Typical screw design is constructed utilizing the functional screw elements (dispersive and distributive types) and conveying screw elements to facilitate forward movement of material in the TSE while subjecting the material mass to effective mixing. The densification of the mass is achieved by carefully selecting the conveying elements with successively narrow pitch. The technique was effectively utilized by scientists in developing a high-dose tablet through densification of the granulation for a low bulk density API (Shah, 2005).

Lodaya et al. (2003) describe a typical process description and process parameters for a Twin-Screw Wet Granulation (TSWG) process. The independent variables in the TSE process are screw design or configuration, screw rpm, temperature, and locations for liquid feed. The granulation characteristics are highly dependent on the screw configuration. Typical key process parameters are powder feed rate, liquid feed rate, and process temperature, and the extruder motor torque is one of useful information to monitor the process consistency. The authors suggest that the process should be run at a steady torque. The maximum torque for any given feed rate, screw design, and rpm should be 80% or below the manufacture-recommended limiting torque.

Figure 23.6 illustrates the schematic of continuous process described in the invention (Ghebre-Sellassie et al., 2002). Ghebre-Sellassie et al. (2002) utilized the TSE capabilities to develop a prototype that integrated the loss-in-weight feeders (Pathak et al., 2000), a TSE, liquid feeders, a wet mill, conveying and leveling devices, a tunnel dryer (radio frequency or microwave drying principle), and a dry milling operation to achieve continuous production of pharmaceutical granulation. Process analytical tools are applied at key steps to ensure that the key process parameters are in control. It is a single-pass, continuous, automated system for producing pharmaceutical granulation. The system incorporates a supervisory control and data assess (SCADA) system that monitors and controls the integrated unit operation. The throughput in such a system can range from a few kilograms to 50 kilograms production of the pharmaceutical granulation per hour. The granulation yield can then be further lubricated if required and compressed or encapsulated as desired.

Multiple loss-in-weight feeders (Pathak et al., 2000) can be utilized to accurately and precisely meter in the raw materials (in particular ratio) into the inlet port of the feeder. The TSE (with optimized screw design) is utilized for mixing and wet granulation with the assistance of the granulation liquid feed introduced into the TSE. The initial screw speed is kept low to quickly determine the water-carrying capacity of the unit mix in the TSE. Slowly, the screw speed is increased along with a simultaneous increase in the feeder metering rate to achieve desired granulation. Once the steady state is achieved, throughput is maintained throughout the process run. The wet granulation is milled through an appropriate-size screen and leveled on the dryer conveyor belt. Radio frequency or microwave drying facilitates the moisture removal along the depth of the granulation bed. The sensors placed at various points in the dryer facilitate the monitoring of the progress in the drying cycle. The PAT tools monitor the inlet and outlet moisture during the drying cycle. Content uniformity is also monitored in a similar manner. Any nonconformity to quality standards is fed back through the SCADA system, and the material is instantly discarded as waste until the automatic adjustments are made to bring quality into control.

HOT-MELT EXTRUSION

Numerous formulation approaches have been published to enhance the solubility of a drug molecule. It is a well-known fact that the amorphous phase of a drug has higher solubility, a higher dissolution rate, and higher bioavailability when compared with the crystalline form of the same drug. Alvarez-Núnez and Leonard (2004) utilized HME followed by milling of the extrudate to create milled solid dispersion (MSD) on the basis of this technique for formulation of amorphous systems. A mixture of a drug compound and polymer that has strong interaction with the drug is heated until homogeneous liquid phase (very likely the polymer starts to melt first, and a drug molecule is dispersed into the polymer matrix) is obtained. The mixture is rapidly cooled down to room temperature to obtain solid dispersion of drug that exists as an amorphous phase. A significant