force/linear inch constant, the compaction force was scaled up to the production unit. Finally, the screw speed to roll speed ratio was kept constant for all units. Using these scale-up factors, reproducibly consistent granules and finished tablets were produced in the laboratory-, pilot-, and production-scale equipment. However, dissolution similarity (f_2 factor) was only established for the laboratory- and pilot-scale formulations but not the production-scale one. Based on the predicted in vivo performance of these formulations, the authors concluded that the production-scale equipment produced a faster releasing formulation compared with smaller units [50]. For successful scale-up, it is important to evaluate compaction rate (kg/min) and applied pressure as well as milling parameters, that is, milling rate (kg/min/screen surface area) and mill speed. The particle size distribution of the processed material provides valuable information about the reproducibility of the process.

Drying

Drying is a commonly employed unit process in the manufacture of solid dosage forms. Drying in the pharmaceutical industry is accomplished using static bed dryers (tray or truck ovens), moving bed dryers (turbo-tray dryers), fluidized bed dryers, and spray dryers. More recently, single-pot systems incorporating high shear mixer-granulators with vacuum, microwave, or infrared drying are also becoming popular [51]. Depending on the desired final product characteristics, any of these dryers may be employed. The commonly used dryers in solid dosage form manufacture (i.e., tray dryers and fluid bed dryers) are discussed here. Critical factors governing the drying process include the EMC of the formulation blend, the exposed surface for solvent transfer, and the vapor carrying capacity of the drying air. Psychometric principles for calculating the vapor carrying capacity of air should be employed in scaling up a drying process. Some important factors while scaling up a tray-drying process are the number of trays, product load per tray (bed thickness), temperature, and humidity of the circulating air inside the oven. Maintaining the same bed thickness (kg/tray) and providing similar drying air capacity will facilitate successful scale-up from pilot-scale to production-scale dryers.

Fluid bed drying processes are more challenging to scale-up [52,53]. Several factors impacting the drying process include airflow, air temperature, bed depth, and product characteristics. The fluidization air volume should be adjusted to keep the same air velocity (ft/min) between different sized units. Inlet temperature, dew point, and the product bed temperature in the scaled-up larger batch should be maintained as in the smaller unit. However, some adjustments to these parameters may be made depending on relative differences in fluidized bed heights between different units.

Milling

Milling is commonly employed to reduce particle size of granulations, bulk drug substances, and excipients to facilitate uniformity of powder mixes. This process is also used to manipulate the dissolution profile of the dosage form. Following wet granulation, wet milling is often employed to improve the granule surface area for more efficient drying. Sizing of granulation is typically accomplished using either low-energy mills (oscillating granulators) or high-energy mills (hammer, conical, and centrifugal impact mills). The hammer mill is the most common and versatile