

COMMUNICATIONS

The effect of added salts on solubilization by a non-ionic surfactant

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The effects of added salts on the properties of aqueous solutions of surfactants have been widely studied. For non-ionic surfactants, salts may have one of two effects. The salt may reduce the critical micelle concentration, lower the cloud point and possibly increase micellar weight. Conversely, the reverse effects may be seen. These effects, which are probably due to solvation/desolvation and complexation, have been examined by Schott & Han (1975, 1976).

In solubilized systems, if micelle size increases in the presence of salt additives, then it might be expected that the amounts of solutes dissolved would be increased because of the larger volume/surface ratios of the micelles. This latter result has often, although not always, been observed (Elworthy et al 1968; Lundberg et al 1979).

If the solute is a non-electrolyte, the addition of salts may introduce another problem associated with the salting-out phenomenon. Salts may either decrease or increase the solubilities of non-electrolytes in water, i.e. "salt-out" or "salt-in" (Long & McDevitt 1952). Salting out can be measured by the Setchenow equation (Setchenow 1889). In a solubilized system the solute is distributed between water and micelle. Hence, any effect which added salt has on solute solubility in water, may affect the total amount dissolved in the solubilized solution.

These effects are important in pharmacy since many solubilized systems contain added salts and the effect of these additives on the total solubility of the drug may be critical.

Presented here are some preliminary solubility/solubilization measurements on aqueous systems containing solute, non-ionic surfactant and added salts. The surfactant used was cetomacrogol 1000, B.P.C., (cetomacrogol), a 1% w/v aqueous solution of which has a cloud-point of 120 °C (see next paragraph). The critical micelle concentration of this surfactant in water is 6×10^{-3} % w/v at 25 °C. The non-electrolyte solutes used were the methyl and propyl esters of *p*-OH benzoic acid (methyl paraben and propyl paraben, respectively). The pH values of all systems were less than 6 so that the esters were present essentially in the undissociated form

and calculations based on data by Watts & Sutherland (unpublished) suggest that after 30 h less than 0.1% of the esters will be hydrolysed. Hydrolysis was therefore not considered to be a problem. All measurements were made at 30 °C.

Table 1 shows the effect of added salts on the cloud-point of a 1% w/v solution of cetomacrogol 1000. Both sodium chloride and magnesium sulphate decreased the cloud-point markedly. In the case of 1 molar magnesium sulphate the cloud-point was so low (< 10 °C) that it was not possible to carry out solubilization studies in this system. Cloud-points for cetomacrogol without salt and in the presence of magnesium nitrate and sodium nitrate, were greater than 100 °C, at atmospheric pressure. The values shown for these systems were obtained with sealed ampoules at greater than atmospheric pressure. Thus, the absolute cloud-points may be approximate, but the relative magnitudes are of the correct order. These findings are similar to those of Schott & Han (1975), who used a different surfactant and found that sodium nitrate lowered the cloud-point slightly and magnesium nitrate raised it emphatically.

In Table 2 the solubilities of the parabens in salt solutions, alone, and in salt solutions containing 1% w/v cetomacrogol are shown. Both sodium chloride and magnesium sulphate salt out the esters significantly, whereas both sodium nitrate and magnesium nitrate

Table 1. Cloud points of 1% w/v cetomacrogol solution and of solutions of 1% w/v cetomacrogol containing added salts.

Salt	Cloud point (°C)
0.5 M Sodium chloride	98.0 ± 1
1.0 M Sodium chloride	84.5 ± 1
1.5 M Magnesium sulphate	63.5 ± 1
1.0 M Magnesium sulphate	< 10
0.5 M Sodium nitrate	111 ± 1*
1.0 M Sodium nitrate	117 ± 1*
0.5 M Magnesium nitrate	120 ± 1*
1.0 M Magnesium nitrate	124 ± 1*
1% w/v Cetomacrogol in water	120 ± 1*

* Correspondence.

* See text for explanation.

Table 2. Solubility/solubilization data for methyl and propyl esters of *p*-hydroxybenzoic acid

Solvent system	(a) Methyl ester			(b) Propyl ester		
	(1) Solubility g litre ⁻¹	(2) Solubility in presence of 1% w/v cetomacrogol	(3) Partition coefficient (K)	(1) Solubility g litre ⁻¹	(2) Solubility in presence of 1% w/v cetomacrogol	(3) Partition coefficient (K)
H ₂ O	2.38	4.11	73	0.37	1.99	445
0.5 M NaCl	1.78	3.31	86	0.32	1.84	477
1.0 M NaCl	1.38	2.78	101	0.25	1.74	590
0.5 M Mg SO ₄	1.72	3.15	83	0.27	1.71	524
1.0 M Mg SO ₄	1.05	—	—	0.16	—	—
0.5 M NaNO ₃	2.57	3.74	46	0.38	1.91	403
1.0 M NaNO ₃	2.33	3.63	56	0.40	1.89	379
0.5 M Mg(NO ₃) ₂	2.46	3.56	45	0.42	1.86	347
1.0 M Mg(NO ₃) ₂	2.10	3.04	45	0.37	1.70	360

either have little effect on solubility, or increase it somewhat, i.e. salt-in. In the presence of cetomacrogol the total solubilities of the esters in all systems are greater than in those systems without surfactant. However, in all systems the total solubilities, in the presence of added salts and surfactant, are less than the solubilities of the esters in the presence of surfactant alone.

In a solubilized system the total amount of solute present is composed of free solute and solute which is bound within the micelle. As an approximation, the free amounts of the esters can be taken as being equal to their solubilities in water and in the various salt solutions. Therefore, the differences between total solubilities in micellar solution and 'free solubilities' give an indication of the solubilities of solutes in the micelles. Such calculations are approximations since addition of surfactant may affect free solubility by affecting structuring of water. Also the addition of salts, by affecting the critical micelle concentration, may affect the distribution of solute. Since the concentration of cetomacrogol used is ≈ 170 times greater than the critical micelle concentration this latter effect is unlikely to be important.

Column 3 in Table 2 shows partition coefficients, (K), calculated from concentrations of solutes in micelles and free solution respectively, using the technique of Smith et al (1974). If the K values of the esters in H₂O/surfactant solutions alone are taken as the base lines, a pattern emerges. For solutions containing sodium chloride or magnesium sulphate the K values are greater than for H₂O/surfactant systems. Conversely, for solutions containing sodium nitrate or magnesium nitrate the K values are less than the values for H₂O/

surfactant systems. It is suggested that the K values are dependent primarily upon changes in micellar size brought about by the added salts. Decreased cloud points and critical micelle concentrations give increases in the total concentrations of micelles and in micellar sizes, leading to a change in distribution, between free and bound solute in favour of the micelle. The opposite is found when cloud points and critical micelle concentrations are little affected.

It may be possible to arrive at a general picture of these effects by extending this work to include measurement of micellar changes, a wider range of added salts, solutes and surfactants, greater concentration ranges of salts and surfactants and a study of the effects of temperature on the systems.

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