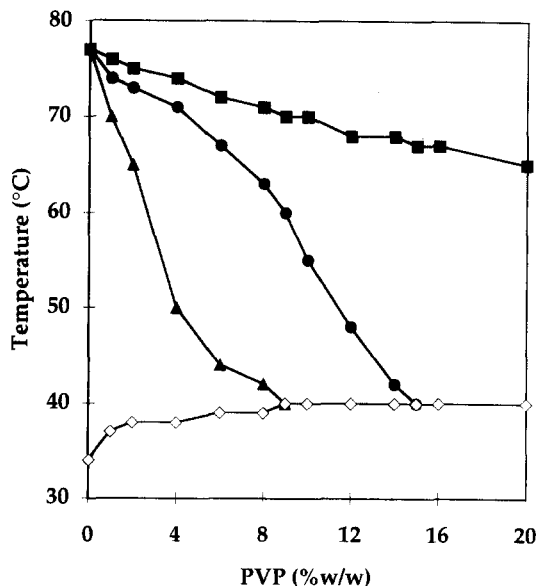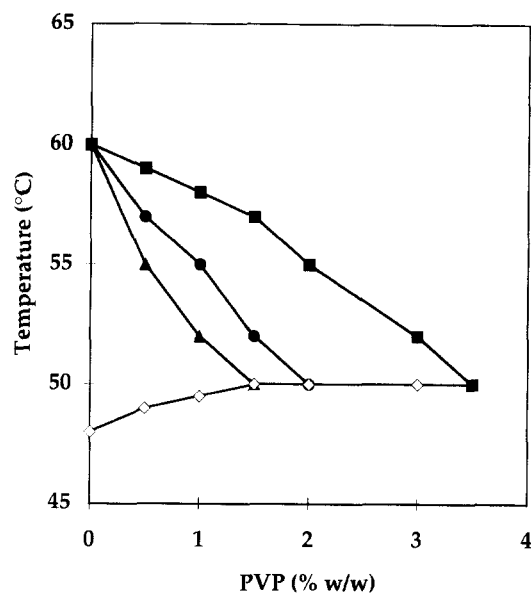

Fig. 4. Effect of PVP concentration and molecular weight on the CP and KP of a 2% w/w solution of surfactant III. The filled symbols represent the CP curves with PVP. Key: (■) PVP 10 000; (●) PVP 40 000; (▲) PVP 360 000. The open symbols (◇) represent the KP curve, which is the same for all the PVPs studied.

Fig. 3. Effect of PVP concentration and molecular weight on the CP and KP of a 2% w/w solution of surfactant II. The filled symbols represent the CP curves with PVP. Key: (■) PVP 10,000; (●) PVP 40 000; (▲) PVP 360 000. The open symbols (◇) represent the KP curve, which is the same for all the PVPs studied.

nonionic surfactant-uncharged polymer systems. The depletion mechanism for polymer-induced flocculation of colloidal dispersions has been explained by several workers (Everett, 1992; Dubin and Tong, 1993; Saito, 1987), and it's potential applicability to micelle-polymer systems has been discussed (Clegg et al., 1994). Although PVP is known to complex with and thus increase the water solubility of a wide variety of solutes (Bühler, 1992), no such attractive interaction was observed with nonionic surfactants.

The lowering of the CP by PVP also appears to depend on the structure of the surfactant; a comparison is shown in Fig. 6, using PVP 10 000. Surfactants I, II and III have the same ethylene oxide content (10 POE units), but varying structure of the hydrophobic group. Comparing surfactant II (POE(10) cetyl ether) with surfactant III (POE(10) stearyl ether), both of which have saturated, unbranched hydrophobic groups, we see that the effect of PVP is stronger on III, the

