# Sub-micron Bovine Serum Albumin particles

*Nano Spray Dryer B-90 HP:*
*Innovative spray drying of proteins with high yields*

## 1. Introduction

Spray-drying was shown to be a rapid, continuous, cost-effective, reproducible and scalable process for the production of dry powders from a fluid. Moreover, in the recent years, spray drying was identified by the pharmaceutical industry as a suitable method to produce protein particles used in pulmonary, nasal and oral delivery [1, 2].

Due to its property, bovine serum albumin (BSA) has many applications in life science disciplines, such as cell culture, in-vitro diagnostics, human and veterinary pharmaceuticals, molecular biology, serology and general research. It is also very well characterized and often used as a model protein in numerous biochemical applications [3].

The possibility to use the Nano Spray Dryer B-90 HP to produce protein sub-micron particles will be investigated here, using BSA as a model protein. The influence of the BSA concentration is studied.

## 2. Experimental

BSA solutions of 10 %, 1 % and 0.1 % were prepared by addition of lyophilized BSA powder (Sigma Aldrich, St Louis, MO, USA) into deionized water before being filtered through a glass fiber filter (Whatman GF/F) under vacuum in order to remove particles that can clog the system. Tween 80 was then added to a obtain 0.05 % [V/V] solution. The BSA solutions were then refrigerated before use. All solutions were prepared as % [w/V] solutions if not mentioned otherwise.

*Table 1: Process parameters.*

| Nebulizer | Large | Medium | Small |
|---|---|---|---|
| **Gas flow rate** | 144-148 L/min | 142-145 L/min | 143-144 L/min |
| **T inlet** | 100 °C | 100 °C | 100 °C |
| **T outlet** | 44-50 °C | 38 - 53 °C | 51-61 °C |
| **Spray rate** | 80 % | 80 % | 80 % |
| **Pressure** | 65 - 68 hPa | 66 - 75 hPa | 64 - 65 hPa |
| **Feed rate** | 90 -100 % | 90 % | 90 % |

Microparticles were prepared by spray drying the BSA solutions using the tall set up of the BUCHI Nano Spray Dryer B-90 HP. During the process, the BSA solution was kept in an ice bath in order to cool it down and to reduce the protein degradation by the heating system. The pump speed was set to reduce residence time around the heating system and therefore to lessen protein degradation. It is also recommended to shorten the tubing bringing the solution into the nebulizer as much as possible to further reduce the residence time around the heating.

The Nano Spray Dryer B-90 HP was operated in open loop with pressurized air with a spray set at 80 % and the frequency at 125 kHz. The used parameters are summarized in Table 1.

## 3. Results

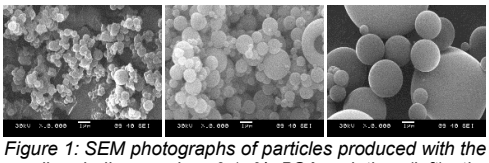

*Figure 1: SEM photographs of particles produced with the small nebulizer and a 0.1 % BSA solution (left), the medium nebulizer and a 1 % BSA solution (middle) and the large nebulizer and a 10 % BSA solution (right).*

BSA particles from 0.133 um to 6.34 um were produced using the nano spray dryer B-90 with yields above 60%.The produced particles are mainly of spherical shape, however some donut shaped particles could also be observed. The drying temperature is shown to have a minor effect on particle size and shape, however the nebulizer diameter and the solution concentration seem to greatly affect the size and the size distribution of the particles.

The particle size and size distribution appear to increase with nebulizer size and with the BSA concentration in the sample solution. This finding is in agreement with this reported by Arpagaus *et a*l. (2012) [4].

Protein degradation by the heat is unlikely since the the outlet temperatures were recorded between 38°C and 61°C and are therefore favorable for spray drying heat sensitive biologicals [4].

## 4. Conclusion

BSA particles from 0.133-6.34 um were produced with the Nano Spray Dryer B-90 HP. Particle size and size distribution were increasing with nebulizer diameter and solution concentration.

Spherical particles were obtained using Tween 80 as a surfactant. Since donut shaped particles were also observed, an optimization of the surfactant concentration or type could be foreseen. The given process parameters may serve as starting values for process optimization and give a clear indication that the material can be successfully spray dried.

## 5. References

[1] S. H. Lee, D. Heng, W. K. Ng, H.-K. Chan, and R. B. H. Tan, “Nano spray drying: A novel method for preparing protein nanoparticles for protein therapy,” *Int. J. Pharm.*, vol. 403, no. 1–2, pp. 192–200, Jan. 2011.

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