2. Aerosol Solvent Extraction System (ASES): Here, the solution is sprayed through the atomization nozzle into a chamber filled with SCF. Expansion of solution occurs within the fine droplets of solvent being sprayed, thus creating supersaturation and precipitation of solids as fine particles.
3. Precipitation with Compressed Antisolvent (PCA): The PCA differs from the GAS process in that much higher mass transfer rate and efficient crystallization are achieved by supplying compressed antisolvent into solution being sprayed (Fusaro et al. 2005). In one study, the authors used supercritical CO_2 as the antisolvent to prepare solid dispersions of phenytoin and PVP K30 from their solutions in acetone or acetone/ethanol mixture by using PCA and conventional spray-drying process. A comparison of intrinsic dissolution rates revealed that solid dispersions prepared using the PCA technique had 68% higher dissolution rate when compared to spray-dried solid dispersions (Muhrer et al. 2006). Process parameters of GAS and PCA techniques have also been manipulated to obtain desired morphology and polymorphs of pharmaceutical actives (Edwards et al. 2001; Jahrmer et al. 2005; Muhrer et al. 2006).

Fusion

Hot-melt extrusion has proven to be a commercially feasible technique, but its application may be limited for processing thermolabile drugs. Even though the extrusion shear rate could be increased to decrease the viscosity of most polymers, high temperatures and long residence time could be detrimental to the product. McGinity and coworkers introduced to a fusion technique called Kinetisol® dispersion, which involved use of a custom built compounder by DisperSol Technologies, LLC (Austin, TX) (DiNunzio et al. 2010b,c). The technique involves the use of impact shear along with heat to manufacture solid dispersion in a very short period of time. A premix of drug and polymer was charged into the compounder, and processing parameters such as maximum rotational speed, ejection temperature, and processing time were studied. All the batches using itraconazole and Kollidon® L100-55 were manufactured at not more than 177°C and 14.1 seconds. The material was quench pressed and milled after discharge. From this study, they concluded that it was possible to manufacture solid dispersions without the use of plasticizers in a very short time. In their following work, they demonstrated that the manufacture of temperature-sensitive compound hydrocortisone was possible using this technique (DiNunzio et al. 2010a).

EXAMPLES OF SOLID DISPERSIONS

As summarized in Table 18.1, FDA has approved approximately 17 products based on solid dispersion technology. Here we will discuss several examples of these.

Surfactant and Lipid-Based Solid Dispersions

Fusion and solvent evaporation are most commonly used techniques to prepare solid dispersions in the laboratory scale. As reported by Serajuddin (1999), these methods have practical limitations in the scale to commercial production. Even methods such as HME, spray drying, and SCF technique described earlier have many challenges. For example, the drug and/or the carrier may not be stable at the high temperature needed for melt extrusion, a common solvent to dissolve both the relatively hydrophobic drug and the relatively hydrophilic carrier for the purpose of spray drying may not be available, and the SCF technology may not be amenable and cost efficient in most cases. The introduction of surface-active and self-emulsifying excipients that are solid at room temperature represents a breakthrough in commercial development of solid dispersions. It has been reported that formulations incorporating these new excipients may not only increase dissolution rates of poorly water-soluble drugs, but they may also be filled as their molten mass directly into hard gelatin capsules, thus eliminating the need for additional unit operations such as milling, blending, sieving, and so forth. Vasanthavada and Serajuddin (2007) recently reviewed the application of surfactants and