Biopharma Group's Lyobead Technology

Introduction

This application note underscores the benefits of employing a lyobead format for lyophilisation process, allowing for the development of a more efficient freeze-drying cycle recipe while highlighting the significance of formulation on the mechanical strength of the lyobead. Additionally, PSD analysis was performed to demonstrate consistency in size during lyobead manufacturing.

Developing a suitable formulation involves the selection of viable excipients and concentrations and plays a crucial role in ensuring the stability and mechanical strength of any freeze-dried product. This importance is amplified in the context of lyobeads as maintaining mechanical robustness is key for the handling and packing process.

Precise dispensing accuracy in diagnostic tests and other applications is paramount, not only for technical precision but also for ensuring patient safety, meeting regulatory standards, and optimising resource usage, all of which are fundamental factors for effective and reliable diagnostics. Using Biopharma Group's LyobeadPRO™ instrument, an internal study was carried out to assess the accuracy and consistency of dispensing.

Cycle efficiency is another advantage when using lyobeads. The lyobeads, with their expansive surface area, exhibit a faster drying rate compared to lyocake. This increased surface area also elevates the likelihood of moisture absorption. Therefore, a meticulous packing process is essential to ensure minimal moisture content in lyobeads.

Biopharma Group's lyobead technology services provides in-depth formulation, cycle development, precise dispensing and optimised packing in a humidity- and temperature-controlled environment.

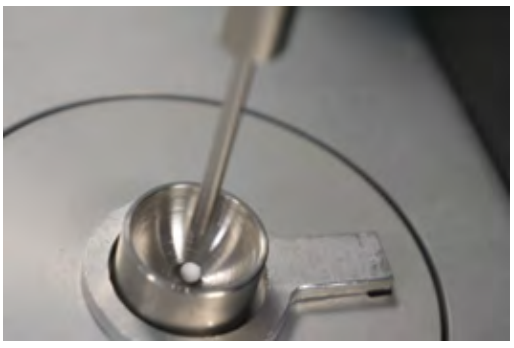

Figure 2: Micropress™ analysis on a lyobead sample.

Figure 1: Close-up droplets using Biopharma Group's LyobeadPRO™

Benefits:

1. Formulation development in lyobeads

Selecting the correct excipient and concentration is crucial for the long-term stability of the freeze-dried product and its mechanical strength. The right formulation holds additional significance in the case of lyobeads, primarily due to the involvement of a handling process in their development. If lyobeads lack mechanical robustness, there is a heightened risk of bead breakage during handling. The study below was conducted using Biopharma Group's MicroPress™ instrument, which assesses the mechanical properties of the freeze-dried product by evaluating the stress level at the fracture point and Young's Modulus The chart below compares the mechanical strength of all several formulations. Table 1 details the excipients used in each formulation. All formulations have the same solid content. However, Formulation 1 exhibits significantly higher mechanical robustness than Formulations 2 and 3. Formulation 1 includes a long-chain polymer, which enhances the mechanical properties of the lyobeads.

Table 1: Description of each excipient

Excipient	Details
A	A polymer of anhydroglucose with the average molecular weight of 75000 g/mol
B	A sugar alcohol with the molecular weight of 182.17 g/mol
C	A trisaccharide with the molecular weight of 504.42 g/mol

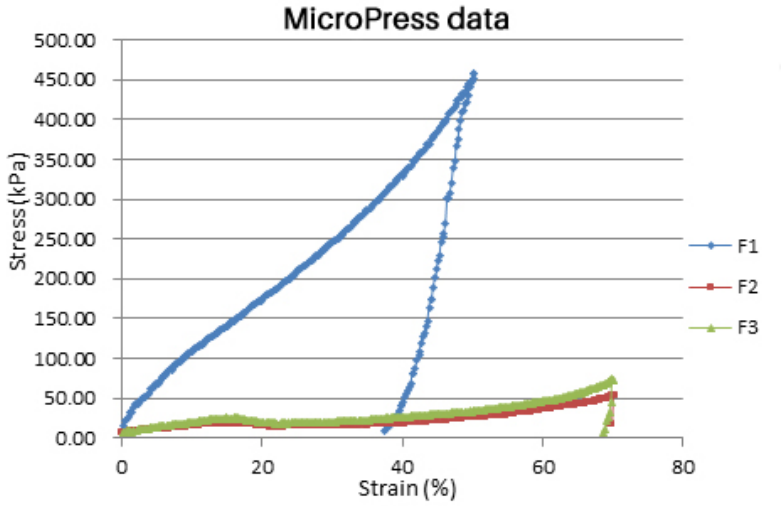

Table 2: Concentration of each excipient in each formulation

Sample Name	Details
F1	10% excipient A
F2	8% excipient B 2% excipient C
F3	10% excipient B 2% excipient C

Figure 3: MicroPress™ data using different formulations Table

2. Assess the accuracy of dispensing Particle Size Distribution (PSD) Analysis

Using Biopharma Group's LyobeadPRO™ instrument, a batch of 20 µL lyobeads was produced using a robust formulation. The analysis of lyophilised beads was conducted using three different analytical methods to assess both size and shape. The lyobeads were photographed using a standard digital camera, and the acquired images were analysed using three distinct techniques.

