Pilot-Scale Investigation of Spray Dried Powders for Direct Compression

Andrew P. Birkmire
GEA Pharma Systems
Columbia, MD USA

Michelle M. Madsen
GEA Niro A/S
Copenhagen, Denmark

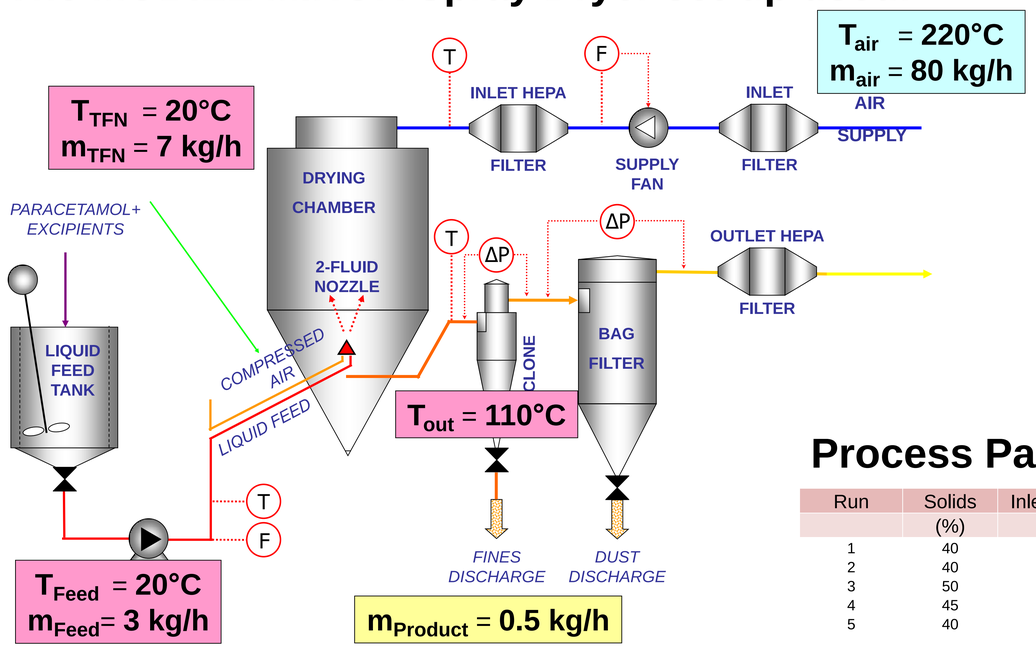
Abstract

Spray drying is an attractive alternative to conventional wet granulation techniques because it is a robust, continuous process that produces free-flowing homogeneous powders and can eliminate many of the conventional batch processes currently used in the Pharmaceutical Industry[1-4]. However, the high cost of many of the Active Pharmaceutical Ingredients (APIs) necessitates development work at a small scale to demonstrate proof-of-concept. It is challenging to produce a free-flowing powder with a small-scale spray dryer due to the short residence time. Large-scale spray drying studies have been performed that successfully produced spray-dried versions of commercially available paracetamol[1]. The aim of this study is to demonstrate what properties comparably produced powders have when produced at a small development scale using spray drying.

Overview

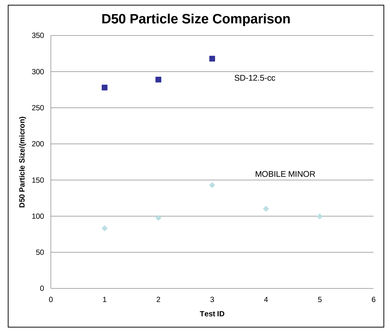
Raw materials remaining from the Master's Thesis project[1] were taken and either mixed with DI Water (Runs #1 and #2) or DI Water and Polyvinylpyrrolidone (PVP – Runs #3-#5) and spray-dried using settings as comparable to Reference 1 as possible in order to as closely mimic the powders produced at commercial scale (SD-12.5-cc) on a pilot-scale spray dryer (MOBILE MINOR). A two-fluid nozzle in counter-current flow (fountain mode) was used as opposed to the pressure nozzle used in the original study as a pressure nozzle at this small scale and with a suspension is not possible due to the required small orifice size. The powders were analyzed for particle size distribution and residual moisture and then tabletted using an eccentric Diaf tabletting machine, adjusted to a tablet compression setting of 5.0 (on a scale of 1-10) on the eccentric arm shaft and a compression rate of ~50 tablets/min. Ten tablets were then analyzed for hardness, porosity, and disintegration.