surfactant with the greater hydrophobicity. Comparing surfactant I (POE(10) oleyl ether) and surfactant III, both of which have the same hydrophilic chain, and very similar molecular weights, we see that the effect of PVP is much weaker for I. This is probably as a result of the unsaturation and branching of the oleyl group, which makes it less hydrophobic, and is consistent with the lower CPs seen for such surfactants (Schott, 1969). The same pattern is seen when looking at the effects of PVP 40 000 on the CPs of surfactants I, II and III. It has been shown that the cmc of nonionic surfactants decreases as the surfactant's hydrophobicity increases (Myers, 1991). Thus, our results show that interaction with PVP is stronger as the amphiphilicity of the surfactant increases. This is analogous to the results with ethoxylated alcohols and polyethylene oxides (Wormuth, 1991), where the miscibility of the two cosolutes decreased strongly upon increasing the amphiphilicity of the surfactant. The effect of PVP 360 000, however, is so strong that it appears to have about the same degree of effect on these three surfactants. Such relationships may be useful in predicting the degree of interaction
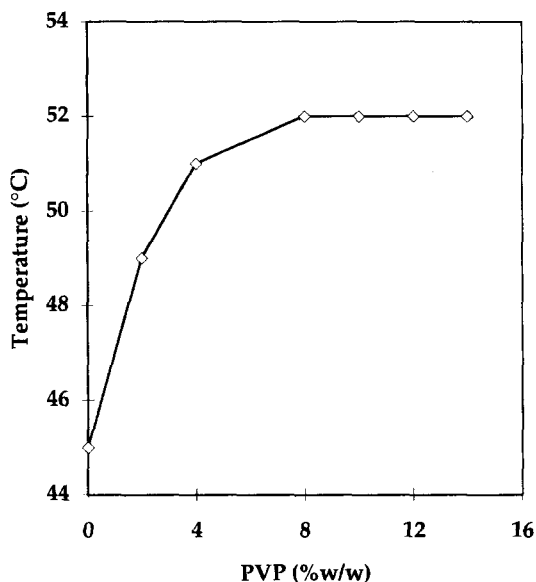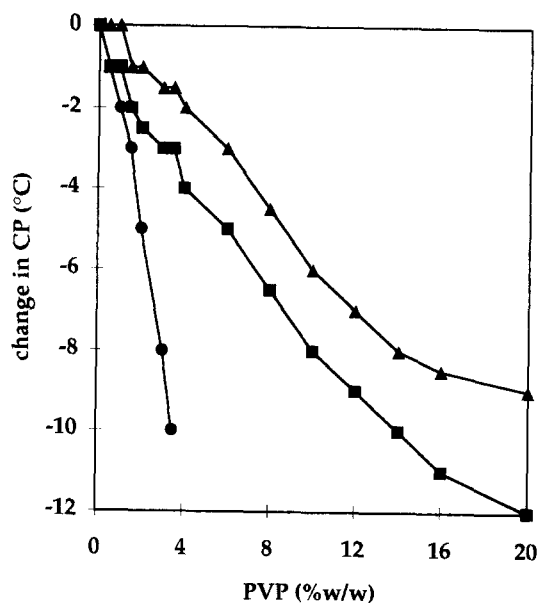

Fig. 6. Effect of surfactant structure on the extent of CP decrease by PVP 10 000. Key: (▲) surfactant I; (■) surfactant II; (●) surfactant III.

between PVP and a variety of nonionic surfactants. Surfactant IV (POE(20) stearyl ether) does not show a CP in the experimental temperature range because of its greater POE content, and requires higher temperatures to decrease hydrogen bonding enough to cause phase separation.

