Atmospheric Spray Freeze Drying (ASFD): A New Approach

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Introduction

The ASFD process has been developed as a new method for manufacturing powder by scientists in Edmonton, Canada. The goal was to reduce drying time and operate at atmospheric conditions with reasonable collection efficiency; this work has also been patented[1]. In contrast with other known atmospheric spray-freeze drying technologies, this new technology combines spray freezing, deposition / collection, and convective flow drying into one step employing co-current gas flow to spray-freeze the solution, convey the frozen powder towards an exit filter and in situ drying. This overcomes the difficulty of fluidizing and elutriating a cohesive frozen powder from a substrate. In this process, a powder cake with uniform thickness builds up on the exit filter after spray-freezing and conveying. The drying of the frozen powder cake follows via streaming a dry gas through the exit filter whilst keeping the temperature below the critical product temperature of the formulation. After drying, the loose free-flowing powder cake can be collected on top of the exit filter at the completion of the process. Atmospheric pressure freeze-drying (ASFD) may therefore be feasible in a wide variety of materials whose solution/suspension can be sprayed, frozen, and dried into a powder cake.

Methods

Biopharma Technology (Winchester, UK) conducted the study using the same ASFD equipment and set up (Figure 1) as published by Wang et al[2]. The freeze-drying cycle was carried out using a VirTis Genesis freeze-dryer equipped with a Wizard2 PC control system. Cycles with the ASFD equipment (10 and 20% w/v) were conducted; a comparative freeze-drying cycle was conducted with 10% w/v skimmed milk. The drying times were compared, along with the type of material produced. Samples were compared by visual inspection, SEM, particle size and surface area. The determination of lyophilisation characteristics for the formulation was completed using the BTL *Lyostat2* freeze-drying microscope. The determination of the particle size and surface area was completed using the Sympatec HELOS/RODOS dry powder sizing instrument with ASPIROS micro-dosing system. The SEM images were taken using the LEO 1530 Field Emission SEM with in-lens secondary electron detector.

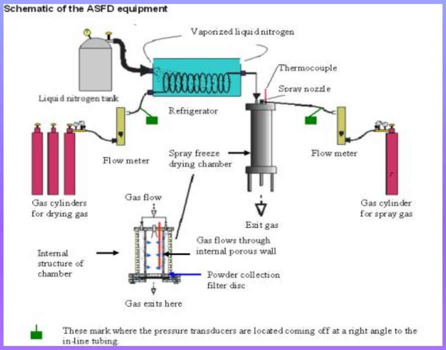

Figure 1 – ASFD schematic

Results and Discussion

Visual inspection showed that the ASFD equipment produces a good fine loose dry powder after each and every run, in contrast with the cohesive cake produced by conventional freeze drying. The total cycle time averaged less than four hours. When a faster flow of drying gas was used in run 3, the material was dried to a moisture content of 2.4% in less than 2.5 hours (sample depth approximately 4mm). The total cycle time for the standard non-optimized freeze drying run was approximately 46 hours, which gave a moisture content of 1.86%.

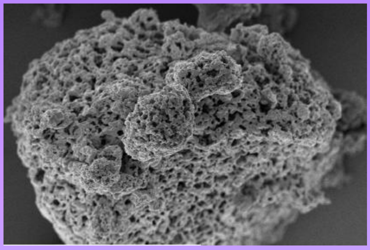

Figure 2 – ASFD material at 5000x

Figure 3 – FD material at 5000x

SEM analysis for the ASFD sample shows the material to have a fine and rounded uneven surface, with peaks and troughs that are observable in the SEM images; see Figures 2 and 3. SEM analysis for the comparable FD sample shows the material to have a smooth surface with sharp edges. This observation is confirmed by the much greater surface area for the ASFD sample. Particle size (µm) for the standard freeze drying run was 43.99; for the two ASFD runs the particle size averaged 25.26. For material dried from 10% solution, the specific surface area (cm^2/cm^3) was 0.36 for the lyophilized cake and 0.86 for the loose dry powder produced by ASFD.

	ASFD run 1 (10%)	ASFD run 2 (10%)	**ASFD run** 3 (20%)	**BTL FD (10%)**
Visual inspection	Fine loose dry powder	Fine loose dry powder	Fine loose dry powder	Good cake
Cycle time (hours)	4	5.5	2.25	46
Moisture (% w/w)	9.30	11.63	2.43	1.86
SEM (Figures 2 and 3)	Material appears to have a fine and rounded uneven surface			Material appears to have smooth surface with sharp edges
Particle size (µm)	25.26		36.15	43.99
Surface area (cm^2/cm^3)	0.86		0.40	0.36
Flow rate (SCFM)	5	5	14	NA

Conclusions

The ASFD method has enabled 15ml of a 20% solution of skimmed milk to be dried in 2.25 hours giving a fine loose dry powder with a final moisture content of 2.4% w/w. The results compare well with the moisture content from the standard freeze drying run in the earlier testing and with the published results by the ASFD inventors. The fast drying time could allow for much greater material throughput and provide a more suitable powder material, reducing the need for milling or grinding. Further work is planned to investigate the drying of proteins and the resulting activity. In addition, testing will explore if fast drying and rapid freezing will permit the use of a less complex formulation.

Acknowledgments

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References

1. Powder Formation by Atmospheric Spray-Freeze Drying USP #7,363,726 B2.
2. Powder Formation by Atmospheric Spray-Freeze Drying" by Wang, ZL et al in Powder Technology, Vol. 170 (2006): 45-52.