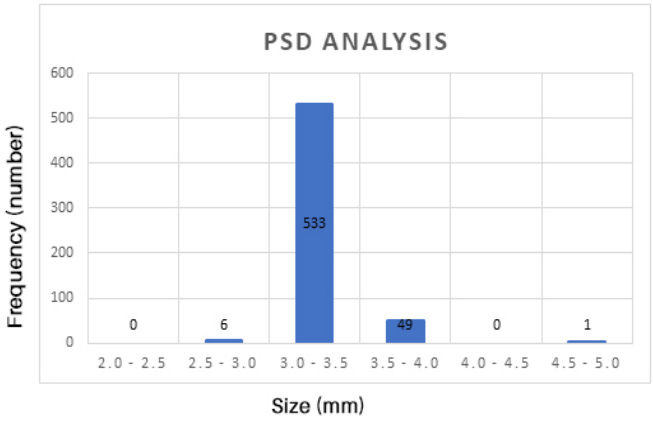

Figure 4: PSD data

Particle number-based size distribution (PSD) data in Figure 4 indicates that 90% of the beads are within the range of 3.0-3.5 mm in diameter, while approximately 10% of the beads exhibit outlier sizes.

The table below presents shape data obtained through Malvern Panalytical Morphologi 4 analysis. When the mean of each parameter is closer to 1, the beads tend to be more spherical. Smaller elongation values indicate less elongated beads. In this dataset, we observed circularity values approaching 1, indicating a higher degree of circularity. Additionally, the table includes data from the analysis using Image J software.

Notably, across different batches, a high level of circularity was observed.

Table 3: Average dataset of shape and size parameters from different batches of the same sample

High Sensitivity Circularity Mean	Aspect Ratio Mean	Elongation Mean	Solidity Mean	Convexity Mean	Diameter D[n, 0.1] (mm)	Diameter D[n, 0.5] (mm)	Diameter D[n, 0.9] (mm)
0.954	0.931	0.069	0.996	0.989	2.58	2.77	2.98

Shape analysis was performed using the Morphologi4 instrument indicates the predominantly spherical nature of lyobeads (figure 5).

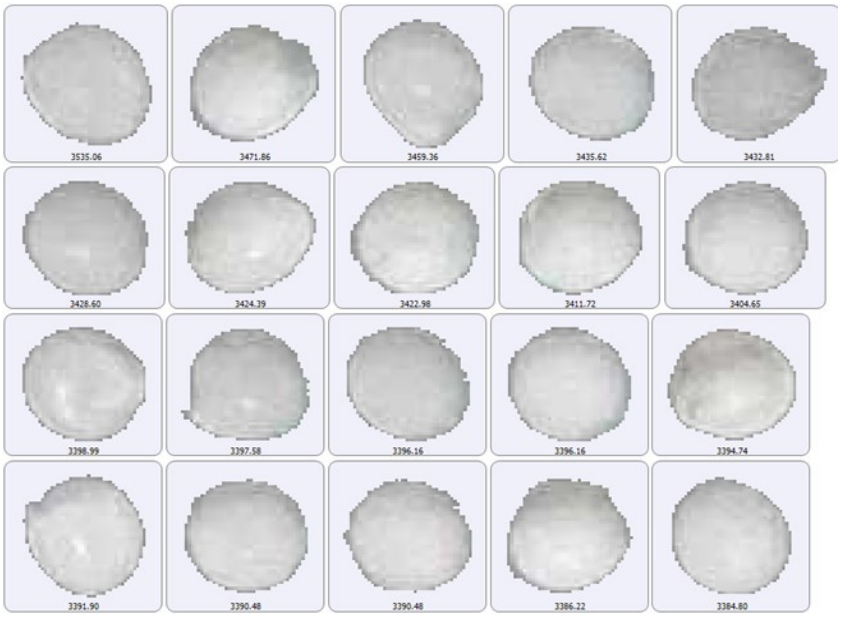

Figure 5: An Example of Captured Particle Images

3. Benefits of lyobeads

Lyobeads offer several advantages, including adaptability to product changes, requiring less R&D investment. They facilitate bulk storage before packaging, support high throughput, and benefit from a large surface area that ensures consistently effective reconstitution.

