Producing ASDs with Pressure Nozzles Using Laboratory Scale Spray Dryers

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PURPOSE

In a previous study, “Designing Spray Dried Particles with a Pressure Nozzle at Small Scale” equipment configuration and process conditions were determined that could produce polymer powders using pressure nozzles in laboratory scale spray dryers. The purpose of this study is to use the knowledge gained from the previous trials to develop a process for generating amorphous solid dispersions (ASD) with pressure nozzles in a laboratory scale spray dryer.

METHOD(S)

The spray drying trials were conducted on a laboratory scale mobile spray dryer, the GSD-200 GENESIS® Spray Dryer. The system was operated in closed loop with a nitrogen gas purge and solvent recovery. The spray gun was a 0.2mm pressure nozzle. Four solutions were prepared, using two active pharmaceutical ingredients (API); ketoconazole (KTZ) and indomethacin (IND), and two polymers; hydroxypropyl methylcellulose acetate succinate (HPMC-AS) and polyvinylpyrrolidone K-30 (PVP K-30). The API:polymer ratio was 1:4. All solutions were 10% solids and organic solvent based (acetone and/or ethanol). A high-pressure positive displacement pump was used to deliver the solutions. Each solution was sprayed at 250 PSI and 46-66 g/m. The drying gas flow was 17 CFM. The inlet and outlet temperatures were formulation dependent. For all trials, at least 350 grams of solution was sprayed (35 grams of solids) and all yields were in the range of 45-65%. Spray times were all between 7 and 11 minutes. The collected samples were analyzed to determine morphology, residual solvent, and particle size distribution. A differential scanning calorimeter (DSC) was used to evaluate morphology. Residual solvent was measured using loss on drying (LOD). Particle size distribution (PSD) was measured using laser diffraction. Table 1 shows the formulations and process parameters.

GSD-200 GENESIS™ Spray Dryer with Extension Insert

RESULT(S)

By choosing compatible formulations and optimizing the processing conditions, all spray dried samples were determined to be amorphous using the DSC to evaluate their morphologies. This was the main objective. Before spray drying, the APIs were analyzed to verify the melting points in their crystalline state (figures 1-2). The collected spray dried material was also analyzed, showing the glass transition temperatures for each sample (figures 3-6). PSD and residual solvent was also analyzed. The average particle size (D50) for all trials was between 13 and 19 microns. This is not a large range, but what is interesting is the strong correlation between particle size and polymer used. Trials 1 and 2 had very similar D50s despite having different APIs. This is also true about trials 3 and 4. The polymer is 80% of the formulation and the API is 20%. This explains why the polymer is more influential than the API. There is also a correlation between particle size and spray rate. The higher the spray rate, the larger the particles. This is not surprising. What is interesting is that the spray rates vary despite each solution being delivered at the same pressure and through the same orifice. This also demonstrates how the chosen polymer impacts particle size. The residual solvent for all four trials was between 2.5% and 4.5%, but no trends were observed.

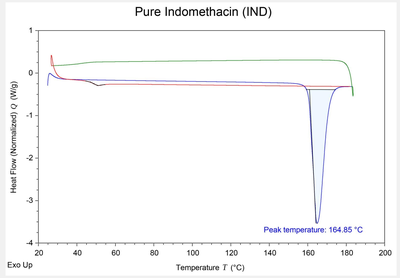


Figure 1

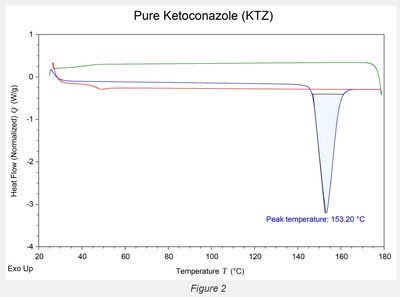


Figure 2

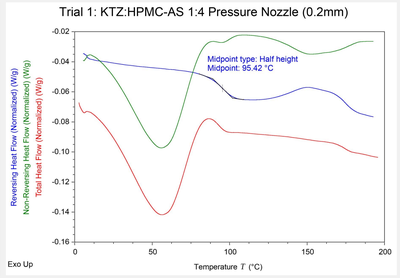


Figure 3

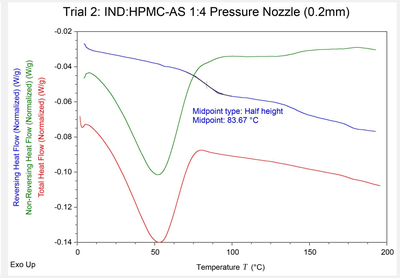


Figure 4

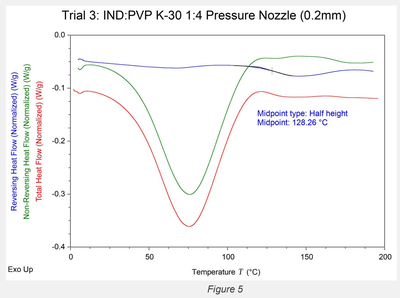


Figure 5

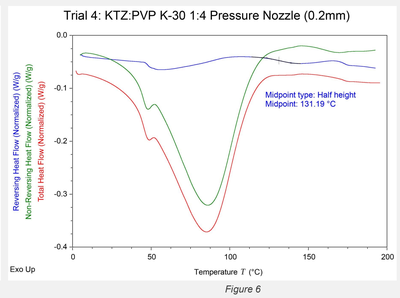
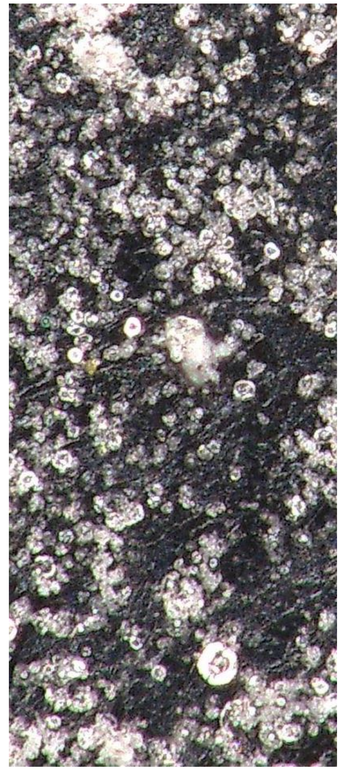


Figure 6

Trial #	API	Polymer	Solvent	Inlet Gas Temp (°C)	Outlet Gas Temp (°C)	Spray Rate (g/m)	Average Particle Size (µm)
1	Ketoconazole	HPMC-AS	Acetone/ Ethanol	110	35-50	65.4	18.24
2	Indomethacin	HPMC-AS	Acetone	90	30-40	55.3	17.18
3	Indomethacin	PVP K-30	Ethanol	180	70-80	46.0	13.41
4	Ketoconazole	PVP K-30	Ethanol	180	70-80	48.6	13.80

Table 1



CONCLUSION(S)

ASD formulations can be studied using a pressure nozzle in a small-scale spray dryer in order to conserve material and expedite the discovery process. As little as 350 grams of solution (only 35 grams of solids) can be used to study the feasibility of an ASD formulation. For 2-fluid spray guns, 350 grams of solution is not necessarily a small amount, but for pressure nozzles, that is very conservative. The ability to process with pressure nozzles in a laboratory sized spray dryer also helps with material recovery and cleaning.

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