The increase in KP of surfactants II, III and IV in the presence of PVP is also similar to what we observed in the PEG-nonionic surfactant systems (Pandit et al., 1995), in that the increase is independent of PVP molecular weight, and depends only on PVP concentration. Proposed explanations for the increase in KP due to a water-soluble polymer were also discussed in our earlier report. Fig. 7 compares the increase in KP for surfactants II, III and IV as a function of PVP concentration. Within the reproducibility of our measurements, all three systems show the same rate of increase with increasing concentrations of PVP, suggesting that the increase in KP is not due to any specific interaction between the surfactant and PVP, but may be due to a change in the solvent properties of water. This may effectively decrease the solubility of the surfactant monomers in water, requiring higher temperatures for the monomer solubility to

Fig. 5. Effect of PVP concentration on the KP of a 2% w/w solution of surfactant IV. The KP curve is the same for all the PVPs studied.

reach the cmc. It may also increase the cmc of the surfactants due to a decrease in the hydrophobic effect, and thus also require higher temperatures for the monomer solubility to reach the cmc. Previous studies of the effect of inorganic salts on KPs of nonionic surfactants also showed a similar small but uniform increase in KP (Schott and Han, 1976).

In any event, the depression of CP and the elevation of KP of nonionic surfactants by PVP dramatically reduce the temperature range in which the surfactants are soluble in water and can form clear, homogeneous solutions. For surfactants exhibiting both a CP and KP, the CP and KP curves meet at a certain critical concentration of PVP, which decreases as the molecular weight of PVP increases. Above this critical PVP concentration, solutions of these surfactants are cloudy at all temperatures.

3.3. Comparison of PEG and PVP in causing phase separation

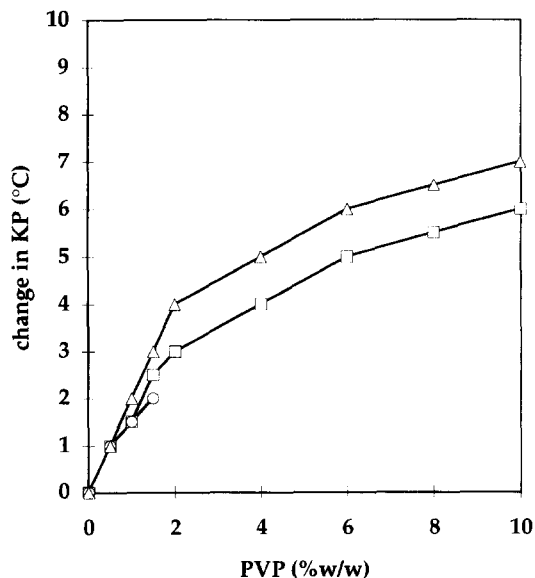Fig. 8 shows a comparison of the ability of PEG 10000 (data taken from Pandit et al., 1995)

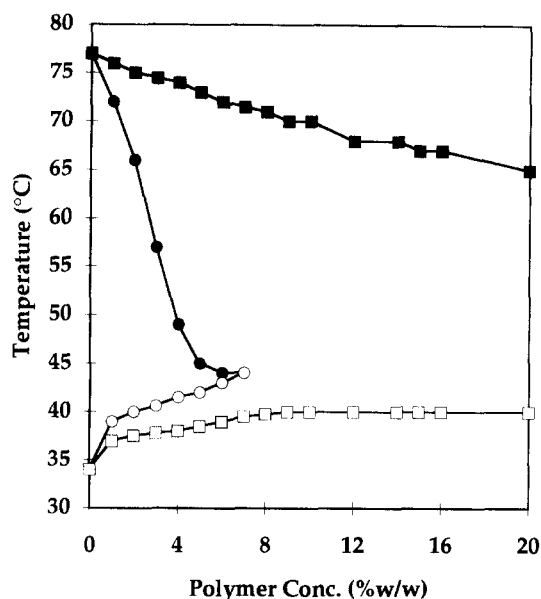
Fig. 8. Comparison of phase separation of surfactant II by PEG 10000 (circles) and PVP 10000 (squares). (PEG data taken from Pandit et al., 1995).

and PVP 10000 to affect phase separation temperatures of surfactant II. It is clearly seen that when comparing polymers of the same nominal molecular weight, PEG is much more effective at lowering CP. This may be related to the differences in the Flory radius of PEG and PVP in water. PEG also appears to be slightly more effective at increasing KP, although this effect is small.