The data below illustrate s a reduction in the cycle's length by approximately 10 days using the lyobead format. A dual gauge freeze-dryer was used to carry out a freeze-drying cycle in both lyobead and lyocake format. The end point of primary and secondary drying is determined by the converging of CM and PVG vacuum gauges. (figures 6 and 7).

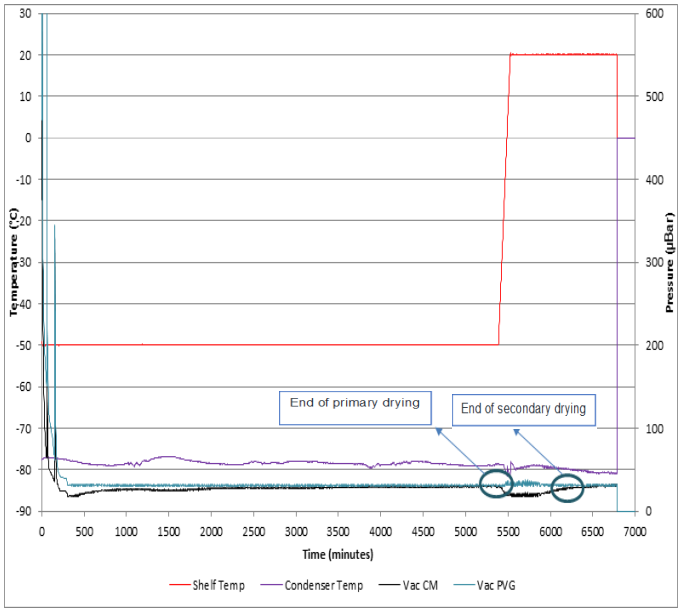

Figure 6: Lyobead Cycle Plot

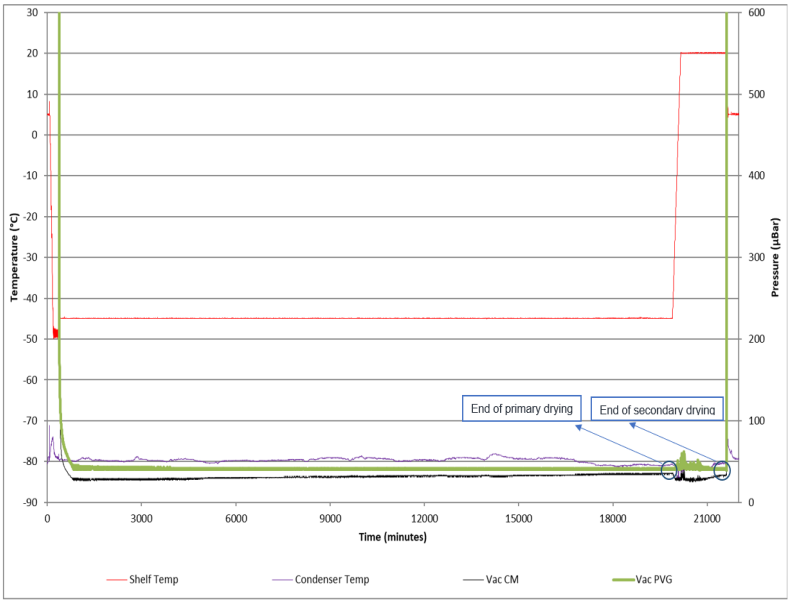

Figure 7: Lyocake Cycle Plot

Conclusion

In the first segment of this application note, MicroPress™ analysis underscores the pivotal role of the sample's formulation in achieving a mechanically robust product in a lyobead format.
In the second part of the application note, using Biopharma Group's LyobeadPRO™ instrument and employing PSD analysis, illuminates it was illustrated that approximately 90% of beads consistently fall within the specified size range.

The third part of the study, the impact of lyobead format on reducing the cycle's length was studied. Using the same sample and applying the lyobead format, a 10-day reduction in the cycle duration was achieved.
Furthermore, the PSD data obtained from ImageJ software reaffirms the consistency of lyobead size, emphasising the reliability of the Biopharma Group's manufacturing process.

Together, these insights deepen our understanding of the critical factors influencing lyobead production and set the stage for enhanced manufacturing precision and uniformity while detailing the clear advantages of moving to lyobead format, especially in Microfluidics which is an evolving technology emergent section of the diagnostics sector.