

**TABLE 13.3**  
**Solubilizing Capacities and Partition Coefficients of Diazepam as a Function of Temperature**

Pluronics	Solubilizing Capacity <sup>a</sup>			Partition Coefficient ( $K_m$ )		
	25°C	37°C	50°C	25°C	37°C	50°C
F-68	0.0253	0.0522	0.1811	272.32	460.37	1292.76
F-88	0.0334	0.1206	0.3167	358.77	1059.43	2464.44
F-108	0.0342	0.3751	0.6771	367.38	3326.63	4294.74

Source: Lin, S.Y. and Yang, J.C., *Acta Pharm. Technol.*, 33, 222–224, 1987.

<sup>a</sup> Units: mol diazepam/mol Pluronic.

**TABLE 13.4**  
**Thermodynamic Parameters for the Solubilization of Diazepam by Pluronic Surfactants**

Temperature	$\Delta G$	F-68			F-88			F-108	
		$\Delta H$	$\Delta S$	$\Delta G$	$\Delta H$	$\Delta S$	$\Delta G$	$\Delta H$	$\Delta S$
25°C	-3.32	-11.61	-27.83	-3.48	-14.53	-37.07	-3.50	-2.74	6.71
37°C	-3.78	—	—	-4.29	—	-33.03	-4.99	—	7.28
50°C	-4.59	—	-21.69	-5.01	—	-29.47	-5.37	—	8.14

Source: Lin, S.Y. and Yang, J.C., *Acta Pharm. Technol.*, 33, 222–224, 1987.

Note: Units of  $\Delta G$  and  $\Delta H$  are kcal/mol, and  $\Delta S$  is cal/K/mol.

surfactants with increasing temperature is believed to be the result of an increase in the micellar aggregation number at higher temperatures, leading to the formation of a larger micelle, capable of entrapping more diazepam.

Lin and Yang (1987) also calculated the thermodynamic parameters of diazepam for micellar solubilization in Pluronic surfactant solutions at different temperatures (Table 13.4). For all systems,  $\Delta G$  was negative, indicating micellar solubilization was spontaneous. The sign of entropy has been associated with the location of solubilized molecules within the micelles. Positive values have been observed for molecules embedded in the micelle center and negative values for adsorption of the molecules on the micelle surface. The results in this paper indicate that in the F-108 and F-88 Pluronics, diazepam molecules can penetrate into the micelle interior, whereas for F-68 and lower concentrations of F-88, diazepam is adsorbed on the micelle surface without penetration into the micellar core.

Croy and Kwon (2004) found increasing temperature from 25°C to 37°C increased the partitioning coefficient and decreased the critical aggregation concentration (CAC) of the polyene antimycotic nystatin in micelles of F-98, P-105, and F-127 (Figure 13.7; Table 13.5). The trend in increased partitioning followed decreased CMC, enlarged core size, and increased aggregate number; hence, the solubility of nystatin improved with the presence of greater available micellar core surface area, indicating amphiphilic nystatin was solubilized at the core-shell interface of these micelles. Croy and Kwon further investigated the effect of temperature on the core polarity of Pluronic micelles, finding the polarity decreased with increasing temperature. Although nystatin partitioning increased at 37°C in the Pluronics, partitioning was much lower in the less numerous F-98 micelles although its core polarity was similar to P-105 and F-127, indicating solubility of nystatin was dependent on total micellar core surface area.