Joshi et al. (2004) demonstrated that the bioavailability of a weakly basic drug in dogs from a solid dispersion in 3:1-PEG–polysorbate 80 mixture was 21-fold higher than that of a capsule containing micronized bulk drug blended with lactose and microcrystalline cellulose. Similarly, Dannenfelser et al. (2004) reported a 10-fold bioavailability of a highly permeable, poorly water-soluble (aqueous solubility ~0.17 μg/mL at 25°C), neutral compound in dogs from a PEG 3350–polysorbate 80 (3:1) solid dispersion as compared to a conventional capsule formulation containing the micronized drug substance. Other reports also confirm enhanced dissolution (Veiga et al. 1993b) and bioavailability (Sheen et al. 1995) of drugs from PEG–polysorbate mixtures.

Tocopheryl Polyethylene Glycol 1000 Succinate

Another surface-active carrier useful for preparing solid dispersion formulations is tocopheryl polyethylene glycol 1000 succinate (TPGS) or d-α-tocopheryl PEG 1000 succinate (Eastman Chemical, TN). Because of its relatively low melting point (~40°C), TPGS may be filled in its molten form in hard and soft gelatin capsules; however, hard gelatin capsules may require band sealing to prevent leakage of the contents. TPGS is used in the soft gelatin capsule formulation of aprenavir (Agenerase®, GSK, NC) to enhance its bioavailability through a combination of increased solubility and permeability enhancement due to excipient-mediated P-glycoprotein efflux inhibition (Yu et al. 1999). Koo et al. (2000) reported that a solid dispersion of an antimalarial drug, halofantrine, provided 5–7 times higher bioavailability than a conventional tablet formulation. In another study conducted in rats, the effect of TPGS on the solubility and permeability of paclitaxel was demonstrated by improving the bioavailability by 4- to 6-fold by coadministration with TPGS as compared to a formulation without TPGS (Varma et al. 2005). Other investigators also reported similar beneficial influences of TPGS on dissolution and absorption of poorly water-soluble drugs (Boudreaux et al. 1993; Sokol et al. 1993; Chang et al. 1996; Wu 1998).

Block Copolymers

There has also been increased focus on the application of block copolymers in solid dispersion formulations of poorly water-soluble drugs (Suni and Cho 1997; Ho et al. 2000; Passerini et al. 2003; Chen et al. 2004; Yin et al. 2005). Various grades of block copolymers are commercially available as poloxamers (Pluronics). Drugs may be formulated by dissolving them in molten block copolymers and filling the liquid in hard gelatin capsules; the molten mass solidifies at ambient room temperature. Recently, Yin et al. (2005) reported a process where a water-insoluble drug, BMS-347070, and a block copolymer, Pluronic F-127, were dissolved in acetone or methylene chloride and then spray dried to form a dispersion of nanosized crystalline drug material within a crystalline, water-soluble matrix. It was hypothesized that the PEO segments of Pluronic F-127 crystallized while the polypropylene oxide segments of the excipient remained amorphous, creating a size-restricted domain in which the drug substance formed physically stable nanocrystals.

Glycerides

Thixotropic gels (TPGS) of mono- and diglycerides have been used as carriers for solid dispersions. In the development of a hard gelatin capsule formulation of a poorly water-soluble drug, propantheline bromide, the drug substance was first dissolved in Miglyol 829 and the solution was then converted to a semisolid form by incorporating colloidal silicon dioxide to increase the viscosity of the fill material. In another study, colloidal silicon dioxide was used as a thickening agent for the mixture of an oil (diesters of caprylic/capric acids; Captex 200), a surfactant (polysorbate 80), and a cosurfactant (C8/C10 mono-/diglycerides; Capmul MCM) (Patil et al. 2004).

PVP and Cellulose-Based Solid Dispersions

Water-soluble synthetic polymers such as polyvinylpyrrolidone (PVP) and cellulose-based polymers such as HPMC have been commonly used to enhance the dissolution rate of poorly water-soluble drugs. PVP has been used extensively not only to enhance the drug dissolution rate