evaporation is ideal for early stages (preclinical to Phase I) of drug development. After removal of the solvent, the resulting ASD is isolated, dried, and milled to the desired particle size. Secondary drying in a vacuum oven or tray dryer is often employed to remove any residual solvent that remains in the final ASD powder.

The main advantage of rotary evaporation is that the thermal decomposition of drug, surfactant and polymer can be prevented as low temperatures are typically required to evaporate organic solvents. Challenges of solvent cast/rotary evaporation method includes difficulty in finding suitable solvent systems for drug substance, surfactant and polymers, and slow rates of solvent removal often leads to drug-polymer phase separation.

Rotary evaporation is used to quickly prepare a large number of samples using mg quantities of material during early stage screening. Small samples allow for larger, more comprehensive screens to be carried out quickly while still providing enough material for meaningful characterization. Potential lead formulations can then be manufactured on a larger scale for further evaluation, including physical and chemical stability studies, *in vitro* release characterization, and *in vitro* studies in animals (Padden et al., 2011).

Spray Drying

ASD preparation by spray drying is also carried out by first dissolving the drug and formulation components (polymers, surfactants) in a pharmaceutically acceptable solvent. The total solids load in the feed solution is typically 5%–25% by weight, and this is generally dictated by API/polymer/surfactant solubility as well as viscosity of the solution. Spray drying converts a solution into a dry powder in a single step. Evaporation of solvent occurs at a very fast rate in spray drying, causing a sudden rise in viscosity that leads to the entrapment of drug molecules in the polymer matrix (Araujo et al., 2010). Because solvent evaporation time is extremely fast (on the order of seconds), spray drying is particularly advantageous for preparing ASDs of compounds with poor thermal stability. Drugs with poor aqueous solubility may be spray dried into very small particles provided that they are soluble in certain solvents suitable for spray drying. Challenges to employing spray drying during discovery and early stages of development include poor flow and compression properties due to the inherent small particle size of the resultant spray dried powder. In addition, the currently available lab scale spray dryers suffer from poor yield and generally cannot work on mg quantities of material (Padden et al., 2011).

Fusion/Hot-Melt Extrusion

The fusion method for ASD preparation involves heating a physical mixture of drug, surfactant, and polymer to form a molten mixture and then cooling and solidifying with rigorous stirring. The hot-melt extrusion method is the modern version of the fusion method in which intense mixing of the components is induced by the extruder. Compared with the traditional fusion method, melt extrusion offers the potential to shape the molten drug-polymer mixture into implants, pellets, or oral dosage forms (Patil et al., 2016). This method requires complete miscibility of the drug and polymer in the molten state. Hot-melt extrusion can be limited in the ability to process heat-sensitive and/or high melting point drugs and it is generally not amenable for manufacturing small quantities (mg to g) needed in preclinical development.

ASDs are inherently metastable systems. The chemical and physical stability of the solid dispersion formulation must be carefully evaluated to ensure that it possesses sufficient handling and storage characteristics for use in the desired study (Six et al., 2004; Vandecruys et al., 2007; Qian et al., 2010). Characterization should include analyses of both solid form and *in vitro* API release in aqueous media. Among numerous methods that are available for characterization of ASDs, polarized light microscopy (PLM), powder X-ray diffraction (pXRD), thermogravimetric analysis (TGA), and differential thermal analysis (DTA) are commonly utilized. Dynamic vapor sorption (DVS), solid-state NMR spectroscopy, Raman spectroscopy, infrared spectroscopy, and isothermal microcalorimetry are also widely employed in ASD characterization.