

TABLE 12.6
Effect of Electrolytes on the Solubility of Furosemide in 5% w/v Polysorbate 80

Concentration (M)	Solubility of Furosemide (mg/100 mL) in Electrolyte				
	NaCl	KCl	MgCl ₂	Na ₂ SO ₄	K ₂ SO ₄
0.00	125.6	125.6	125.6	125.6	125.6
0.01	130.2	127.0	128.2	129.9	131.0
0.02	131.9	129.8	131.4	133.7	134.4
0.05	132.3	131.9	135.5	139.6	144.6
0.10	133.2	132.5	136.4	149.9	147.5
0.20	134.1	134.1	141.4	157.8	160.9

Source: Taken from Shihab, F. A. et al., *Int. J. Pharm.*, 4, 13–20, 1979.

between anionic surfactant (SDS) micellar solutions and several familiar metal salt solutions (Al₂(SO₄)₃, FeCl₃, CaCl₂, and MgCl₂) were investigated. Precipitates were formed in all systems except SDS-MgCl₂. The forming of these precipitates was attributed to adsorption-charge neutralization (Al⁺), bridge connection (SDS-FeCl₃) and low solubility product of Ca(DS)₂ crystal respectively. SEM photographs of the precipitates can serve as additional vivid proofs of the above-mentioned conclusion.

Nature and Concentration of Surfactant and Solute

The effect of various surfactants—the cationics (cetyltrimethylammonium bromide [CTAB] and cetyl pyridinium chloride [CPC]), the anionic (sodium lauryl sulfate [SLS]), and the nonionic (polysorbate 80 [Tween 80])—on the solubility and ionization constants of some sparingly soluble weak acids of pharmaceutical interest was studied (Gerakis et al., 1993). Benzoic acid (and its 3-methyl-, 3-nitro-, and 4-tert-butyl-derivatives), acetylsalicylic acid, naproxen, and iopanoic acid were chosen as model drugs. The cationics, CTAB and CPC, were found to considerably increase the ionization constant of the weak acids (ΔpK_a ranged from -0.21 to -3.57), while the anionic, SLS, showed a negligible effect and the nonionic, Tween 80, generally decreased the ionization constants. Solubility of the acids increased in aqueous micellar and in acidified micellar solutions.

Eda et al. (1996, 1997) studied the solubilization of isomeric alkanols in ionic surfactant micelles using a piezoelectric gas sensor method. The surfactants used included SLS and CTAB. The solutes were 1-, 2-, 3-, and 4-alkanol, as well as branched and cyclic alkanols. Free energy change of transfer of the alkanols from water to micelles was found to be in the order of 1- < 2- < 3- < 4-alkanol < branched alkanol < cyclic alkanol. The results seem to indicate that a bulkier alkanol was less favorably solubilized in the micelle. The results also agreed with the principle of hydrophobicity that a bulky alkyl group is less hydrophobic than a slender alkyl group with the same number of carbons, since the bulky one has a smaller surface area that is accessible to water. However, additional correlation work between the micelle/water and octanol/water partition coefficients showed a good correlation for the transfer free energy from water to micelle and from water to octanol ($r = 0.97-0.98$). This result indicates that the solubilization of alkanols in micelles depends only on the hydrophobicity of alkanols and that there is no effect of the molecular shape of alkanols on the solubilization in the micelles. Hence, a flexible micelle solubilization model for alkanols was proposed (Figure 12.12).

Some surfactant micelles exhibit concentration-dependent growth. That is, the micelles at concentrations much higher than the CMC are larger than those at concentrations smaller than the CMC. In the case where the solute is located within the hydrophobic core of the micelle, the micellar solubilization capacity increases with increasing alkyl chain length. Table 12.7 illustrates this