Investigation of Process Loss During Foam Drying of Bacteria

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INTRODUCTION

Vacuum foam drying was first used to preserve biologicals in the 50's . Unlike conventional freeze drying, the drying is carried out from the liquid state at temperatures above the freezing point under vacuum that promotes foam formation. The technology avoids excursions to extreme temperatures that can damage sensitive biologicals, facilitates a quick drying cycle, and provides potential long term stability at ambient temperature. We have been able to achieve years of stability at room temperature for various live viruses using the technology. One of the challenges in vacuum foam drying of biologicals is process loss. No systematic studies have been performed and the mechanisms of process loss remain unclear. In the present study, we have investigated the cause of process loss during vacuum foam drying of *Listeria monocytogenes* and the impact of drying cycle optimization on reducing the loss.

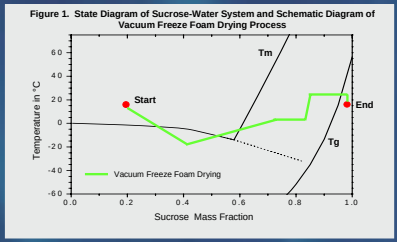
OBJECTIVES

- Process loss mapping during vacuum foam drying of *Listeria monocytogenes*
- Investigate the impacts of drying parameters on the process loss
- Examine the effect of Tg on the process loss

METHODOLOGY

- *Listeria monocytogenes* was formulated with sucrose or trehalose and vacuum foam dried in 10 ml glass vials using a VirTis Genesis lyophilizer. The drying process was initiated by foaming under vacuum at a shelf temperature above 0°C and continuous drying under the same condition, followed by a secondary drying step at higher temperature. As shown in Figure 1, the foam freezes shortly following foaming due to evaporative cooling. Furthermore, in contrast to lyophilization, the sample is drying above Tg during most of the drying cycle.
- Vials were sampled at different drying stages using a sample thief without interruption of the drying cycle.
- The viability of the bacterium was determined by a plate count assay. The process loss was calculated by subtracting the viability recovered immediately after sampling from the initial viability before drying.
- The residual moisture content was determined gravimetrically for the early drying stage sampling, and by Karl Fischer titration for the late drying stage samples.

Figure 1. State Diagram of Sucrose-Water System and Schematic Diagram of Vacuum Freeze Foam Drying Process



RESULTS

Figure 2. Loss in Viability During Vacuum Freeze Foam Drying

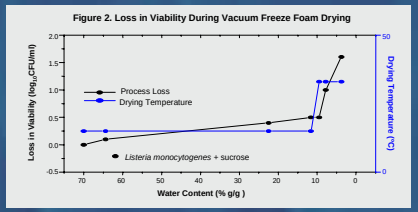


Figure 3. Omitting Secondary Drying Step at Elevated Temperature Reduced Process Loss

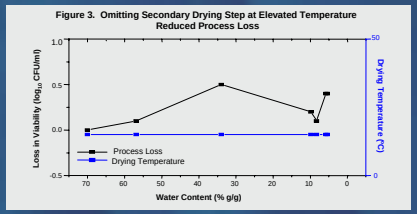


Figure 4. Stepwise Increase of Drying Temperature Reduced Process Loss

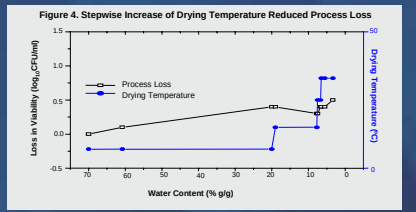
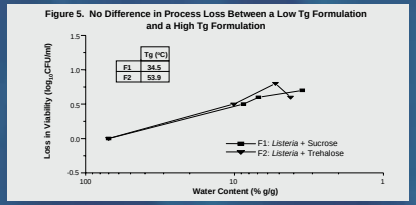
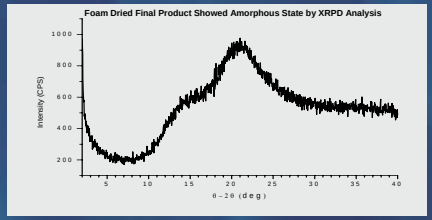


Figure 5. No Difference in Process Loss Between a Low Tg Formulation and a High Tg Formulation



Dried Foam Cake

Foam Dried Final Product Showed Amorphous State by XRPD Analysis



SUMMARY AND CONCLUSION

- Process loss was not due to freezing, boiling, or foaming.
- A major loss occurred when moisture content fell below 10%, coinciding with the initiation of a secondary drying step at elevated temperature.
- The process loss during vacuum foam drying *Listeria monocytogenes* was due to combined desiccation stress and thermal stress.
- Drying cycle optimization can significantly reduced process loss.