In conclusion, we have shown evidence that there is a repulsive interaction between alkylpolyoxyethylene ether surfactants and PVP in water, similar to that seen with PEGs. The interaction with PVP is weaker than that with PEG for the same nominal molecular weight of polymer. The result of the interaction is a lowering of the CP and an elevation of the KP of the surfactant, which effectively decreases the temperature range where the surfactants form clear solutions in water. The reduction of CP depends on the molecular weights of PVP, and on the structure of the hydrophobic group of the surfactant. The reduction of KP is independent of the molecular weights of PVP and surfactant, and depends only upon the concentration of PVP. The lowering of

Fig. 7. Effect of surfactant structure on the extent of KP increase by PVP. Key: (□) surfactant II; (◦) surfactant III; (△) surfactant IV.

CP may be explained as a repulsive interaction due to depletion flocculation. The mechanism of the observed increase in KP is not yet clear. In fact, the significance of KPs for nonionic surfactants, and their alteration by additives needs to be investigated further.

Acknowledgements

References

Boscher, Y., Lafuma, F. and Ouivoron, C., Light-scattering studies of hydroxyethylcellulose in water/nonionic surfactant binary mixtures. *Polym. Bull.*, 9 (1983) 533–536.

Brackman, J.C., van Os, N.M. and Engberts, J.B.F.N., Polymer-nonionic micelle complexation. Formation of poly(propylene oxide)-complexed n-octyl thioglucoside micelles. *Langmuir*, 4 (1988) 1266–1269.

Buhler, V., *Kollidon. Polyvinylpyrrolidone for the Pharmaceutical Industry*, BASF Aktiengesellschaft, Ludwigshafen, 1992.

Clegg, S.M., Williams, P.A., Warren, P. and Robb, I.D., Phase behavior of polymers with concentrated dispersions of surfactants. *Langmuir*, 10 (1994) 3390–3394.

Dubin, P. and Tong, P. (Eds.), *Colloid-Polymer Interactions*, ACS Symposium Series 532, American Chemical Society, Washington D.C., 1993.

Everett, D.H., *Basic Principles of Colloid Science*, Royal Society of Chemistry, London, 1992.

Goddard, E.D. and Ananthapadmanabhan, K.P. (Eds.), *Interactions of Surfactants with Polymers and Proteins*, CRC Press, Boca Raton, 1993.

Karlstrom, G., Carlsson, A. and Lindman, B., Phase diagrams of nonionic polymer-water systems. Experimental andtheoretical studies of the effects of surfactants and other solutes. *J. Phys. Chem.*, 94 (1990) 5005–5015.

Myers, D., *Surfaces, Interfaces and Colloids. Principles and Application*, VCH Publishers, New York, 1991.

Pandit, N.K., Kanjia, J., Patel, K., and Pontikes, D.G., Phase behavior of aqueous solutions containing nonionic surfactant-polyethylene glycol mixtures. *Int. J. Pharm.*, 122 (1995) 27–33.

Penders, M.H.G.M., Nilsson, S., Piculell and Lindman, B., Clouding and diffusion of nonionic surfactants in agarose gels and solutions. *J. Phys. Chem.*, 97 (1993) 11332–11338.

Saito, S., Polymer-Surfactant Interactions. In *Nonionic Surfactants-Physical Chemistry, Surfactant Science Series*, Vol. 23, Dekker, New York, 1987.

Schott, H. Hydrophile-lipophile balance and cloud points of nonionic surfactants. *J. Pharm. Sci.*, 58 (1969) 1443–1449.

Schott, H. and Han, S.K., Effect of additives on solutions of nonionic surfactants IV. Krafft points. *J. Pharm. Sci.*, 65 (1976) 979–981.

Shinoda, K. *Principles of Solution and Solubility*, Dekker, New York, 1978.

Wormuth, K., Patterns of phase behavior in polymer and amphiphile mixtures. *Langmuir*, 7 (1991) 1622–1626.