

Lyophilization Process Monitoring

1. Introduction

Lyophilization (freeze-drying) is an essential technology for preserving the quality of delicate, heat-sensitive products such as pharmaceuticals and foods. However, optimizing and controlling this process is extremely complex. Traditional methods have faced the challenge of not knowing the results until after the process is complete, making it impossible to respond immediately if problems occur.

Real-time monitoring using a mass spectrometer (MS) is gaining attention as a powerful means to solve the challenges of the lyophilization process. A key feature is its ability to directly measure the partial pressures of water vapor and residual solvents within the lyophilization chamber. This allows for an accurate understanding of the progress of both primary and secondary drying phases.

The ability to grasp the drying status in real-time makes it possible to appropriately end the process as soon as drying is complete. This prevents product degradation from over-drying and avoids unnecessary energy consumption. Furthermore, if any abnormal moisture remains, it can be detected early and drying conditions can be adjusted promptly, minimizing quality variations between batches. This ensures long-term product stability and significantly reduces the risk of quality defects.

This note introduces a case study of monitoring a lyophilization process in real-time using the ASTON mass spectrometer.

Note: While some data is disclosed in this report with customer cooperation, detailed process conditions are confidential.

2. Experimental Method

1. Connect the ASTON (with its inlet system) to the lyophilization process chamber (Figure 1).
2. Measure the residual gases inside the lyophilization chamber.
3. Start the lyophilization process and subsequently begin measurement with ASTON.
4. Perform real-time monitoring of the lyophilization process.

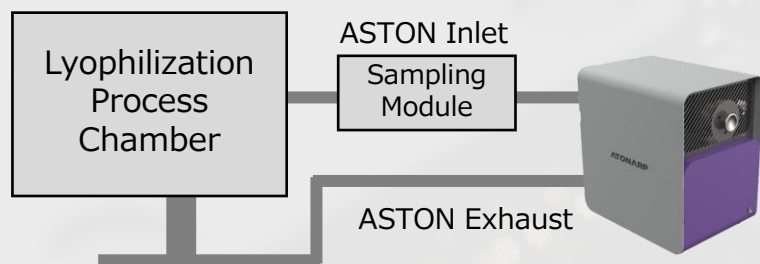


Figure 1. System Configuration

Table 1. ASTON Measurement Conditions

Ionization	EI
Electron Energy	70 eV
Scan Mode	Full Scan
Step Size	1 u

3. Result

When the residual gases inside the lyophilization chamber were measured, components such as water H₂O and nitrogen N₂ were detected (Figure 2). Subsequently, as the lyophilization process began, the primary and secondary drying phases could be visually confirmed.

In the primary drying phase, it was observed that water H₂O rose sharply, remained high, and then gradually decreased. As the water decreased, air N₂ was supplied to maintain a constant pressure in the chamber, and this event was also captured (Figure 3).

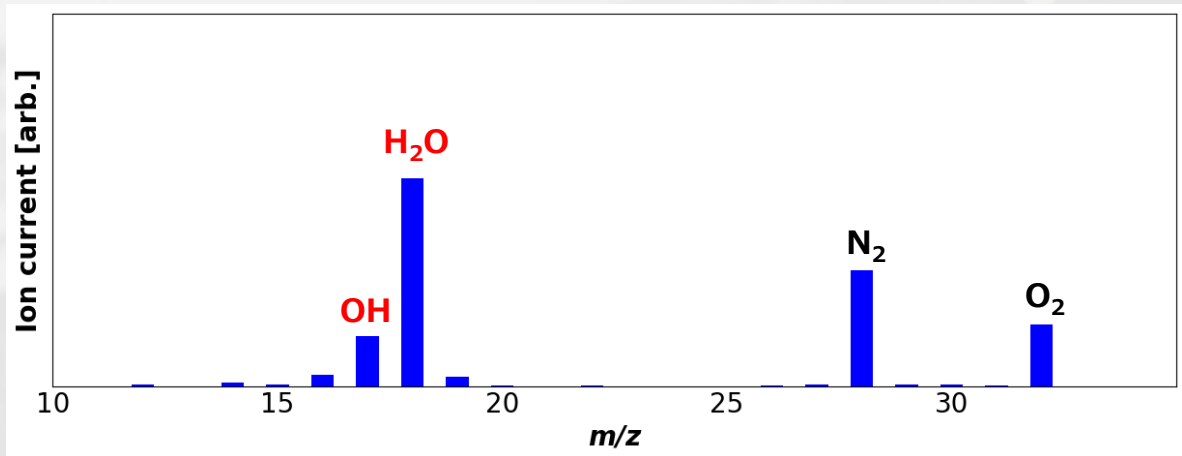


Figure 2. Residual Gases in Lyophilization Chamber

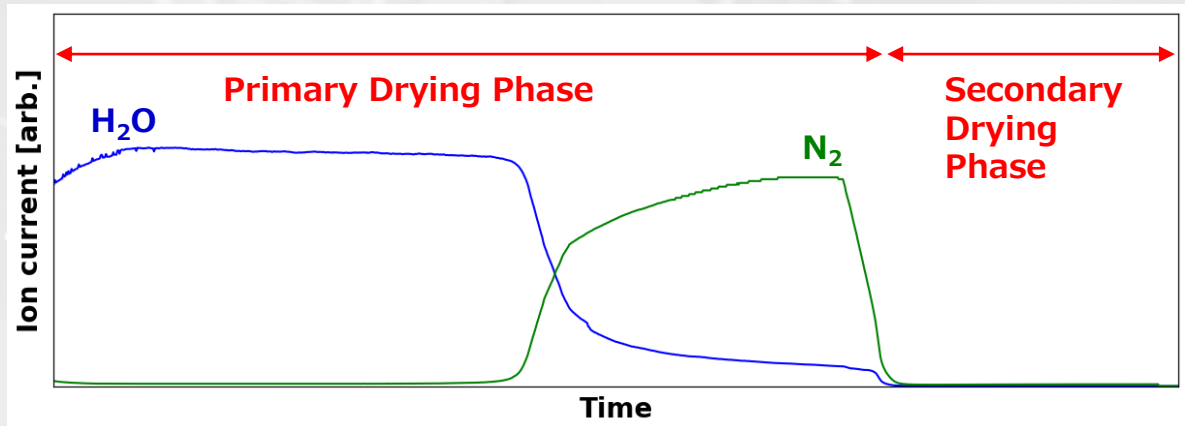


Figure 3. Lyophilization Process

4. Conclusion

Real-time monitoring with the ASTON mass spectrometer serves as a powerful tool for Process Analytical Technology (PAT), which is promoted by the U.S. Food and Drug Administration (FDA), enabling data-driven, scientific process management. It can also simultaneously monitor the behavior of organic solvents, such as tert-butanol (TBA), along with water in real-time, contributing to the optimization of drying processes for more complex formulations.

