reduce skin irritation. The synergistic behavior of surfactant mixtures may also be exploited to reduce the total amount of surfactant used in a particular application, thus reducing both cost and environmental impact. In addition, as environmental regulations on producing and releasing new materials become more restrictive, it may be preferable from a regulatory perspective to combine existing surfactants rather than introducing new ones (Shiloach and Blankschtein, 1998a).

Surfactant mixtures are also often employed in drug solubilization since such mixtures exhibit high solubilization potential for lipophilic drugs and also are physiologically relevant (Humberstone et al., 1996; Krishnadas et al., 2003; Rhee, 2007). Christensen et al. (2004) applies solubilization in mixed micelles to *in vitro* lipid digestion models to simulate drug in an *in vivo* setting. Mixtures of surfactants can lead to changes in the size and shapes of micelles, as well as to increases in the amount of oil solubilized in some surfactant solutions (Florence, 1981; Hammad and Muller, 1998; Sugioka and Moroi, 1998). Mixed micelles act as solubilizing vehicles for nonswelling amphiphilic such as long-chain fatty acids and cholesterol. As early as 1969, Small et al. (1969) have studied simple and mixed bile salt micelles using NMR. They found that the hydrophobic side of the bile salt molecule containing methyl groups is hindered in its molecular form by the addition of lecithin. Furthermore, by assuming a disk-shaped micelle model in which the outer perimeter of bile salt molecules encloses a small disc of lecithin molecules, they found that as the molar ratio of lecithin increases, the diameter of the micellar disc would increase. This leads to a decrease in the fraction of lecithin molecules in contact with bile salts.

Naylor et al. (1993) studied the ability of lecithin to modify the rate and mechanism of dissolution of hydrocortisone in the presence of sodium taurocholate (NaTC) solutions. They found that in the presence of lecithin, the CMC of NaTC dropped owing to the *more effective solubilization capacity of the mixed micelle*. Furthermore, the CMC value dropped more on saturation with hydrocortisone, implying some interaction between hydrocortisone and the NaTC/lecithin micelles. These results indicated that in the NaTC-only system, wetting effects predominated dissolution, whereas in the NaTC/lecithin system, the dissolution rate of hydrocortisone was enhanced mainly through solubilization.

Humberstone et al. (1996) investigated the solubilization and intrinsic dissolution of halofantrine hydrochloride (Hf·HCl), a highly lipophilic phenanthrenemethanol antimalarial with poor and erratic absorption of Hf after oral administration, using micellar composition (NaTC alone) and mixed micellar composition (NaTC and lecithin). Studies were initiated based on the fact that food increases the oral bioavailability of Hf in humans approximately three- to fivefold. The solubility and intrinsic dissolution rate of Hf·HCl were investigated as a function of bile salt concentration (NaTC, 0–30 mM) and micellar composition (4:1 NaTC:lecithin). At premicellar (fasted) concentrations of NaTC (<5 mM), the solubility and intrinsic dissolution rate were very low (<15 μg/mL; <0.01 μg s^{-1} cm^{-2}). At NaTC concentrations typical of the postprandial state, the solubility and dissolution rate improved dramatically. For example, solubility in 30 mM NaTC increased approximately 1000-fold relative to buffer control, with even greater enhancement (3000-fold) associated with mixed micellar systems. These data suggest that the improved absorption of Hf·HCl in the fed state is most likely due to the increased solubilization and dissolution of the drug in the presence of mixed micelles containing bile salts.

Comparison of Solubilizing Capacity Among Different Types of Micelles

Hammad and Muller (1998) investigated the solubility of clonazepam in bile salt/soya phosphatidylcholine-mixed micelles (BS/SPC-MM). The solubility of clonazepam in different micellar systems was studied as a function of the concentration. The linear increase in clonazepam solubility is attributed to the parallel increase in the number of micellar species available to solubilize clonazepam (Alkan-Onyuksel et al., 1994). Hammad and Muller (1998) also compared the solubilization capacity of BS/SPC-MM with other surfactant systems such as pluronic F68, sugar ether, and BS. It was found that BS/SPC-MM was proven superior in enhancing the solubility of clonazepam. At a concentration of 10%, 3.5-, 30-, 40-, and 50-fold increases in clonazepam solubility were