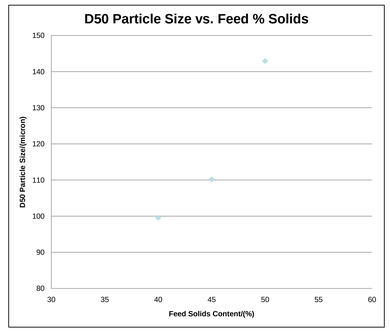
The MOBILE MINOR Spray Dryer set-up used:

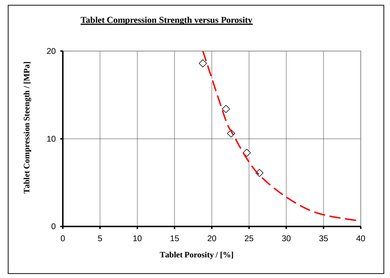


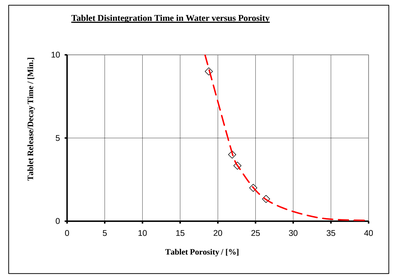
Results and Discussion

Five successful runs were performed on the MOBILE MINOR spray dryer using the #6 fountain nozzle and an inlet temperature of 220 and an outlet temperature of 110 degrees C[Ref. 1]. Runs #1 and #2 were a control with no additional PVP from the OTC formulation and Runs #3-#5 contained the additional 2.5% PVP used in the Thesis work at three different feed solids concentrations, 40, 45, and 50%. The residual moisture levels in the powders were comparable to those produced on the SD-12.5-cc, in the range of 2.5-3.5% vs. 1.7-3.2% at the commercial scale. The particle size, however, was much smaller than can be produced at the large scale. This is a known limitation of small-scale spray drying and is due to the shorter residence time of the droplets at the smaller scale. The D50 particle size produced in these tests was between 85-140 micron, whereas 275-320 micron D50 particles were produced on the SD-12.5-cc. Due to the reduced size of the particles, the resulting tablets had lower compression strengths (5-20 vs. 160-260 MPA) and shorter disintegration times (2-9 vs. 14-103 min.). Higher solids content in the feed yielded larger particles. Addition of 2.5% PVP resulted in tablets with improved disintegration times.









Process Parameters:

Run	Solids	Inlet Temp.	Outlet Temp.	Atom. Press.	Atom. Rate	Airflow	Total Sprayed	Spray Rate	Run Time	Cyclone	Moisture	d(10)	d(50)	d(90)
	(%)	(C)	(C)	(bar)	(kg/hr)	(kg/hr)	(g)	(g/min)	(min)	(g)	(%)	(micron)	(micron)	(micron)
1	40	220	110	1	7	80	376.7	34.25	11	83	2.87	18.594	83.1183	199.0634
2	40	220	110	0.7	5	80	374.5	35.67	10.5	70.4	2.49	13.0965	97.6668	218.5996
3	50	220	110	1	7	80	622	50.98	12.2	144.7	2.74	26.3912	142.9505	335.7943
4	45	220	110	1	7	80	761.4	49.44	15.4	140.8	3.27	22.5507	110.1807	254.6499
5	40	220	110	1	7	80	857.3	33.75	25.4	141.3	3.42	23.1925	99.5538	272.6016

Conclusions

Powders similar to, except smaller in size and with slightly higher moisture contents, were produced on a pilot scale spray dryer as were previously produced at a commercial scale. This is a result of the shorter residence time and method of atomization available at the smaller scale. Higher solids concentration in the feed yielded larger particles. Addition of 2.5% PVP in the feed produced tablets with improved disintegration times. Proof-of-concept of pilot-scale spray drying development work of direct compression formulations was demonstrated to be feasible.

References

1. Madsen, Michelle M. Spray Dried Pharmaceutical Powders for Direct Tablet Compression. Master's Thesis, University of Copenhagen, Denmark, 4/2007.
2. Gohel, M. C. "A Review of Co-Processed Directly Compressible Excipients." J Pharm Pharmaceutical Sciences 8(1):76-93, 2005.
3. Raff, A. M., et. Al. "Spray-Drying of Tablet Granulations I." Presented to the Pharmacy Subsection, AAAS, Chicago meeting, December1959.
4. Avachat, A. and V.J. Ahire. "Characterization and Evaluation of Spray-Dried Co-Processed Excipients and Their Application in Solid Dosage Forms." Indian Journal of Pharmaceutical Sciences, 2007 Vol. 69, Iss. 1, pp 85-90.